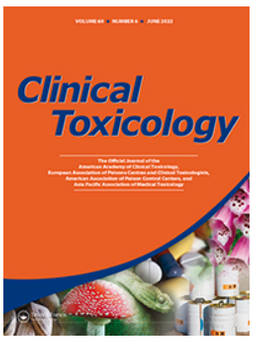

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SHORT COMMUNICATION

Emerging synthetic cannabinoids detected by a drug checking service in Toronto, Canada

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ABSTRACT

Background: Toronto's Drug Checking Service (DCS) provides people who use drugs with information on the chemical composition of their substances and conducts real-time monitoring of the unregulated drug supply. Presented are first known data of three newly detected synthetic cannabinoids (SCs) in Toronto, Ontario.

Methods: The present data are from samples analyzed between April and November 2020. Samples were collected at partnering harm reduction agencies in Toronto and analyzed using gas or liquid chromatography-mass spectrometry. An intake survey queried about the sample characteristics on submission, including expected drug(s).

Results: Samples were analyzed between 1 April and 20 November 2020 ($N = 19$), which marks the period immediately following imposed COVID-19 border and movement restrictions in Canada. The newly detected, unexpected SCs were ACHMINACA ($n = 15$), AB-FUBINACA ($n = 3$), and 4-fluoro-MDMB-BUTINACA ($n = 1$). Fentanyl was expected in 74% ($n = 14$). Most SCs were detected in samples containing fentanyl or related analogues ($n = 18$; 95%), or benzodiazepine-related drugs (i.e., etizolam and flualprazolam) ($n = 15$; 79%).

Conclusions: This information can inform overdose prevention efforts and drug market monitoring of SCs in Toronto and regions served by the same drug trafficking routes. The detection of SCs during a period marked by COVID-19-related restrictions can contribute to efforts to identify global drug market trends during this time.

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Introduction

The presence of synthetic cannabinoids (SCs) has increased in unregulated drug markets globally, including North America [1]. SCs are potent agonists of the cannabinoid-1 receptor (CB-1) relative to delta-9-tetrahydrocannabinol (Δ9-THC) [2]. Other plausible receptor activity (i.e., cannabinoid-2, and *N*-methyl-D-aspartate) has yet to be confirmed. Consumption of potent SCs may lead to presentation of severe cardiac, renal, and gastrointestinal symptoms; decline in cognition and mental status (e.g., acute dissociative, psychotic features); central nervous system depression (e.g., respiratory depression); and withdrawal [2–5]. Notably, SCs are not detectable on conventional urine drug screens. Therefore, as increasingly potent SCs enter the unregulated drug supply, their detection is critical to inform responses to overdose and related effects.

Herein, we report on new SCs detected in drug samples submitted to Toronto's Drug Checking Service (DCS) in Toronto, Canada, in the period following restrictions related to the COVID-19 pandemic in Ontario [6], during which global drug trafficking patterns are believed to have been affected [7–9].

Methods

The protocol and rationale for Toronto's DCS have been previously described [10]. Samples are provided voluntarily by service users at partnering harm reduction agencies in downtown Toronto, transported to clinical laboratories at St. Michael's Hospital or the Centre for Addiction and Mental Health, and analyzed using gas chromatography- or liquid chromatography–high-resolution mass spectrometry. A target analysis for known reference standards is used with a 96–99% match based on the GC-MS software (Agilent GC6890N/MS5975). These results are supplemented by intake survey responses from service users or staff. This includes information such as expected drug, unexpected effect, and sample characteristics on submission. Results are

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Table 1. Expected contents, co-occurring drugs, unexpected effects, and appearance (as reported when submitting samples to Toronto's Drug Checking Service), of substances found to contain newly-detected synthetic cannabinoids ACHMINACA, AB-FUBINACA, and 4-Fluoro-MDMB-BUTINACA ($N = 19$).

Date analyzed	Expected Drug	Co-occurring drugs detected[a]	Unexpected effect	Sample type/Appearance
ACHMINACA ($n = 15$)				
20-May-20	Do not know	Caffeine CBD Etizolam Fentanyl	n/a	Used equipment
20-May-20	Do not know	Caffeine CBD Etizolam Fentanyl	n/a	Used equipment
20-May-20	Fentanyl	6-MAM Caffeine Etizolam Fentanyl Flualprazolam	n/a	Used equipment
20-May-20	Fentanyl	Caffeine CBD Etizolam Fentanyl	n/a	Used equipment
26-May-20	Fentanyl	Caffeine Etizolam Fentanyl	Overdose	Used equipment/Purple
29-May-20	Heroin	Caffeine Cocaine Etizolam Fentanyl Heroin	n/a	Used equipment/"Brown-ish" liquid in cooker
3-Jun-20	Fentanyl	Caffeine CBD Fentanyl	n/a	Used equipment
3-Jun-20	Ketamine Fentanyl	Caffeine Etizolam Fentanyl Ketamine	n/a	Used equipment/ Brown liquid in cooker
5-Jun-20	Fentanyl	Caffeine Etizolam Fentanyl Flualprazolam Oxycodone Phenacetin	n/a	Used equipment
18-Jun-20	Fentanyl	Caffeine Etizolam Fentanyl	n/a	Used equipment/Fuchsia residue
9-Jul-20	Fentanyl	Caffeine CBD Etizolam Fentanyl	n/a	Used equipment/Purple residue
9-Jul-20	Fentanyl	Caffeine Etizolam Fentanyl Methamphetamine	n/a	Used equipment/Purple residue
22-Jul-20	Fentanyl	Caffeine Etizolam Fentanyl	n/a	Substance/Green
4-Sep-20	Fentanyl	6-MAM Caffeine Codeine Fentanyl Heroin	Overdose	Used equipment/White
25-Sep-20	Fentanyl	6-MAM Caffeine Cocaine Despropionyl-fentanyl (4-ANPP) Fentanyl Heroin Phenacetin	n/a	Used equipment
AB-FUBINACA ($n = 3$)				
2-Nov-20	Carfentanil	Caffeine Despropionyl fentanyl (4-ANPP) Diphenhydramine Etizolam Fentanyl	Very strong	Used equipment

(*continued*)

Table 1. Continued.

Date analyzed	Expected Drug	Co-occurring drugs detected[a]	Unexpected effect	Sample type/Appearance
4-Nov-20	Fentanyl	Caffeine Despropionyl fentanyl (4-ANPP) Etizolam Fentanyl Hydromorphone	n/a	Used equipment
20-Nov-20	Fentanyl	Acetyl fentanyl Caffeine CBC Cocaine Deschloroetizolam Despropionyl fentanyl (4-ANPP) Etizolam Fentanyl THC	n/a	Used equipment/Purple
4-Fluoro-MDMB-BUTINACA ($n = 1$)				
17-Apr-20	Phenidate	None	Drowsy/sedated	Substance/Off-white/Gray

[a]Acronyms used in order of appearance: CBD: Cannabidiol; 6-MAM: 6-monoacetylmorphine; CBC: cannabichromene; THC: tetrahydrocannabinol.

communicated to service users and aggregated for drug market analysis within 24–48 h. For this study, we limited results to the period of April 1 to November 20, 2020, coinciding with the implementation of COVID-19 restrictions in Ontario [11].

Results

Among 1104 samples analyzed by Toronto's DCS during the indicated period, we identified 19 samples (2%) that contained ACHMINACA, AB-FUBINACA, or 4-Fluoro-MDMB-BUTINACA. Among those, 11% ($n = 2$) were a substance (e.g., powder) and 89% ($n = 17$) were used equipment (e.g., cooker, filter), 18% ($n = 3$) of which were reused. Sample appearances were described as brown, fuchsia, grey, green, purple, or white. Survey data indicate that an unexpected effect following use was reported for 21% ($n = 4$), described in Table 1. Spectral results for selected samples containing each SC are shown in Figure 1(a–c).

ACHMINACA (EC_{50} unknown) was detected in 15 samples. Of these, 93% ($n = 14$) were used equipment, 21% ($n = 3$) of which were reused, and 7% ($n = 1$) were a substance. Upon submission, service users identified the expected drug as fentanyl in 73% ($n = 11$), heroin in 7% ($n = 1$), fentanyl with ketamine in 7% ($n = 1$), or unknown in 13% ($n = 2$), as seen in Table 1. Of the samples that contained ACHMINACA, fentanyl and caffeine were detected in all (100%) and etizolam (benzodiazepine-related drug) was detected in 80% ($n = 12$). Two samples were associated with overdose, both expected to contain fentanyl.

AB-FUBINACA (EC_{50} =1.8–23.2 nM[3][12]) was detected in three used equipment samples expected to contain fentanyl ($n = 2$) or carfentanil ($n = 1$) on submission. Fentanyl, caffeine, and etizolam were detected in each sample that contained AB-FUBINACA. One sample had the unexpected effect of being "very strong."

4-Fluoro-MDMB-BUTINACA (EC_{50} =0.2 nM[13]) was detected in one substance sample expected to contain phenidate, a central nervous system stimulant. 4-Fluoro-MDMB-BUTINACA was the only drug detected. This sample was reportedly associated with drowsiness.

Discussion

Toronto's DCS detected three SCs (AB-FUBINACA, 4 F-MDMB-BUTINACA and ACHMINACA), during a period marked by COVID-19 restrictions. To our knowledge, this is their first detection in Toronto's unregulated drug supply. Their presence raises important clinical and public health concerns, especially given that the majority were detected in combination with high-potency opioids (in comparison to morphine) and benzodiazepine-related substances. While the pharmacological potencies of AB-FUBINACA and 4 F-MDMB-BUTINACA have been established [3,12,13], there is no published reporting for ACHMINACA, suggesting a need for further study. The presented data provide insight for laboratories seeking to update toxicology reference libraries and inform decisions on the drug screen testing menu.

Raising awareness of SCs in the unregulated drug supply is critical for people who use drugs and service providers alike. Current urine-based screening has no diagnostic utility, therefore, therapeutic management (i.e., treating symptomology given lack of antidote) is contingent on clinical suspicion of an SC-implicated intoxication. There is limited evidence of continuous naloxone infusion to improving symptomology and may vary depending on the SC involved [14,15]. The combination of respiratory depression, physiological impairment, and altered mental status that SCs may elicit when interacting with high potency opioids or benzodiazepine-related drugs suggests protocols on overdose response for a range of substances should be developed or adapted. Guidance from interdisciplinary experts, including peers, will likely aid in effective response, alongside investing in and ensuring harm reduction organizations are fully equipped to address these attendant harms.

In Toronto, these SCs were found to be present after the implementation of COVID-19 restrictions [11], a period associated with an increased incidence of overdose mortality [16]. Their presence implies the continued importance of prioritizing the welfare of

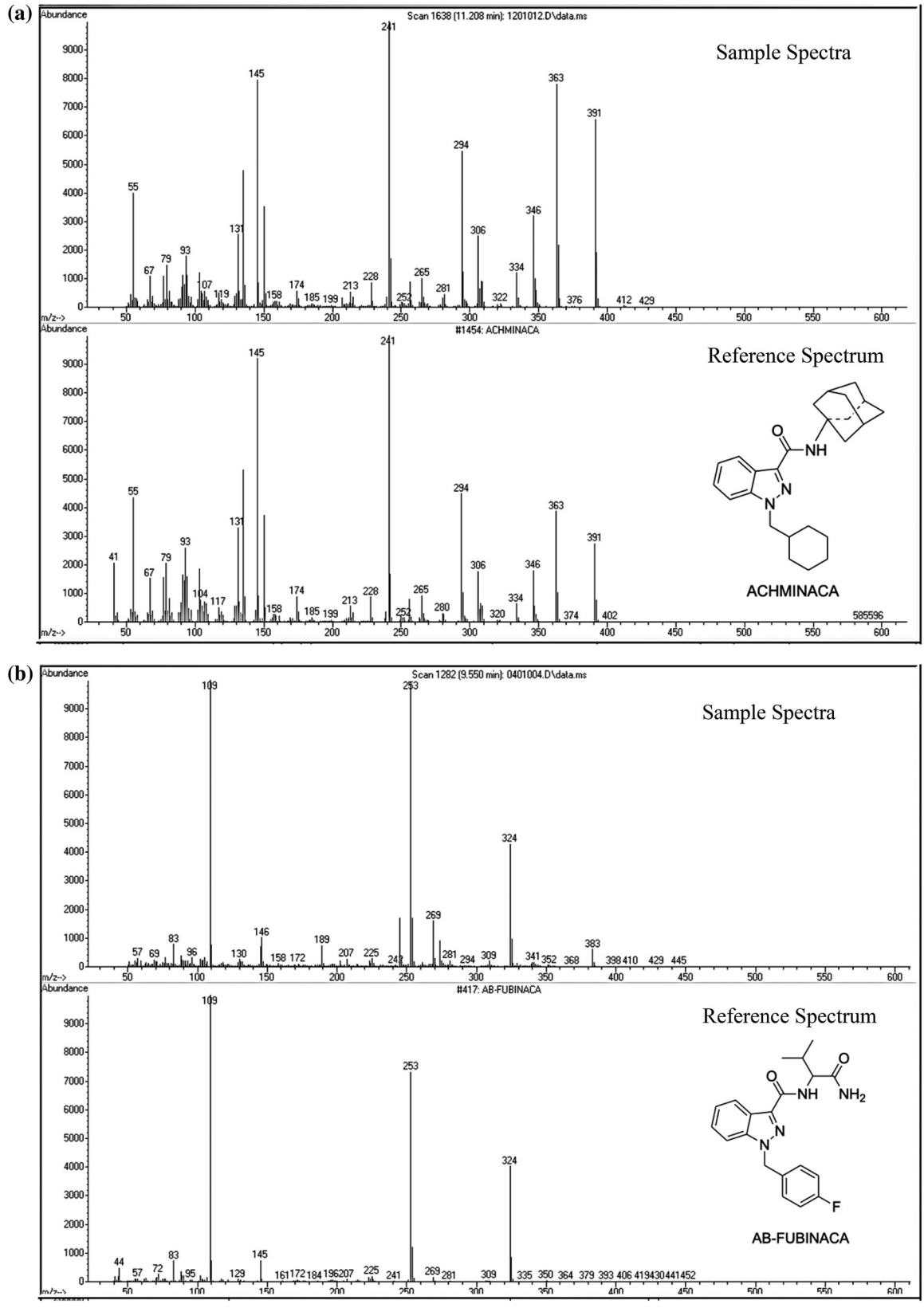

Figure 1. GC–MS mass spectra (a) ACHMINACA (MW = 391.6) (b) AB-FUBINACA (MW = 368.4), and (c) 4-fluoro-MDMB-BUTINACA (MW = 363.4) in selected samples depicted in top panels. Reference mass spectrum shown in bottom panels. Each analysis produced results with 96–99% match based on the GC-MS software utilized (Agilent GC 6890 N/MS 5975). Retention time is shown at the top middle description of each spectra shown (e.g., ACHMINACA =11.208 min).

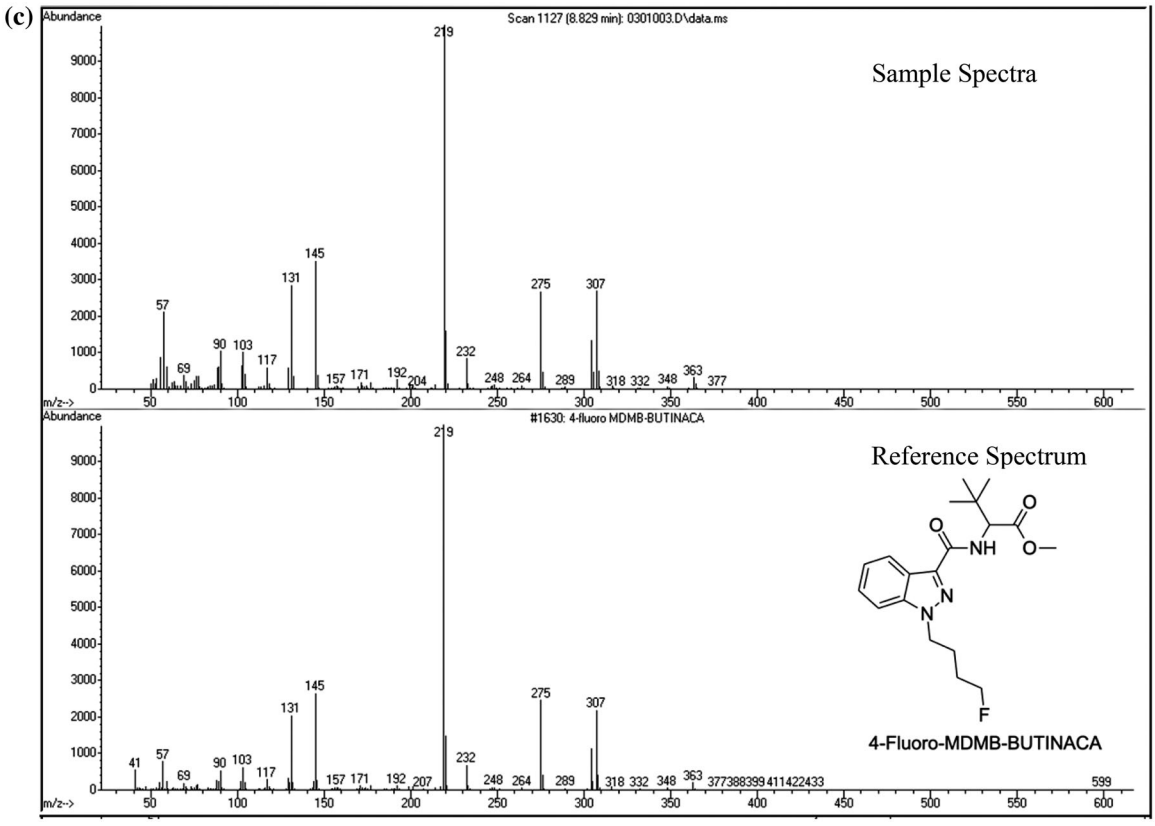

Figure 1. Continued.

people who use drugs by providing rapid, reliable data on the composition of unregulated substances. Toronto's DCS collaborated with Toronto Public Health and distributed alerts notifying the public of the detection of SCs in expected opioid samples [17]. As the COVID-19 pandemic persists, drug market changes will inevitably continue [3,4]. An evaluation of Toronto's DCS to uncover associated behavioral changes and monitor drug market trends continues throughout this time.

Limitations of the study include the potential for sampling bias, limiting the generalization of findings across our geographic setting. Equipment samples may contain multiple substances from reuse. Self-report of unexpected effects is subject to recall bias. Limitations of mass spectrometry include accessibility, cost, speed of result dissemination, destruction of sample for analysis, and restricted compound identification to library references. Only qualitative results confirming presence were provided and quantification was not implemented. Additionally, we are unaware if these SCs might have been in the supply (undetected) prior to launch in October 2019.

These findings demonstrate the need for clinical laboratories to participate in monitoring and surveillance of unregulated drug markets in response to the overdose epidemic.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1] Ti L, Tobias S, Maghsoudi N, et al. Detection of synthetic cannabinoid adulteration in the unregulated drug supply in three canadian settings. Drug Alcohol Rev. 2021;40(4):580–585.

[2] Seely KA, Lapoint J, Moran JH, et al. Spice drugs are more than harmless herbal blends: a review of the pharmacology and toxicology of synthetic cannabinoids. Prog Neuropsychopharmacol Biol Psychiatry. 2012;39(2):234–243.

[3] Adams AJ, Banister SD, Irizarry L, et al. "Zombie" outbreak caused by the synthetic cannabinoid AMB-FUBINACA in New York. N Engl J Med. 2017;376(3):235–242.
[4] Manini AF, Krotulski AJ, Schimmel J, et al. Respiratory failure in confirmed synthetic cannabinoid overdose. Clinical Toxicology. 2022;60;(4):524–526.
[5] Alon MH, Saint-Fleur MO. Synthetic cannabinoid induced acute respiratory depression: case series and literature review. Respir Med Case Rep. 2017;22:137–141.
[6] Ontario enacts declaration of emergency to protect the public: significantly enhanced measures will help contain spread of COVID-19. Toronto: Queen's Printer for Ontario; 2020.
[7] Gomis B. How the illicit drug trade is adapting to the coronavirus pandemic [Internet]. World Politics Review. 2020. Available from: https://www.worldpoliticsreview.com/articles/28696/how-the-illicit-drug-trade-is-adapting-to-the-coronavirus-pandemic
[8] WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020 [Internet]. World Health Organization. 2020. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19–-11-march-2020
[9] United Nations Office on Drugs and Crime (UNODC). COVID-19 and the drug supply chain: from production and trafficking to use [Internet]. UNODC. 2020. Available from: https://www.unodc.org/documents/data-and-analysis/covid/Covid-19-and-drug-supply-chain-Mai2020.pdf
[10] Maghsoudi N, McDonald K, Stefan C, et al. Evaluating networked drug checking services in toronto, Ontario: study protocol and rationale. Harm Reduct J. 2020;17(1):9–10.
[11] Ontario orders the mandatory closure of all non-essential workplaces to fight spread of COVID-19 [Internet]. Ontario Newsroom, Office of the Premier. 2020. Available from: https://news.ontario.ca/en/release/56435/ontario-orders-the-mandatory-closure-of-all-non-essential-workplaces-to-fight-spread-of-covid-19
[12] World Health Organization Expert Committee on Drug Dependence: forty-second report. WHO technical report series. Geneva: Word Health Organization; 2020 (License: CC BY-NC-SA 3.0 IGO. AB-FUBINACA; no. 1026).
[13] World Health Organization Expert Committee on Drug Dependence: forty-second report. WHO technical report series. Geneva: Word Health Organization; 2020 (License: CC BY-NC-SA 3.0 IGO. 4F-MDMB-BINACA; no. 1026).
[14] Jones JD, Nolan ML, Daver R, et al. Can naloxone be used to treat synthetic cannabinoid overdose? Biol Psychiatry. 2017;81(7): e51–e52.
[15] Richards JR, Schandera V, Elder JW. Treatment of acute cannabinoid overdose with naloxone infusion. Toxicol Commun. 2017;1; 1(1):29–33.
[16] Ontario Drug Policy Research Network; Office of the Chief Coroner for Ontario/Ontario Forensic Pathology Service; Ontario Agency for Health Protection and Promotion (Public Health Ontario); Centre on Drug Policy Evaluation. Preliminary patterns in circumstances surrounding opioid-related deaths in Ontario during the COVID-19 pandemic [Internet]. Toronto (ON): Ontario Drug Policy Research Network. 2020. Available from: https://www.publichealthontario.ca/-/media/documents/o/2020/opioid-mortality-covid-surveillance-report.pdf?sc_lang=en
[17] Toronto's Drug Checking Service. Synthetic cannabinoid circulating in Toronto's unregulated drug supply: ACHMINACA [Internet]. Centre on Drug Policy and Evaluation. 2020. Available from: https://drugchecking.cdpe.org/alert/achminaca/