Published in final edited form as:

Forensic Sci Int. 2019 January ; 294: e25–e27. doi:10.1016/j.forsciint.2018.10.019.

The Unexpected Identification of the Cannabimimetic, 5F-ADB, and Dextromethorphan in Commercially Available Cannabidiol E-liquids

Justin L Poklis, B.S.^{a,*}, Haley A Mulder, M.S.F.S.^b, and Michelle R Peace, Ph.D.^b

^aVirginia Commonwealth University, Department of Pharmacology & Toxicology, 410 North 12th Street, Room 754, Box 980613, Richmond, VA 23298-0613, USA

^bVirginia Commonwealth University, Department of Forensic Science, 1015 Floyd Avenue, Room 2015, Richmond, VA 23284

Graphical Abstract:

Keywords

Electronic cigarettes; Electronic liquids; cannabidiol; 5-fluoro MDMB-PINACA; dextromethorphan; DART-MS

Introduction

Electronic cigarettes (e-cigarettes) were developed as an alternative method for nicotine delivery and have had a significant surge in popularity. Electronic liquids (e-liquids) are formulations used in e-cigarettes, and consist of a ratio of propylene glycol and vegetable glycerin, a pharmaceutical and/or herbal remedy and, usually, a flavoring agent. When the e-cigarette is activated, the e-liquid is vaporized, followed by a rapid condensation into an aerosol that is inhaled (1). E-cigarettes have been reported to be an effective delivery system for drugs other than nicotine (DOTN).

*Corresponding Author Justin L. Poklis, Department of Pharmacology & Toxicology, Virginia Commonwealth University, Box 980613, Richmond, VA 23298-0613, USA, Phone: 804-827-0571, justin.poklis@vcuhealth.org, mulderha@vcu.edu, mrpeace@vcu.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Cannabidiol (CBD), a cannabinoid, is an active ingredient of *C. sativa* and *C. indica* and has been promulgated as having potential anti-convulsant, anti-nociceptive, and anti-psychotic properties (2). In the United States CBD is, minimally, legal with a prescription in 46 states and the District of Columbia. CBD products are available in numerous forms, including e-liquids, and are sold at various retail stores and on the internet. These products can contain up to 0.3% tetrahydrocannabinol (THC), the active major psychoactive component of marijuana. The U.S. Food and Drug Administration recently approved CBD oral solution for the treatment of seizures associated with two rare and severe forms of epilepsy. In the health section of the January 12, 2015 issue of the New York Times, the use of e-cigarettes and marijuana was reported as “a union that seems all but inevitable”. In a study at of 1542 undergraduates that were self-reported e-cigarette users, approximately 7% stated they had used the device to consume a substance other than nicotine. Nearly 80% of this group reported use of a cannabinoid or some derivative of cannabis (3). The e-liquids used in e-cigarettes have been demonstrated to be an effective route of administration for cannabinoids (4). The inhalation of CBD through an aerosol produced by an e-cigarette may be advantageous over traditional smoking methods and ingestion. Previous studies have evaluated the discrepancies in labeled cannabinoid concentrations versus actual concentrations in commercially available products (2, 4–8). Presently there is limited to no manufacturing standards to ensure safety and quality of product cannabinoid infused e-liquids products.

The synthetic cannabinoid 5-fluoro MDMB-PINACA (5F-ADB) is a cannabimimetic (9), meaning that the chemical structure may not resemble naturally occurring cannabinoids, but has some similar pharmacological activity by binding with the CB1 and/or CB2 receptors. 5F-ADB is reported to produce euphoric and other psychoactive effects similar to that of THC. 5F-ADB has been reported in series of five non-fatal clinical intoxications after smoking “Spice” or “herbal preparation” to cause anxiety, confusion, psychomotor agitation, psychosis and tachycardia (10). In 2014, the Drug Enforcement Agency (DEA) reported 2,311 incidents involving medical intervention or death involving 5F-ADB which resulted in its status as Schedule I drug in January 2017.

Dextromethorphan (DXM) is used in numerous cough and cold medications for its anti-tussive effects. It can cause agitation, ataxia, hypertonic, sedation and may produce dissociative hallucinations at high doses. The abuse potential of DMX was recognized in the 1960s. Since the late 1990s, adolescents have been increasingly abusing dextromethorphan products. The number of cases of adolescent abuse reported to the California Poison Control System from 1999 through 2004 increased 10-fold (11). A more recent study from the Toxicological Laboratory and Poison Information Center in Krakow noted that the most often cause of poisoning for patients 13–18 of over the counter medications was acetaminophen and dextromethorphan. An average of 30 DXM poisonings a year were reported for the years of 2010–2015 (12).

Presented is the evaluation of nine CBD e-liquids from a single manufacturer for cannabinoids and other psychoactive compounds. Two commercial e-liquids were submitted to our laboratory, Liquid Gold Strawberry and Diamond CBD Vape Additive, from an outside source that suspected they contained active ingredients other than CBD. The same

two products and an additional seven products were then purchased directly from the manufacturer, diamondcbd.com. These e-liquids were analyzed using a Direct Analysis in Real Time coupled to a JEOL JMS T100LC Accu-TOF (DART-MS) and an Agilent GC-MS 6890N/5973 Mass Selective Detector (Agilent, Santa Clara, CA, USA) (GC/MS). Active ingredients were identified using commercial standards based upon retention time and mass spectral comparisons.

Methods

The nine CBD infused e-liquids were initially screened for the presence of cannabinoids, and other possible psychoactive components using previously published method (13). In brief, The CBD e-liquids were mixed by hand for 20 s before a capillary tube was dipped into an aliquot of each e-liquid prior to introduction into the helium stream of a DART-MS five times. Each sample was analyzed in positive-ion mode with a helium stream temperature of 300 °C. The flow rate was 2.3 L/min with a discharge electrode needle voltage at 150 V and grid electrode at 250 V. The ion guide peak voltage was 400 V, reflectron voltage was 900 V, orifice 2 was set to 5 V, and the ring lens was set to 3 V with orifice 1 operated in function switching mode at 20, 30, 60, or 90 V with a single data file created for all four voltages. The range of masses measured was from 40 to 1,000 Da. Each e-liquid was analyzed five separate times to ensure reproducibility of the results. The data was analyzed by the creation of averaged, background subtracted, centroided mass spectra that was calibrated using the PEG 600. DART-MS controlled by Mass Center software version 1.3.4 m (JEOL Inc., Tokyo, Japan). Identification of psychoactive components were made when the exact mass was detected within 5 mDa of its calculated monoisotopic mass $(M+H)^+$, and were confirmed using primary references materials (Cerilliant, Round Rock, Texas and Cayman Chemical, Ann Arbor, Michigan) that was used to match its fragmentation pattern in function switching mode.

The contents of the nine CBD infused e-liquids were confirmed for the presence of cannabinoids, and other psychoactive components using a GC/MS. The CBD e-liquids were prepared by mixing for 20 s before aliquoting and diluting 1:1000 with HPLC grade methanol (Thermo fisher, Waltham, MA). With each analytical run, reference standards were prepared and analyzed at 100 ng/mL for CBD, THC, 5F-ADB and DXM along with a drug free sample. The chromatographic separation was performed on a HP-5MS column 30 m × 0.25 mm id × 0.25 µm (Agilent, Santa Clara, CA, USA). The injection port was set to 250 °C and the run was made in splitless mode. The initial temperature was set to 120 °C, with a ramp of 300 °C at 10 °C/min, and a hold time of 12 min, for a total run time of 30 min. The identification of the psychoactive components in the e-liquids was based on the combination of retention time and mass spectrum.

Results

All the e-liquids were determined to contain CBD. Two of the nine were determined to contain THC. Four of the nine were determined to contain 5F-ADB and one contained DXM (Table 1).

Discussion

The website where these e-liquids were purchased stated that these products were “100% natural CBD extracts” and provided no indication that these products contained any other active substances. The detection of THC in two products was expected as CBD products may contain up to 0.3% THC, and both naturally occur in cannabis plant material. However, the detection of 5F-ADB and DXM was unexpected. The addition of 5F-ADB and DXM compounds to the CBD products may lead to unexpected psychoactive effects. Uninformed users may mistakenly associate these effects with CBD. The inclusion of these drugs in e-liquids can lead to dangerous consequences; particularly when the users are unaware, and the product are used for therapeutic reasons. 5F-ADB was a Schedule I drug when both the Liquid Gold and Diamond CBD Vape Additive products were purchased. The formulation for Diamond CBD Vape Additive had changed from time the original sample was purchased, resulting in the detection of DXM rather than 5F-ADB.

Conclusion

The finding of both 5F-ADB and DXM were both unexpected. There was no indication on the website, box or labeled e-liquid containers to indicate that these products contained any psychoactive substance other than CBD. The analysis of these products illustrates the potential quality control issues that can occur in an unregulated industry. CBD products are believed by many users to offer health benefits, but the detection of a dangerous cannabimimetic, 5F-ADB, and DXM in the analyzed products illustrates the need for oversight of CBD products.

Acknowledgments

Funding: This work was supported by the National Institutes of Health [P30DA033934]; and National Institute of Justice, Office of Justice Programs [2016-DN-BX-0150]. The opinions, findings, and conclusions or recommendations expressed in this abstract are those of the author(s) and do not necessarily reflect those of the Department of Justice.

References

- [1]. Peace MR, Baird TR, Smith N, Wolf CE, Poklis JL, Poklis A, Concentration of nicotine and glycols in 27 electronic cigarette formulations. *JAT* 40 (2016) 403–407. doi: 10.1093/jat/bkw037. [PubMed: 27165804]
- [2]. Peace MR, Butler KE, Wolf CW, Poklis JL, Poklis A, Evaluation of two commercially available cannabidiol formulations for use in electronic cigarettes. *Front Pharmacol*, 7 (2016) 279, doi: 10.3389/fphar.2016.00279 [PubMed: 27621706]
- [3]. Kenne DK, Fischbein RL, Tan ASL, Banks M, The Use of Substances Other Than Nicotine in Electronic Cigarettes Among College Students. *Substance Abuse*, 2017 doi: 10.1177/1178221817733736
- [4]. Varlet V, Concha-Lozano N, Berthet A, Plateel G, Favrat B, De Cesare M, Lauer E, Augsburger M, Thomas A, Giroud C, Drug vaping applied to cannabis: is “Cannavaping” a therapeutic alternative to marijuana? *Sci Rep*, 6 (2016) 25599. doi: 10.1038/srep25599 [PubMed: 27228348]
- [5]. Bonn-Miller MO, Loflin MJE, Thomas BF, Marcu JP, Hyke T, Vandrey R, Labeling accuracy of cannabidiol extracts sold online. *JAMA*, 318 (2017) 1708–1709. doi: 10.1001/jama.2017.11909. [PubMed: 29114823]

- [6]. Vandrey R, Raber JC, Raber ME, Douglass B, Miller C, Bonn-Miller MO, Cannabinoid dose and label accuracy in edible medical cannabis products. *JAMA*, 313 (2017) 2491. doi: 10.1001/jama.2015.6613
- [7]. Peace MR, Stone JW, Poklis JL, Turner JB, Poklis A, Analysis of a commercial marijuana e-cigarette formulation. *JAT*, 40 (2016) 374–378. doi: 10.1093/jat/bkw021. [PubMed: 27059691]
- [8]. Giroud de Cesare M, Berthet A, Varlet V, Concha-Lozano N, Favrat B, E-cigarettes: a review of new trends in cannabis use, *Int J Environ Res Public Health* 12 (2015) 9988–10008. doi: 10.3390/ijerph120809988. [PubMed: 26308021]
- [9]. Hasegawa K, Wurita A, Minakata K, Gonmori K, Yamagishi I, Nozawa H, Watanabe K, Suzuki O, Identification and quantitation of 5-fluoro-ADB, one of the most dangerous synthetic cannabinoids, in the stomach contents and solid tissues of a human cadaver and in some herbal products, *Forensic Toxicol* 33 (2015) 112–121. 10.1007/s11419-014-0259-0
- [10]. Barceló B, Pichini S, López-Corominas V, Gomila I, Yates C, Busardò FP M FP, Pellegrini. Acute intoxication caused by synthetic cannabinoids 5F-ADB and MMB-2201: A case series. *Forensic Sci. Int*, 273 (2017) e10–e14. doi: 10.1016/j.forsciint.2017.01.020. [PubMed: 28190538]
- [11]. Bryner JK, Wang UK, Hui JW, Bedodo M, MacDougall C, Anderson IB. Dextromethorphan abuse in adolescence: an increasing trend: 1999–2004. *Arch Pediatr Adolesc Med* 160 (2006) 1217–22. [PubMed: 17146018]
- [12]. Gomółka E, Hydzik P, Szkolnicka B. [Poisonings with paracetamol, salicylates and dextromethorphan – problem evaluation based on data from Toxicological Laboratory and Poison Information Center in Krakow in 2010–2015]. *Przegl Lek* 73 (2016) 813–7.
- [13]. Peace MR, Mulder HA, Baird TR, Butler KE, Friedrich AK, Stone JW, Turner JB, Poklis A, Poklis JL, Evaluation of Nicotine and the Components of e-Liquids Generated from e-Cigarette Aerosols, *JAT*, (In Press)

Highlights:

- Analysis of unregulated cannabidiol e-liquids potentially used for medical or health reasons
- Four CBD only e-liquids determined to contain 5F-ADB or dextromethorphan.
- Illustrates the potential quality control issues that occur in an unregulated industry

Table 1.

Detection of CBD and other psychoactive compounds in CBD e-liquids

Sample (Received for Analysis)	CBD	THC	5F-ADB	DXM
Liquid Gold Strawberry	X		X	
Diamond CBD Vape Additive	X		X	
Samples (Purchased)	CBD	THC	5F-ADB	DXM
Liquid Gold Strawberry	X		X	
Liquid Gold Jungle Juice	X	X	X	
Diamond CBD Vape Additive	X			X
Blue CBD 250 mg	X			
Blue CBD 1000 mg	X			
Diamond CBD 50 mg	X			
Diamond CBD 1000 mg	X	X		
X - Indicates Detection				