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Long-term monitoring of drug consumption patterns during the COVID-19 pandemic in a small-sized community in Brazil through wastewater-based epidemiology

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HIGHLIGHTS

- Time-weighted concentrations of several drugs were estimated using POCIS sampling.
- An urban Brazilian WWTP was monitored for one year during the COVID-19 pandemic.
- All the priority compounds for WBE defined by the SCORE group were monitored.
- Drug consumption was correlated with human mobility.

ARTICLE INFO

Handling Editor: Keith Maruya

Keywords:
Wastewater-based epidemiology
POCIS sampling
COVID-19
Illicit drugs
Long-term monitoring

ABSTRACT

The abuse of legal and illegal drugs is a global public health problem, also affecting the social and economic well-being of the population. Thus, there is a significant interest in monitoring drug consumption. Relevant epidemiological information on lifestyle habits can be obtained from the chemical analysis of urban wastewater. In this work, passive sampling using polar organic chemical integrative samplers (POCIS) was used to quantify licit and illicit drugs biomarkers in wastewater for the application of wastewater-based epidemiology (WBE). In this WBE study, a small urban community of approximately 1179 inhabitants was monitored from 18 March 2020 to 3 March 2021, covering the mobility restriction and flexibilization periods of the COVID-19 pandemic in Brazil. Consumption was estimated for amphetamine, caffeine, cocaine, MDMA, methamphetamine, nicotine, and THC. The highest estimated consumption among illicit drugs was for THC (2369 ± 1037 mg day⁻¹ 1000 inh⁻¹) followed by cocaine (353 ± 192 mg day⁻¹ 1000 inh⁻¹). There was a negative correlation between consumption of caffeine, cocaine, MDMA, nicotine, and THC with human mobility, expressed by cellular phone mobility reports (P-value = 0.0094, 0.0019, 0.0080, 0.0009, and 0.0133, respectively). Our study is the first long-term drug consumption evaluation during the COVID-19 pandemic, with continuous sampling for almost a whole year. The observed reduction in consumption of both licit and illicit drugs is probably associated with stay-at-home orders...

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https://doi.org/10.1016/j.chemosphere.2022.134907
Received 27 January 2022; Received in revised form 18 April 2022; Accepted 6 May 2022
Available online 10 May 2022
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1. Introduction

Illicit drug consumption is a worldwide health and social problem (EMCDDA, 2019; UNODC, 2019). In addition, the use of some licit drug compounds, such as tobacco, has relevant impacts on the population’s health (Gao et al., 2018). In this context, the knowledge of the illicit and licit drug consumption behavior of a given population is of paramount importance for the planning and monitoring of demand and damage reduction activities, as well as for law enforcement intelligence (Bannwarth et al., 2019; Fallati et al., 2020). Classic monitoring of the consumption of drugs at the population level is based on epidemiological, sociological, and criminological indicators (EMCDDA, 2016). Considering the complexity and inherent uncertainty of these indicators, the analysis of wastewater was proposed as a more objective and representative strategy for the estimation of drug consumption by a population served by a wastewater treatment plant (WWTP). In this approach, named wastewater-based epidemiology (WBE), concentrations of biomarkers of drug use in wastewater are measured and the amount of drug intake by the population is estimated through retrospective calculations (Bannwarth et al., 2019; Fallati et al., 2020). The fundamental aspect of WBE is that human excrements (urine and feces) contain compounds and their biotransformation products originating from consumed products, such as illicit drugs, pharmaceuticals, food, tobacco, among others (Hernández et al., 2018; van Wel et al., 2018). The retrospective estimation of drug consumption by WBE demands the knowledge of the biomarker concentration in the wastewater, the wastewater inflow in the WWTP, the size of the served population by the WWTP, and the conversion factors from measured biomarker concentration to the consumed product (Lorenzo and Pico, 2019).

Several WBE studies were already reported, mainly focused on illicit drugs (Huizer et al., 2021). The priority compounds for WBE defined by the Sewage Analysis CORe group Europe (SCORE) are 3,4-methylene dioxyamphetamine (MDMA, ecstasy), amphetamine (AMP), methamphetamine (MAMP), cocaine (COC), and cannabis (SCORE, 2021). The first European study on illicit drug use by analyzing wastewater biomarkers was carried out in 2011 (Thomas et al., 2012). Monitoring was repeated in subsequent years to expand spatial coverage, increasing the number of monitored cities from 19 in 2011 to 73 in 2017 (González-Mariño et al., 2020). The human biomarker used in a WBE study should preferably be a specific metabolite of the compound under investigation, thus ensuring that its presence derives only from human excretion and not from exogenous sources, be excreted mainly through urine, and presenting concentration levels in wastewater in the ng L⁻¹ range, to ensure its detection. A biomarker must also be sufficiently stable in wastewater (Gracia-Lor et al., 2017). To estimate tobacco consumption, cotinine (COT) is usually monitored and quantified, as 70–80% of the consumed nicotine (NIC) is metabolized to this metabolite, which is subsequently hydroxylated to trans-3′-hydroxycotinine (Rodríguez-Alvarez et al., 2014). COC consumption is estimated using benzoylecgonine (BZE) wastewater concentrations, which is relatively stable in wastewater (Gracia-Lor et al., 2017). Anhydroecgonine methyl ester (AEME), a pyrolysis product of COC is indicative of the use of smoked cocaine (crack) (Bisceglia et al., 2010). Amphetamine stimulants are generally monitored as the parent compounds (Gracia-Lor et al., 2017). The main urinary metabolite of THC, the most relevant psychoactive compound in cannabis, is 11-nor-9-carboxy-A¹-tetrahydrocannabinol-glucuronide (THC-COOH-glu) (Zuccato et al., 2008). However, THC-COOH-glu is unstable in wastewater due to the presence of β-glucuronidase enzymes from fecal bacteria and the unconjugated form is then measured in WBE studies (Castiglioni et al., 2006; D’Asenzo et al., 2003; Heberer, 2002). The same occurs with applies to COT-glucuronide, the biomarker of NIC consumption (Castiglioni et al., 2015). Caffeine (CAF) can be monitored as the parent compound (Senta et al., 2015).

The retrospective calculation of drug consumption in WBE requires the knowledge of the average concentration of the biomarker along the 24 h of the day. The large majority of the reported WBE studies used composite active sampling to obtain representative wastewater concentrations (Hahn et al., 2021). This sampling strategy demands the use of expensive automatic samplers, properly installed with environmental protection and power supply (Allan et al., 2006). A cost-effective alternative to automatic composite sampling is the use of passive samplers, particularly the polar organic chemical integrative sampler (POCIS) (Alvarez et al., 2004). POCIS samplers are less affected by short-term fluctuations of biomarker concentrations in wastewater and allow pre-concentration of the analytes, leading to very low quantification limits (Fedorova et al., 2014; Morin et al., 2013). However, the use of POCIS requires the calibration of the sampling rates for the compounds of interest (Magi et al., 2018). Recently, our group described an analytical method based on POCIS sampling for the measurement of all priority compounds of SCORE in wastewater (Hahn et al., 2022). Only a few studies have compared automatic composite sampling with POCIS sampling. Criquet et al. (2017), compared POCIS (Bond Elut Plexa sorbent) and automated composite sampling for the determination of 65 substances (pesticides and pharmaceuticals) in an urban river, with 2-week sampling campaigns. The authors reported a good agreement between the two sampling methods, with 75% of the measurements showing ratios between 0.33 and 3. The concentrations measured with POCIS were, in general, between the maximum and minimum levels measured in the composite samples. Bishop et al. (2020), compared POCIS (Oasis HLB sorbent) and automated composite sampling for measuring prescription and illicit drugs concentrations in the influent of a WWTP. These authors reported an underestimate of the concentrations using POCIS when compared to the median concentrations of the composite sample, with only 48% of the concentrations within a three-fold difference. However, the POCIS membrane occlusion (sampled over 30 days) reported by the authors may have affected the performance of the sampling device.

At the beginning of the year 2020, the World was affected by the COVID-19 pandemic. The initial control of the spread of the disease was based on non-pharmacological measures, and more than 100 Countries instated personal mobility restrictions (Reinstadler et al., 2021). The impact of these measures on the demand and supply in the illicit drug market is still unknown. The SCORE group reported stability or slight increase in COC and AMP consumption in Europe during 2020 when compared to 2019, whereas the consumption of MDMA and MAMP were reduced. Cannabis use appeared to have been less affected during the pandemic mobility restriction periods. However, this study was based on sampling performed during only one week in most evaluated cities (SCORE, 2021). To date, there is no long-term continuous WBE for illicit drugs performed during the COVID-19 pandemic.

In this context, this study describes a WBE study evaluating all priority SCORE drugs during a whole year in 2020–2021 in a Brazilian mid-size city, comparing the estimated drug consumption with human mobility reports. To this end, POCIS sampling associated with liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS)
was used for the measurement of 8 human drug consumption biomarkers in wastewater of a WWTP.

2. Material and methods

2.1. Reagents, materials and POCIS samplers

Analytical standards of COT and CAF were purchased from Sigma Aldrich (Saint Louis, USA), BZE, AEME, AMP, MAMP, MDMA, and 11-nor-9-carboxy-Δ²-THC (THC-COOH) were purchased from LGC Standards (Luckenwalde, Germany). The deuterated internal standard cocaine-d₃ (COC-d₃) was supplied by Cerilliant (Round Rock, USA). Benzylecgonine-d₃ (BZE-d₃), amphetamine-d₃ (AMP-d₃), methamphetamine-d₃ (MAMP-d₃), 3,4-methylenedioxyamphetamine-d₃ (MDMA-d₃), and 11-nor-9-carboxy-Δ²-THC-d₃ (THC-COOH-d₃) were purchased from LGC Standards. Caffeine-d₃ (CAF-d₃) was supplied by Toronto Research Chemicals (Toronto, Canada). COT, CAF, CAF-d₉, were purchased as powders and the other standard were purchased as methanolic solutions at 1 or 0.1 mg mL⁻¹. Methanol, acetonitrile, and dichloromethane were purchased from Merck (Darmstadt, Germany). Isopropanol was supplied by Honeywell (Muskegon, USA). Formic acid and ammonium formate were bought from Sigma-Aldrich. Ammonium hydroxide was from Química Moderna (Barueri, Brazil). Ultrapure water and ammonium formate were bought from Sigma-Aldrich. Formic acid was supplied by Honeywell (Muskegon, USA). Formic acid in methanol. Eluates 2 and 3 were evaporated at 45 °C. Bond Elut Certify® cartridges were purchased from Agilent (Santa Clara, USA) and Oasis® HLB sorbent was purchased from Waters (Milford, USA). POCIS samplers were sandwiched between two polyethersulphones membranes, obtained from Pall, Ann Arbor, USA, and clamped between two stainless steel rings. Bond Elut Certify® cartridges and Oasis® HLB cartridges were purchased from Waters

2.2. POCIS extraction and analysis by LC-MS/MS

POCIS extraction and analysis were performed as recently described by Hahn et al. (2022). The Oasis® HLB sorbent was removed from the POCIS sampler and extracted three times with 4 mL of methanol. The methanolic extract was added with 50 μL of the internal standard working mixture and submitted to a solid-phase extraction (SPE) dual clean-up procedure. First, the methanolic extract was applied to a Bond Elut Certify® (130 mg, 3 mL⁻¹) cation exchange cartridge and this eluate (eluate 1) was collected. The Bond Elut Certify® was washed sequentially with 2 mL of aqueous 2% formic acid and 2 mL of methanol, followed by analyte elution (eluate 2) with two aliquots of 1 mL of dichloromethane: isopropanol: ammonia (80:20:2; v/v/v) (anion exchange cartridge, followed by cartridge washing with 2 mL of 5% ammonia in methanol: water (50:50; v/v) and 2 mL methanol. Finally, the Oasis® Max cartridge was eluted (eluate 3) with two aliquots of 1 mL of 2% formic acid in methanol. Eluates 2 and 3 were evaporated at 45 °C to dryness and recovered with 200 μL of a mixture of water: methanol (50:50; v/v). The mass balance was determined by comparing the recovery of the analytes at the end of the extraction process with the expected recovery. The recoveries were determined by the ratio of the area of the target compound to the area of the internal standard used for calibration. The recoveries were 90 ± 5% for COT and MDMA, 95 ± 5% for AMP, 93 ± 5% for AEME, 87 ± 5% for BZE, and 85 ± 5% for MDMA-d₃.

2.3. Analytical quality assurance

Calibration curves, with five concentration levels, were prepared in mixture of water: methanol (50:50, v/v). The concentration of the calibrators for AMP, MAMP, and AEME was 5, 12.5, 50, 125, and 250 ng g⁻¹. Calibration levels for COT and MDMA were 25, 62.5, 250, 625, and 1250 ng g⁻¹. BZE and THC-COOH calibrators had concentration levels of 250, 625, 2500, 6250, and 12,500 ng g⁻¹. The concentrations of CAF calibrators were 1000, 2500, 10,000, 25,000, and 50,000 ng g⁻¹. All calibrators contained a mixture of deuterated internal standards, with the concentrations of 0.05 (AMP-d₃ and MAMP-d₃), 0.25 (COC-d₃ and MDMA-d₃), 2.5 (BZE-d₃ and THC-COOH-d₃), and 10 (CAF-d₉) μg mL⁻¹. Weighted linear regression curves were used to estimate the concentration of the analyte in the influent water at the beginning of the sampling period. The relative error between measured and expected concentration was within the range of –19.8 to 20.4%. The reproducibility of the triplicate POCIS samplers used in the same sampling period ranged from 9.6 for COT to 27.8% for CAF. Internal standard-corrected matrix effects were in the range of –11.8 to 22.8% (AMP), with a maximum CV% of 5.6% (MAMP), with exception of AEME. This latter compound presented an ion enhancement effect in the range of 33.4–42.5%, which, despite being relatively large, was within a narrow range.

2.4. Laboratory calibration of POCIS sampling rate

The sampling rates (Rₚ in L day⁻¹) of the POCIS samplers for the target analytes were estimated through laboratory calibration experiments (Li et al., 2010; Rodayan et al., 2016). The POCIS samplers were exposed to water buffered to pH 8.1 (the average pH of the wastewater at the WWTP), added with the analytes. Positive and negative controls were also processed. The samplers were exposed to the water containing the analytes for 8 days, with daily aliquots used for the quantification of the compounds. Rₚ values were confirmed by the mass balance of the amount of the analyte accumulated in the POCIS in the calibration studies. The overall absorbance rate constant (k, L day⁻¹), represented by the regression slope, was calculated for each triplicate experiment from ln-transformed concentration graphs (y-axis) over time (x-axis). The dissipation constant (kₑ, L day⁻¹) was obtained at the positive control experiment and was subtracted from k to obtain the constant of adsorption (kₐ, L day⁻¹). The Rₚ for each analyte was calculated by multiplying kₑ by the water volume present in the experimental vessel. Rₚ values were 0.043, 0.050, 0.060, 0.079, 0.081, 0.085, 0.140, and 0.254 L day⁻¹ for AMP, COT, AEME, BZE, MAMP, CAF, MDMA, and THC-COOH, respectively. Details of the calibration experiment
experiment were described by Hahn et al. (2022).

2.5. POCIS sampling of wastewater and TWA concentration calculations

A set of three POCIS samplers were fixed into a perforated PVC tube and were submerged in the wastewater at a raw sewage inlet of a WWTP located in Novo Hamburgo, Brazil. This WWTP serves an average estimated urban population of 1179 people, according to the hydro chemical parameter biological oxygen demand over five days (BOD5). The number of inhabitants was established by dividing the BOD5 by 60 g day\(^{-1}\) inh\(^{-1}\), as an estimate of the amount produced by one person (Rico et al., 2017). Measurements of BOD5 in each sampling period allowed the use of a dynamic population size marker. The values ranged from 778 to 1679 inhabitants served by the WWTP during the evaluation period. The structure containing the POCIS samplers was substituted every 14 days. The sampling campaign started in March 2020 and finished in March 2021. Over this time, 24 sets of 3 POCIS samplers were used for sampling and analysis. After removal from the wastewater, the samplers were briefly washed with tap water and transferred to plastic bags. The samplers were disassembled, and the sorbent was extracted on the same day of removal from the wastewater. Data on wastewater inflow, temperature, and pH were provided by the sanitation company responsible for the WWTP.

The weight averaged concentration in wastewater (\(C_{\text{WIA}}\), ng L\(^{-1}\)) of the target compounds was calculated using equation (1). In this equation, \(C\) is the concentration of the compound in the sorbent (ng g\(^{-1}\)), \(M\) is the mass of sorbent in the POCIS (g), \(R\) is the sampling rate of the compound (L day\(^{-1}\)) and \(t\) is the POCIS exposure time (days).

\[
C_{\text{WIA}} = \frac{C \times M}{R \times t}\]

Equation 1

2.6. Back-calculation of drug consumption

The estimate of drug consumption by the population served by the WWTP (\(C\), expressed in ng mg \(^{-1}\) 1000 inh \(^{-1}\)) was obtained by multiplying the \(C_{\text{WIA}}\) (average of the three measurements) by the daily wastewater inflow in the WWTP (\(Q\), m\(^3\) day\(^{-1}\)) and by a specific correction factor (\(f\)), which considers the fraction of the original compounds excreted as the biomarker, as well as the ratio between molecular masses of the drug to the biomarker (Gracia-Lor et al., 2020). The result of this multiplication is divided by the number of people served by the WWTP and multiplied by 1000, to obtain a normalized value (van Nuijs et al., 2011; Zuccato et al., 2008), according to equation (2). The correction factors used in the study are presented in Table 1. Considering the low estimated mean residence time of the wastewater in the investigated sewer system (0.05–2 h), and given the known stability of the chosen biomarkers in wastewater (Senta et al., 2014, 2015), the estimated \(C\) values reasonably reflect the consumption rates for the various substances.

\[
C = \frac{(C_{\text{WIA}} \times Q \times f)}{1000} \text{ inh}\]

Equation 2

2.7. Mobility reports and its relationship with drug consumption

Community mobility reports for the city of Novo Hamburgo from 18 March 2020 to 3 March 2021 were obtained from Google LLC (Mountain View, USA), at www.google.com/covid19/mobility (Accessed 18 October 2021). Report insights are created with aggregated and anonymized datasets from users who have enabled the location history setting. The reports presented data on mobile phone mobility through city locations related to different human activities, classified as workplaces, supermarkets and pharmacies, parks, residential, public transport, and retail and recreation. The mobility variations are expressed as a percentage (%) and indicate the difference in the number of visitants along the day in the given location in comparison with a reference value from the pre-pandemic period (3 January 2020 to 6 February 2020), where no restriction in mobility was effective in the evaluated region. The evaluated time range included the introduction of the first human mobility reduction measures during the COVID-19 pandemic in the evaluated region, where the first stay-at-home recommendations by local authorities were stated on 16 March 2020, and the period of easing of mobility restrictions, after 3 August 2020. The mobility variation for each POCIS sampling period, expressed as %, was obtained by averaging the mobility variation of all the 14 days of sampling and is presented in Table 2. The parks and public transport mobility data were not evaluated due to incomplete data. The normality of the drug consumption data was tested using the Kolmogorov-Smirnov test. Parametric tests for correlation and regression analyses and group comparisons were used due to data normality. The relation between drug consumption estimates (y-axis) and the mobility variation (x-axis) was evaluated by simple and multiple linear regression, with regression adequacy evaluated through P-values (significance level of 95%) and correlation coefficients (\(r\)). For the multiple linear regression, the estimated consumption of each drug was related to all location categories at the same time. In addition, consumption data were divided into 2 groups, before and after the flexibilization period decreed in the city of Novo Hamburgo. The pre-flexibilization period was from 18 March to 5 August 2020 and the post-flexibility period was from 5 August 2020 to 3 March 2021. To evaluate whether there are differences between these two groups, the Student’s t-test for independent samples was used. Statistical analyses were performed using SPSS version 24 (IBM Corporation, USA).

3. Results and discussion

Wastewater sampling using POCIS is a useful alternative for WBE studies in resource-limited settings, once more sophisticated automatic composite samplers are not required. However, just a few previous studies for WBE of illicit drugs consumption using POCIS sampling were reported (Baz-Lomba et al., 2017; Harman et al., 2011) and none of these studies evaluated the consumption of THC, the most commonly used illicit drug of abuse (UNODC, 2021). Particularly in Brazil, only composite sampling was reported, with short-term evaluations, for COC (da Silva et al., 2018; Maldaner et al., 2012; Sodré et al., 2018). In this study, a sampling campaign of almost a whole year was applied. Long-term WBE studies can provide a valuable outline of the drug consumption profile of a locality and are less affected by point

| Drug  | Biomarker | Percentage of drug dose excreted as the biomarker (%) | Molar mass ratio | Correction factor (\(f\)) | Reference |
|-------|-----------|------------------------------------------------------|-----------------|--------------------------|-----------|
| AMP   | AMP       | 36.3                                                 | 1               | 2.77                     | Gracia-Lor et al. (2016) |
| CAF   | CAF       | 2.4                                                  | 1               | 41.7                     | Basel (2000)       |
| COC   | BZE       | 29                                                   | 1.05            | 3.59                     | Castiglioni et al. (2013) |
| Ecstasy | MDMA     | 22.5                                                 | 1               | 4.4                      | Gracia-Lor et al. (2016) |
| MAMP  | MAMP      | 22.7                                                 | 1               | 4.4                      | Gracia-Lor et al. (2016) |
| NIC   | COT       | 30                                                   | 0.92            | 3.1                      | Castiglioni et al. (2015) |
| THC   | THC-COOH  | 0.5                                                  | 0.91            | 182                      | Gracia-Lor et al. (2016) |

\(a\) Average for the most frequent intake route.

\(b\) Ratio between the molecular mass of the drug and the biomarker.

\(c\) Sum of the free and conjugated form.
The wide variation of R values for the same compounds even when similar sorbents are used.

Human mobility variation (%) in the city of Novo Hamburgo for each POCIS sampling period, with respect to pre-pandemic period.

The temperature of the wastewater was 10.7°C and the pH was 7.4 during the sampling campaign. Table 3 summarizes the estimated C_WA and amount of consumed drug for all sampling periods of the study. Among the monitored compounds, only MAMP was not detected in any sampling period. AEME was detected in only 4 sampling periods. AMP, BZE, CAF, COT, MDMA, and THC-COOH were measured in all POCIS extracts. CAF monitoring started in 27 May 2020.

To date, the majority of WBE studies for illicit drugs were performed using composite sampling, with sampling campaigns of up to one week (Hahn et al., 2021). The long-term profiling of consumption behavior of illicit and illicit drugs was reported only by few studies. Two of them used POCIS sampling and were performed in the same WWTP in Oslo, Norway. Among the compounds evaluated in this study, Harman et al. (2011), evaluated the consumption of AMP, MAMP, MDMA, and COC whereas Baz-Lomba et al. (2017), estimated the consumption of COC and MAMP. This study is the first long-term monitoring of the consumption of THC, CAF, and NIC based on WBE with POCIS sampling.

The highest estimate of illicit drug consumption was found for THC (2369 mg day⁻¹ 1000 inh⁻¹), followed by COC (353 mg day⁻¹ 1000 inh⁻¹), with much lower consumption of AMP and MDMA. Important to note that AMP can be present in wastewater as a metabolite of drugs such as fenproporex, used illegally in Brazil as an appetite suppressant and as a stimulant by truck drivers (Leyton et al., 2019), and lisdexamfetamine dimesylate, a prescription drug used to treat attention deficit/hyperactivity disorder. AEME, a pyrolytic metabolite of COC, was measured only in 4 consecutive sampling periods, from 11 November 2020 to 6 January 2021. This finding indicates the use of COC in the form of crack by the evaluated population, but in a small proportion of the overall consumption. The low frequency of AEME detection and the very high proposed correction factor described in the literature to estimate crack consumption, which leads to significant uncertainty, prevented us to use this marker for consumption estimates (Baker et al., 2014). In this context, we used the correction factor of 3.59, which considers that COC was used by the intranasal route, with 29% of the dose excreted as BZE (Castiglioni et al., 2013).

The estimates of consumption presented in Table 3 correspond to the amounts of active drugs taken. The actual amount of pure drug in a consumption unit is not easily estimated due to wide variations in the patterns of use and varying purity of the street products (Zuccato et al., 2008). However, considering the average dose of 125, 100, 30, and 100 mg for smoked THC, intranasal COC, oral AMP, and oral MDMA, respectively, the calculated consumed amount would be 19 cannabis dosages day⁻¹ 1000 inh⁻¹, 3.5 COC dose day⁻¹ 1000 inh⁻¹, 0.14 AMP dose day⁻¹ 1000 inh⁻¹, and 0.22 MDMA dose day⁻¹ 1000 inh⁻¹ (Daglioglu et al., 2019; Zuccato et al., 2008).

The consumption of COC in Brazilian cities was previously estimated, using 24 h composite sampling performed over 1–8 days (da Silva et al., 2018; Maldaner et al., 2012; Sodré et al., 2018). These studies estimated higher consumptions of COC, from 700 mg day⁻¹ 1000 inh⁻¹ to 6229 mg day⁻¹ 1000 inh⁻¹, with the latter referring to a composite sample collected in the last day of Carnival (da Silva et al., 2018). Important to note that POCIS sampling provides an average concentration over the sampling period and is less affected by point variation in the use of a given drug. Also, differences on the socio-economical, cultural, and demographic characteristics of the evaluated populations could also affect the consumption estimates.

The CAF consumption estimate had an average of 48 mg day⁻¹ inh⁻¹, lower than the estimate of 115.7 mg day⁻¹ inh⁻¹ of the Brazilian Institute of Geography and Statistics (IBGE), related to Brazilians over 10 years old (Sartori and da Silva, 2016). Similar observation was made regarding tobacco use, where the estimated consumption of 1.56 mg day⁻¹ inh⁻¹ of NIC is below the expected value considering the frequency of tobacco consumption previously reported in the Brazilian adult population, of 9.8% (Lopes et al., 2021). These differences in the estimates of CAF and NIC consumption could be attributed to the reduced income of the population during the mobility reduction period due to the COVID pandemic and to the demographic characteristics of the population served by the WWTP, with an unknown percentage of children.

The COVID-19 pandemic resulted in the enforcement of human variabilities (Krizman-Matasic et al., 2019).

The lack of standardization of POCIS calibration procedures and influence of environmental factors can result in significantly different R values for the same compounds even when similar sorbents are used (Baz-Lomba et al., 2017). The wide variation of R values observed in the literature characterize the high dependency of experimental calibration conditions and the semi-quantitative nature of drug consumption estimation using POCIS (Hahn et al., 2021). In this study, C_WA were estimated using lab constructed POCIS samplers with Oasis® HLB sorbent, whose calibration was recently described (Hahn et al., 2022). The wastewater was sampled in a WWTP from a mid-sized Brazilian city from 18 March 2020 to 3 March 2021, with 24 sampling periods of two weeks. In each sampling period, three POCIS samplers were extracted and analyzed by LC-MS/MS, with method validation details recently described (Hahn et al., 2022). The temperature of the wastewater was 17–27 °C and the pH was 7.4–8.5 during the sampling campaign. Table 3 summarizes the estimated C_WA and amount of consumed drug for all sampling periods of the study. Among the monitored compounds, only MAMP was not detected in any sampling period. AEME was detected in

| Sampling period (2020–2021) | Retail and Recreation | Workplaces and Pharmacies | Supermarkets and Pharmacies | Residential |
|-----------------------------|-----------------------|---------------------------|-----------------------------|-------------|
| 18 Mar. to 1 Apr.           | -49%                  | -31%                      | -8%                         | 17%         |
| 1 Apr. to 15 Apr.          | -62%                  | -47%                      | -12%                        | 22%         |
| 15 Apr. to 29 Apr.          | -52%                  | -34%                      | -11%                        | 18%         |
| 29 Apr. to 13 May           | -43%                  | -25%                      | -2%                         | 15%         |
| 13 May to 27 May            | -37%                  | -19%                      | -1%                         | 14%         |
| 27 May to 10 June           | -34%                  | -15%                      | 5%                          | 13%         |
| 10 June to 24 June          | -29%                  | -16%                      | 5%                          | 13%         |
| 24 June to 8 July           | -45%                  | -19%                      | -2%                         | 16%         |
| 8 July to 22 July           | -45%                  | -19%                      | 0%                          | 15%         |
| 22 July to 5 Aug.           | -43%                  | -16%                      | 1%                          | 14%         |
| 5 Aug. to 19 Aug.           | -30%                  | -12%                      | 6%                          | 12%         |
| 19 Aug. to 2 Sept.          | -29%                  | -10%                      | 8%                          | 11%         |
| 16 Sept. to 30 Sept.        | -26%                  | -5%                       | 11%                         | 9%          |
| 30 Sept. to 14 Oct.         | -25%                  | -4%                       | 15%                         | 9%          |
| 14 Oct. to 28 Oct.          | -21%                  | -3%                       | 16%                         | 7%          |
| 28 Oct. to 11 Nov.          | -19%                  | -4%                       | 18%                         | 7%          |
| 11 Nov. to 25 Nov.          | -13%                  | 3%                        | 23%                         | 7%          |
| 25 Nov. to 9 Dec.           | -12%                  | 3%                        | 23%                         | 7%          |
| 9 Dec. to 23 Dec.           | -8%                   | 4%                        | 26%                         | 7%          |
| 23 Dec. to 6 Jan.           | -27%                  | -30%                      | 11%                         | 9%          |
| 06 Jan. to 20 Jan.          | -26%                  | -9%                       | 3%                          | 7%          |
| 20 Jan. to 3 Feb.           | -25%                  | -5%                       | 1%                          | 6%          |
| 3 Feb. to 17 Feb.           | -20%                  | -4%                       | 6%                          | 4%          |
| 17 Feb. to 3 Mar.           | -31%                  | -9%                       | 8%                          | 7%          |
mobility restrictions in most countries of the world. The state of health emergency in the city of Novo Hamburgo, Brazil, was declared on 18 March 2020 by the city mayor. Soon after, on 23 March 2020, the state of public calamity was instated, with mandatory closure of all workplaces, commercial, and educational facilities, excluding essential activities. The higher reduction in human mobility in the city was observed at the beginning of the restrictions, between 1 April 2020 and 15 April 2020, with a 62% reduction in mobility in retail and recreation activities and a 47% reduction in workplace mobility. The first confirmed COVID-19 case in the city was reported on 29 March 2020, with the first death the next day. Different levels of restrictions in human mobility were effective since then, until 3 August 2020, when non-essential activities were authorized to reopen partially. The human distancing levels do not depend only on government recommendations, but also on individual decisions. The level of human mobility in an urban location can be derived from cellular phone mobility, as applied in other studies (Reinstadler et al., 2021; Zhu et al., 2020). Fig. 1 presents the amounts of drugs consumed over the study and the registered human mobility in different activities, which were significantly correlated.

In this study, wastewater was sampled from 18 March 2020 to 3 March 2021, covering the period of most severe mobility restrictions and the period where some of the restrictions were lifted, what happened just after the middle of the year of 2020. There is very limited data about the drug consumption of the evaluated population before COVID-19 mobility restrictions (Hahn et al., 2022). The results of the simple and multiple correlation analyses relating to the amount of

Table 3

| Sampling period (2020–2021) | AMP Consumption | CAF Consumption | COC Consumption | MDMA (Ecstasy) Consumption | NIC Consumption | THC (Cannabis) Consumption |
|-----------------------------|-----------------|-----------------|-----------------|-----------------------------|----------------|---------------------------|
| 18 Mar. to 1 Apr.           | 6.4 ± 4.0       | –               | –               | 325.7 ± 264.1              | 7.0 ± 6.9      | 208.3 ± 145.9             |
| 1 Apr. to 15 Apr.           | 10.3 ± 5.8      | –               | –               | 382.3 ± 280.7              | 13.1 ± 11.8    | 184.6 ± 117.1             |
| 15 Apr. to 29 Apr.          | 11.5 ± 6.7      | –               | –               | 509.8 ± 384.9              | 14.5 ± 13.4    | 250.5 ± 163.3             |
| 29 Apr. to 13 May           | 7.3 ± 4.0       | –               | –               | 410.4 ± 289.9              | 24.7 ± 21.4    | 247.6 ± 151.0             |
| 13 May to 27 May            | 5.3 ± 2.5       | –               | –               | 245.7 ± 152.5              | 21.4 ± 16.3    | 211.2 ± 113.2             |
| 27 May to 10 June           | 7.6 ± 4.1       | 5135 ± 41,856   | 246.5 ± 173.0   | 12.7 ± 10.9                | 203.4 ± 123.3  | 39.2 ± 1395.6             |
| 10 June to 24 June          | 4.5 ± 2.7       | 1941 ± 17,326   | 207.0 ± 159.0   | 8.9 ± 8.4                  | 124.6 ± 82.7   | 26.7 ± 1039.8             |
| 24 June to 8 July           | 4.7 ± 3.7       | 1046 ± 12,613   | 252.0 ± 261.6   | 12.4 ± 15.8                | 139.4 ± 125.0  | 44.6 ± 2349.6             |
| 8 July to 22 July           | 4.1 ± 2.7       | 1422 ± 14,167   | 176.7 ± 151.6   | 8.8 ± 9.3                  | 119.4 ± 88.5   | 56.9 ± 2473.6             |
| 22 July to 5 Aug.           | 3.3 ± 1.5       | 1129 ± 7930     | 223.3 ± 135.0   | 7.2 ± 5.4                  | 167.6 ± 87.5   | 75.6 ± 2316.4             |
| 5 Aug. to 19 Aug.           | 3.0 ± 1.7       | 3458 ± 28,885   | 221.9 ± 159.6   | 5.5 ± 4.9                  | 149.4 ± 92.8   | 51.8 ± 1888.7             |
| 19 Aug. to 2 Sept.          | 2.5 ± 1.2       | 2324 ± 16,972   | 250.2 ± 157.3   | 5.4 ± 4.1                  | 180.7 ± 98.1   | 58.2 ± 1855.8             |
| 16 Sept. to 30 Sept.        | 4.6 ± 2.8       | 9385 ± 85,995   | 348.8 ± 275.1   | 6.5 ± 6.3                  | 197.7 ± 134.7  | 28.0 ± 1121.6             |
| 30 Sept. to 14 Oct.         | 3.4 ± 2.2       | 6826 ± 66,893   | 395.4 ± 333.6   | 3.4 ± 3.5                  | 204.8 ± 149.2  | 43.3 ± 1852.4             |
| 14 Oct. to 28 Oct.          | 6.4 ± 3.9       | 9119 ± 83,642   | 407.8 ± 322.0   | 19.8 ± 19.2                | 270.7 ± 184.6  | 65.4 ± 2616.5             |
| 28 Oct. to 11 Nov.          | 5.9 ± 3.7       | 9616 ± 91,494   | 573.7 ± 470.0   | 40.7 ± 40.9                | 292.0 ± 206.5  | 48.8 ± 2027.9             |
| 11 Nov. to 25 Nov.          | 6.1 ± 4.3       | 5750 ± 60,208   | 601.1 ± 541.9   | 20.9 ± 23.1                | 309.4 ± 240.9  | 60.2 ± 2752.6             |
| 25 Nov. to 9 Dec.           | 11.3 ± 6.2      | 6213 ± 51,222   | 563.5 ± 400.0   | 42.9 ± 37.3                | 296.3 ± 181.6  | 72.9 ± 2622.8             |
| 9 Dec. to 23 Dec.           | 12.6 ± 9.9      | 7364 ± 87,179   | 610.2 ± 621.9   | 40.9 ± 51.1                | 292.5 ± 257.5  | 76.7 ± 3961.1             |
| 23 Dec. to 6 Jan.           | 7.9 ± 4.7       | 6787 ± 59,750   | 823.8 ± 624.3   | 53.7 ± 49.9                | 351.4 ± 230.0  | 118.0 ± 4534.4            |
| 6 Jan. to 20 Jan.           | 2.8 ± 1.8       | 8459 ± 81,171   | 791.6 ± 654.0   | 75.5 ± 76.5                | 439.9 ± 313.8  | 98.1 ± 4101.7             |
| 20 Jan. to 3 Feb.           | 13.0 ± 10.0     | 3069 ± 35,688   | 847.8 ± 848.8   | 47.5 ± 58.3                | 342.0 ± 295.6  | 89.1 ± 4523.3             |
| 3 Feb. to 17 Feb.           | 7.2 ± 3.9       | 1224 ± 9910     | 547.3 ± 381.6   | 17.4 ± 14.9                | 269.8 ± 162.4  | 60.5 ± 2139.4             |
| 17 Feb. to 3 Mar.           | 10.1 ± 6.7      | 5891 ± 59,013   | 486.4 ± 419.5   | 19.7 ± 20.8                | 231.7 ± 172.5  | 71.3 ± 3115.5             |
| Average                     | 6.7 ± 4.2       | 5061 ± 29,847   | 47,995 ± 27,748 | 435 ± 353 ± 192 ± 22.1 ± 22.1 ± 20 237 ± 163 ± 65 ± 58.7 ± 2369 ± 1037 | 22.1 ± 19 21 ± 79 ± 23 | 6 ± 23 | 1037 | 6 ± 23 |

* Estimated using THC as biomarker.
* Estimated using BZE as biomarker.
* Estimated using COT as biomarker.
* Estimated using THC-COOH as biomarker.
consumed drug and human mobility reduction during the study are summarized in Tables 4 and 5, respectively. No significant correlations were observed for AMP consumption, in both analyses, the drug less consumed among the evaluated compounds. COC daily consumption presented a negative correlation with the human mobility level at residential locations on simple ($r = 0.5999, P$-value $= 0.0019$) and multiple ($r = 0.7412, P$-value $= 0.0207$) correlation analyses. In addition, COC daily consumption also had a positive significant correlation with retail and recreation mobility in simple correlation analysis, and a negative correlation with workplaces mobility on multivariate analysis. In both tests, we observe that the contribution (regression slope) of the residence mobility category is much greater than the other significant variables to the consumption of COC. So, even if the circulation in the workplace and recreation and leisure locations has increased over time, the major impact in the increase of COC consumption was probably the reduction of the permanence of the population in their residences. Particularly, COC consumption presented a trend to increase along with the increase of mobility in public activities, markedly after the end of August 2020. This observation was confirmed by the finding of the

Fig. 1. Drug consumption and human mobility in different location categories during the WBE sampling study (18 March 2020 to 3 March 2021).

Table 4
Summary of simple correlation analysis between daily drug consumption (mg day$^{-1} 1000$ inh$^{-1}$) and human mobility (% of pre-pandemic mobility) in the city of Novo Hamburgo from 18 March 2020 to 3 March 2021.

| Drug Location category | $r$ | Intercept | Slope | Average $P$-value of linear regression$^a$ |
|------------------------|-----|-----------|-------|----------------------------------------|
| AMP retail and recreation | 0.1711 | 5.1263 | 2.9891 | 0.4242 |
| workplaces | 0.0682 | 4.3634 | 1.2564 | 0.7516 |
| supermarkets and pharmacies | 0.1121 | 4.0298 | 2.5967 | 0.6020 |
| residential | 0.1862 | 5.2627 | -9.7240 | 0.3836 |
| CAF retail and recreation | 0.6164 | 95356.63 | 177613.10 | 0.0049 |
| workplaces | 0.4706 | 62554.39 | 159353.82 | 0.0420 |
| supermarkets and pharmacies | 0.6654 | 25205.91 | 237439.74 | 0.0019 |
| residential | 0.5792 | 96002.47 | -508828.06 | 0.0094 |
| COC retail and recreation | 0.4765 | 564.2563 | 677.2497 | 0.0186 |
| workplaces | 0.3031 | 414.5278 | 454.2131 | 0.1499 |
| supermarkets and pharmacies | 0.3201 | 314.9191 | 603.0578 | 0.1272 |
| residential | 0.5999 | 633.0945 | -2547.6456 | 0.0019 |
| MDMA retail and recreation | 0.4454 | 42.4721 | 65.2149 | 0.0292 |
| workplaces | 0.2639 | 27.6461 | 40.7460 | 0.2127 |
| supermarkets and pharmacies | 0.2899 | 18.5757 | 56.2579 | 0.1694 |
| residential | 0.5280 | 47.5249 | -231.0105 | 0.0080 |
| NIC retail and recreation | 0.5243 | 242.6507 | 254.1022 | 0.0085 |
| workplaces | 0.3729 | 189.2170 | 190.5381 | 0.0727 |
| supermarkets and pharmacies | 0.3729 | 148.2715 | 239.5335 | 0.0727 |
| residential | 0.6334 | 264.2398 | -917.3735 | 0.0009 |
| THC retail and recreation | 0.3646 | 3243.7641 | 2800.2071 | 0.0798 |
| workplaces | 0.2161 | 2607.2109 | 1749.9063 | 0.3105 |
| supermarkets and pharmacies | 0.2674 | 2198.5598 | 2722.0729 | 0.2065 |
| residential | 0.4979 | 3626.6973 | -11426.5233 | 0.0133 |

$^a$ Significant correlations are presented in bold.
correlation analyses, characterizing that the longer people stayed at home, lesser COC was consumed. The human mobility level in the city in retail and recreation activities increased from correlation analyses, characterizing that the longer people stayed at home, lesser COC was consumed. The human mobility level in the city in Novo Hamburgo from 18 March 2020 to 3 March 2021.

Table 5
Summary of multiple correlation analysis between daily drug consumption (mg day\(^{-1}\) 1000 inh\(^{-1}\)) and human mobility in all location categories in the city of Novo Hamburgo from 18 March 2020 to 3 March 2021.

| Drug | Location category | r      | F-value   | Slope   | Average P-value of linear regression |
|------|------------------|--------|-----------|---------|--------------------------------------|
| AMP  | retail and recreation workplaces | 0.2913 | 0.7779 | 9.8479 | 0.6011 |
|      | supermarkets and pharmacies residential | -8.8073 | 0.3682 | 2.1841 | 0.7854 |
|      | -11.6261 | 0.7402 |
| CAF  | retail and recreation workplaces | 0.7416 | 0.0181 | -183.139 | 0.3193 |
|      | supermarkets and pharmacies residential | -40388 | 0.6795 | 327500 | 0.0458 |
|      | -587245 | 0.1000 |
| COC  | retail and recreation workplaces | 0.7412 | 0.0032 | 52512 | 0.6250 |
|      | supermarkets and pharmacies residential | -13002 | 0.0277 | -39180 | 0.6582 |
|      | -4976.6 | 0.0207 |
| MDMA | retail and recreation workplaces | 0.6752 | 0.0164 | 123.69 | 0.3143 |
|      | supermarkets and pharmacies residential | -130.32 | 0.0482 | -78.126 | 0.4384 |
|      | -347.28 | 0.1363 |
| NIC  | retail and recreation workplaces | 0.7267 | 0.0048 | 181.35 | 0.6286 |
|      | supermarkets and pharmacies residential | -361.64 | 0.0727 | -134.29 | 0.4639 |
|      | -1540.4 | 0.0374 |
| THC  | retail and recreation workplaces | 0.6604 | 0.0223 | -2754.8 | 0.6712 |
|      | supermarkets and pharmacies residential | -6924.4 | 0.0493 | 2418.3 | 0.6515 |
|      | -31720 | 0.0154 |

Significant correlations are presented in bold.

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Correlation analysis also had a significant positive correlation with mobility in retail and recreation activities (r = 0.4454, P-value = 0.0292), and a significant negative correlation with residential mobility (r = 0.5280, P-value = 0.0080) in simple regression analysis. In addition, a significant negative correlation of MDMA daily consumption with workplace mobility (r = 0.6752, P-value = 0.0482) was found in multiple regression analysis, which shows that MDMA use was particularly affected by the closure and reopening of club parties and raves, which restarted at the end of 2020. THC daily consumption had a significant negative correlation with residential mobility in both simple (r = 0.4979, P-value = 0.0133) and multiple correlations (r = 0.6604, P-value = 0.0154), and a negative significant correlation with workplace mobility in multiple analysis (r = 0.6604, P-value = 0.0493). CAF daily consumption presented a negative correlation with the human mobility level at residential locations (r = 0.5792, P-value = 0.0094), and positive significant correlations with retail and recreation, workplace, and supermarket and pharmacies location mobilities in simple correlation analysis. CAF consumption was highly correlated with mobility at retail locations (r = 0.67). Reduced consumption in the end-of-year holidays is probably associated with people temporally moving away from their homes in this period. CAF daily consumption also presented a positive significant correlation with supermarket and pharmacies mobilities in the multiple regression analysis. These data indicate that CAF consumption was affected by overall mobility and not by modifications in particular human activity. Both CAF and NIC consumption presented a strong negative correlation with the human mobility level at residential locations and positive significant correlations with retail and recreation. As these compounds are originated from licit consumed products, the reduction in consumption is probably associated with reduced access, which can be due to the closure of commercial facilities during some time of the evaluated period, but also to the reduced income of the population due to the shutdown of companies and unemployment. The smaller NIC consumption when people were mostly at home may also be due to respect for family members who do not smoke. Thus, the decrease in the population’s permanence in residential locations due to the flexibility of stay-at-home recommendations during 2020 had a greater impact on the increase in the consumption of licit and illicit drugs than the change of mobility in other location categories. In general, we observed that overall drug consumption was reduced during the stay-at-home period.

In the evaluation of the period before and after the mobility flexibilization, significant higher drug consumption was observed, except for AMP, as presented in Table 6. From the 4 sampling periods of the pre-pandemic period, the consumption averages were 7.2, 375.3, 20.5, 134.0, and 2660 mg day\(^{-1}\) 1000 inh\(^{-1}\) for AMP, COC, MDMA, NIC, and THC, respectively. Even considering the limited amount of data available from pre-pandemic drug consumption estimates, we can observe an increase in consumption after easing mobility restrictions when compared to the pre-pandemic period, except for THC, which presented similar behavior in both periods.

There are a few studies evaluating drug use patterns during the COVID-19 pandemic employing WBE. Reinstadler et al. (2021), evaluated the consumption of illicit drugs and pharmaceuticals in Innsbruck, Austria, for 35 days in March–April 2020 using 24 h composite wastewater samples. The study found a reduction in the consumption of recreational drugs like COC, AMP, MDMA, MAMP, and alcohol, probably related to the closure of touristic and recreational activities. On the other hand, the consumption of CAF and NIC remained similar to those found before the pandemic. Been et al. (2021), evaluated AMP, MAMP, MDMA, BZE, and THC-COOH levels in wastewater from seven cities from The Netherlands, Belgium, Spain, and Italy during the early COVID-19 pandemic employing WBE. Reinstadler et al. (2021) evaluated AMP, MAMP, MDMA, BZE, and THC-COOH levels in wastewater from eleven cities from The Netherlands, Belgium, Spain, and Italy during the early COVID-19 pandemic employing WBE. Reinstadler et al. (2021) evaluated AMP, MAMP, MDMA, BZE, and THC-COOH levels in wastewater from eleven cities from The Netherlands, Belgium, Spain, and Italy during the early COVID-19 pandemic employing WBE.

Table 6
Student’s t-test for independent samples to compare drug consumption (mg day\(^{-1}\) 1000 inh\(^{-1}\)) before (18 March to 5 August) and after mobility flexibilizations (5 August to 3 March) in the city of Novo Hamburgo.

| Drug | Consumption before flexibilization (mean ± SD) | Consumption after flexibilization (mean ± SD) | P-value* (t) |
|------|---------------------------------------------|---------------------------------------------|-------------|
| AMP  | 3.8 ± 1.6                                   | 4.5 ± 2.8                                   | 0.477       |
|      | (−0.724)                                    |                                             |             |
| CAF  | 18.778 ± 13.338                             | 58.430 ± 26.925                             | 0.006       |
|      | (−3.117)                                    |                                             |             |
| COC  | 225.2 ± 83                                  | 443.5 ± 198                                 | 0.002       |
|      | (−3.705)                                    |                                             |             |
| MDMA | 11.9 ± 4.9                                  | 29.3 ± 23                                   | 0.016       |
|      | (−2.719)                                    |                                             |             |
| NIC  | 119.7 ± 38                                  | 194.3 ± 67                                  | 0.002       |
|      | (−3.717)                                    |                                             |             |
| THC  | 1773 ± 575                                  | 2794 ± 1098                                 | 0.014       |
|      | (−2.680)                                    |                                             |             |

Significant difference between the compared periods are presented in bold.
60% reduction in COC consumption in Castellon (Spain). However, an increase in drug consumption was observed in other locations, like an increase in COC consumption in Milan. Montgomery et al. (2021), evaluated the consumption of illicit and prescription drugs from March to June 2020, during the early COVID-19 lockdowns in the states of Kentucky and Tennessee, USA. The study performed sampling of wastewater for 4 periods of 10 consecutive days and compared the estimated drug consumption of June with March 2020, during the lockdown period. The authors found an increase of 72% in hydrocodone consumption in the latter wastewater collections, but decreases in the consumption of the illicit drugs MAMP and COC, of 16 and 42%, respectively. Bade et al. (2021), evaluated the consumption of MAMP, MDMA, COC, THC, and alcohol through wastewater analysis from 20 WWTP in Australia from February to June 2020, during a national lockdown, and compared the finding with pre-pandemic estimates. The estimates of MAMP consumption presented decreases of up to 50%, but cannabis consumption increased significantly. Authors suggest that the observed changes in consumption were possibly linked to reduced supply of imported substances, with increased use of locally produced drugs.

Our study is the first long-term continuous drug consumption evaluation during the COVID-19 pandemic. We hypothesize that the observed reduction of the consumption of both drugs of illicit and licit compounds in the low-income community monitoring in this study, differently from the study performed in Developed Countries, was mostly related to reduced availability of financial resources of the population. Differently from what was observed in Europe and USA, the supply of COC and THC, the more commonly consumed illicit drugs of abuse in Brazil, were probably not significantly affected by border closures during COVID-19 pandemic. The increase in consumption was probably due to the relaxation and return of recreational activities, with the reduction in permanence in residential locations.

4. Conclusions

Consumption estimates of AMP, CAF, COC, MAMP, MDMA, NIC, and THC were obtained after POCIS sampling in a small WWTP in Southern Brazil with continuous days of monitoring for almost a whole year during the COVID-19 pandemic. The most consumed illicit drugs were THC and COC, with average yearly intakes of 2369 and 353 mg day−1 1000 inh−1, respectively. The consumption of illicit and licit drugs by the population served by the WWTP was correlated with the human population served by the WWTP. The study performed sampling of wastewater for 4 periods of 10 consecutive days and compared the finding with pre-pandemic estimates. The estimates of MAMP consumption presented decreases of up to 50%, but cannabis consumption increased significantly. Authors suggest that the observed changes in consumption were possibly linked to reduced supply of imported substances, with increased use of locally produced drugs.

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding sources and Acknowledgements

This research is supported by the National Institute of Science and Technology in Forensic Sciences (MCTI/CNPq/CAPES/FAPS 16/2014 - INCT program, CNPq 465450/2014-8). This work is also part of another project financially supported by CNPq (427723/2018–3). RZH, MFB, LLFL, and AS are recipients of CAPES scholarships. RL is recipient of a CNPq research scholarship. Authors thank Prof. Daniela Müller de Quevedo for the support with statistical analyses.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2022.134907.

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