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SHORT COMMUNICATION

Synthetic cannabinoid receptor agonists profile in infused papers seized in Brazilian prisons

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Abstract

Purpose Synthetic cannabinoid receptor agonists (SCRAs) are a class of varied compounds that mimic the effects of natural cannabinoids found in cannabis. Because they have a wide range of diverse structures, they vary widely in their potency. The abuse of new psychoactive substances (NPS) in prisons was reported in many European countries and in the USA. In the present study, we have described the identification of SCRAs in 56 infused paper sheet samples, seized mainly in Brazilian prisons between 2016 and 2020.

Methods The materials were seized by local or federal law enforcement and analyzed by São Paulo State Police or Brazilian Federal Police using gas chromatography–mass spectrometry, attenuated total reflection-Fourier transform infrared spectroscopy, liquid chromatography–high-resolution mass spectrometry or nuclear magnetic resonance spectrometry.

Results Most of these samples (87.5%) were seized in 2019–2020; seven different SCRAs were identified in samples, and the most frequently identified substances were MDMB-4en-PINACA (23.6%) and 5F-MDMB-PICA (36.4%), the newest SCRAs emerging recently.

Conclusions As observed in Europe and the USA, Brazil also shows the prevalence of indazole-3-carboxamides and indole-3-carboxamides among SCRAs seizures in the prison system. This phenomenon is spreading all over the world at this moment. These data on the prevalence could help to alert judicial authorities to shutting down the introduction of NPS, including SCRAs, into prisons to ensure safety and security for avoiding health risks of prisoners and staff, leading to positive effects in this population. To our knowledge, this is the first demonstration of SCRAs smuggling into prisons in Latin America.

Keywords Synthetic cannabinoid receptor agonists · New psychoactive substances (NPS) · 5F-MDMB-PICA · MDMB-4en-PINACA · Abuse in prisons

Introduction

New psychoactive substances (NPS) are illicit substances not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, and they are designed to mimic the effects of traditional drugs such as cannabis, cocaine, and amphetamine, which may pose a public health threat. Typically, NPS are more potent than the drugs that they mimic and include a wide and diverse range of chemical structures, even within the same effect group. Therefore, their pharmacodynamics, pharmacokinetics, and intensity of effects remain unpredictable, and they sometimes have severe adverse health consequences, mostly neurological symptoms, including death [1–3].

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Up to August 2020, over 1000 individual NPS have been reported, and since 2015 more than 500 NPS were reported per year to the United Nations Office for Drugs and Crime (UNODC) Early Warning Advisory. The main groups of NPS reported are stimulants and synthetic cannabinoid receptor agonists (SCRAs); these two groups correspond to 64% of the reports [4].

The growth in the number of substances seems to be stabilizing since 2013, due to efforts by several countries to curb the advance of the NPS through new legislation or updates to existing ones, mainly with the aim of making the production, possession, and supply of a large number of structural analogs illegal [5, 6]. Over the last 10 years, Brazil reported the identification of 116 NPS, being the country that most reported substances among the region of South America, Central America and Caribbean [7].

SCRAs are a class of structurally varied compounds that mimic the effects of natural cannabinoids found in cannabis (mostly Δ^9-tetrahydrocannabinol, THC). Their pharmacodynamics consists of interaction with human cannabinoid type 1 and type 2 G-protein coupled receptors, CB_1 and CB_2. Because they have a wide range of diverse structures, SCRAs vary widely in their potency and efficacy [5, 8]. The first synthetic analog was synthesized in 1990 with a potency 100 times the THC, while identifications of SCRAs in herbal blends sold for recreational use started almost 20 years later. Nowadays, these NPS also have been detected in powders, infused paper and e-liquids for using electronic cigarette [5, 9, 10].

Convulsions, paralysis, tachycardia, hypertension, myocardial infarction, arrhythmias, psychosis, auditory and visual hallucinations, agitation, anxiety, depression, suicidal ideation and self-harm are some of the health risks associated with SCRAs; diagnoses of bipolar disorder, personality disorders, the onset of schizophrenia and related disorders have also been associated with the use of these substances. In addition, regular users exhibit aggressive behavior and other psychotic symptoms, especially among those already affected by addiction or mental illness [2, 11]. Recently, cases of vitamin K-dependent coagulopathy and bleeding have been reported in patients who had smoked SCRAs just before the onset of symptoms, with hemoptysis, hematuria, epistaxis and mucocutaneous bleeding being the most common. Biological samples from these individuals indicated the presence of brodifacoum, a super warfarin rodenticide [12–14].

Between 2016 and 2018, half of all NPS cases reported to the UNODC Early Warning Advisory on NPS – Toxicology Portal (Tox-Portal) involved synthetic opioids or SCRAs. According to UNODC, 5F-MDMB-PINACA (5F-ADB), 5F-MDMB-PICA and AMB-FUBINACA (FUB-AMB) were the most frequently reported SCRAs and featured in fatalities as well as clinical admissions in 2019 as the second most commonly identified substance in fatal cases (28%) and assessed to have contributed to death in the majority of cases [6]. 5F-MDMB-PICA was also the most seized SCRAs in EU, Norway and Turkey in 2017 and the most reported in the first quarter of 2020 by USA [15, 16]. In Florida—the third most populous state of the USA—over 56 and 36 kg of SCRAs were seized in 2016 and 2017, respectively [17].

Most NPS tend to be transient, however, patterns in use of SCRAs among marginalized, vulnerable and socially disadvantaged groups have been observed, including homeless people and those in prisons or on probation, especially because of the low cost, easy availability and high potency of these substances [18]. NPS use in prisons was reported by USA and 22 countries in Europe, and it features as an important challenge. It has been classified as the new "drug of choice" among European prisoners probably due its lack of odor, allowing it to be smoked undetected, besides avoiding detection by traditional drug screening. Due to its higher potency, small doses can cause the effects expected by the user, facilitating the smuggling of these substances into prisons, once the dosage unit can be a piece of 1 cm^2 (LSD-like blotter paper), allowing the administration of the drug by other routes such as sublingual and in the eye [19]. In Brazil, the Penitentiary Administration Secretariat of São Paulo State reported several attempts of smuggling infused papers containing SCRAs, usually made by the prisoner's relatives who, in some cases, hide the drug in their underwear and genitals [20–22]. Moreover, admission of patients from nearby prisons suffering the effects of NPS misuse has become frequent. This pattern of use associated with unpredictable pharmacodynamics, high potency and health risks could lead to serious negative consequences, such as unintentional overdose events and casualties [1, 3, 16, 23].

The number of cases of self-harm, suicide attempts, aggression, and ambulance call-outs reached alarming levels, as well as the use of drugs in prisons, also associated with organized crime, bullying, debt and suicides [2]. Furthermore, family members and friends of prisoners who are addicted or in debt are coerced to send money or smuggle more drugs into prisons. Incidents involving NPS also carry a higher risk of hospitalization as compared with traditional drugs, being associated with a high prevalence of fatalities [2]. In addition, psychotic events resulting from the use of SCRAs also affect the prison staff, because users can present hallucinations and depression, leading to fear, self-harm, suicidal ideations, paranoia, inability to be with others, and other risky behaviors. Moreover, a study conducted in UK applied a questionnaire among professionals working in prisons or related sectors; episodes involving outbreak of anger, hallucinations and psychosis were the main reasons for 67% of individuals to believe NPS had a significant impact on their work [2].

In the present study, we described the identification of SCRAs in 56 infused paper sheet samples, seized in Brazilian prisons between 2016 and 2020.

Materials and methods

Fifty-six infused paper sheet samples were seized, between 2016 and 2020, by the São Paulo State Police or Brazilian Federal Police, mainly in the prisons located in São Paulo state. SCRAs were identified in forensic chemistry laboratory by gas chromatography–mass spectrometry (GC–MS), attenuated total reflection-Fourier transform infrared spectroscopy (ATR-FTIR), liquid chromatography–high-resolution mass spectrometry (LC–QTOF-MS) or nuclear magnetic resonance (NMR), according to laboratories standard operational procedures and the Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) recommendations. Figures 1 and 2 depict examples of infused paper sheets seized in the Brazilian prison system and submitted to forensic chemistry analysis.

Results

Several seizures of SCRAs are being carried out in Brazilian prisons over the years. Since 2016, at least 48 seizures were made in the prisons of São Paulo state, all of them in infused paper form. During the same period, the Brazilian Federal Police seized other six infused paper samples containing SCRAs. Most of these samples (87.5%) were seized between 2019 and 2020. Seven different SCRAs were identified in samples (Table 1), and the most frequently identified substances were MDMB-4en-PINACA (23.6%) and 5F-MDMB-PICA (36.4%). In seized samples, more than one NPS was detected, combining 4F-MDMB-BINACA and 5F-MDMB-PICA; MDMB-4en-PINACA and 5F-MDMB-PICA; and, ADB-FUBINACA and 25I-NBOH (hallucinogenic phenylethylamine).

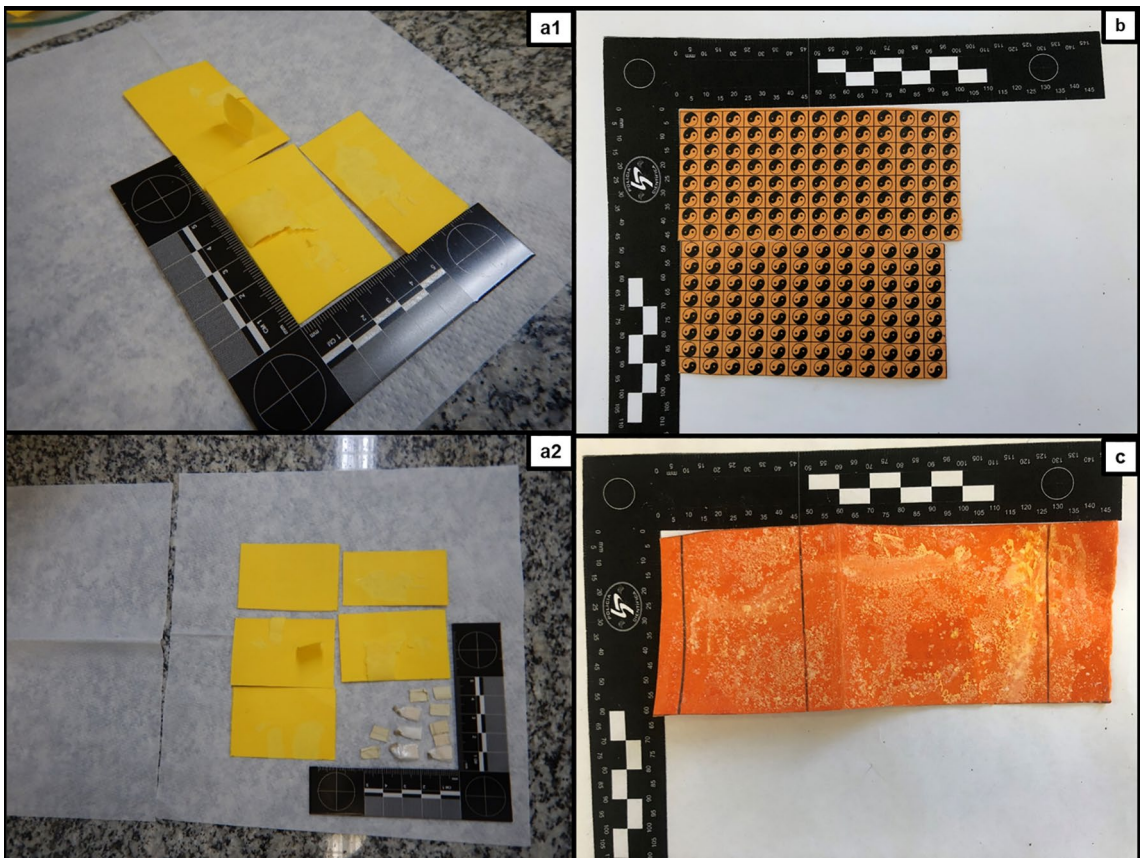

Fig. 1 Infused paper samples seized in Brazilian prisons containing 5F-MDMB-PICA. Yellowish papers seized by Brazilian Federal Police with approximately 24 cm^2 per sheet (**a1** and **a2**). Blotter paper ("LSD-like") with yin-yang logo, seized by Sao Paulo State Police, each square (single dose) of which was of approximately 1 cm^2 (**b**); orange-colored paper seized by Sao Paulo State Police at the state prison with approximately 84 cm^2 per sheet (**c**)

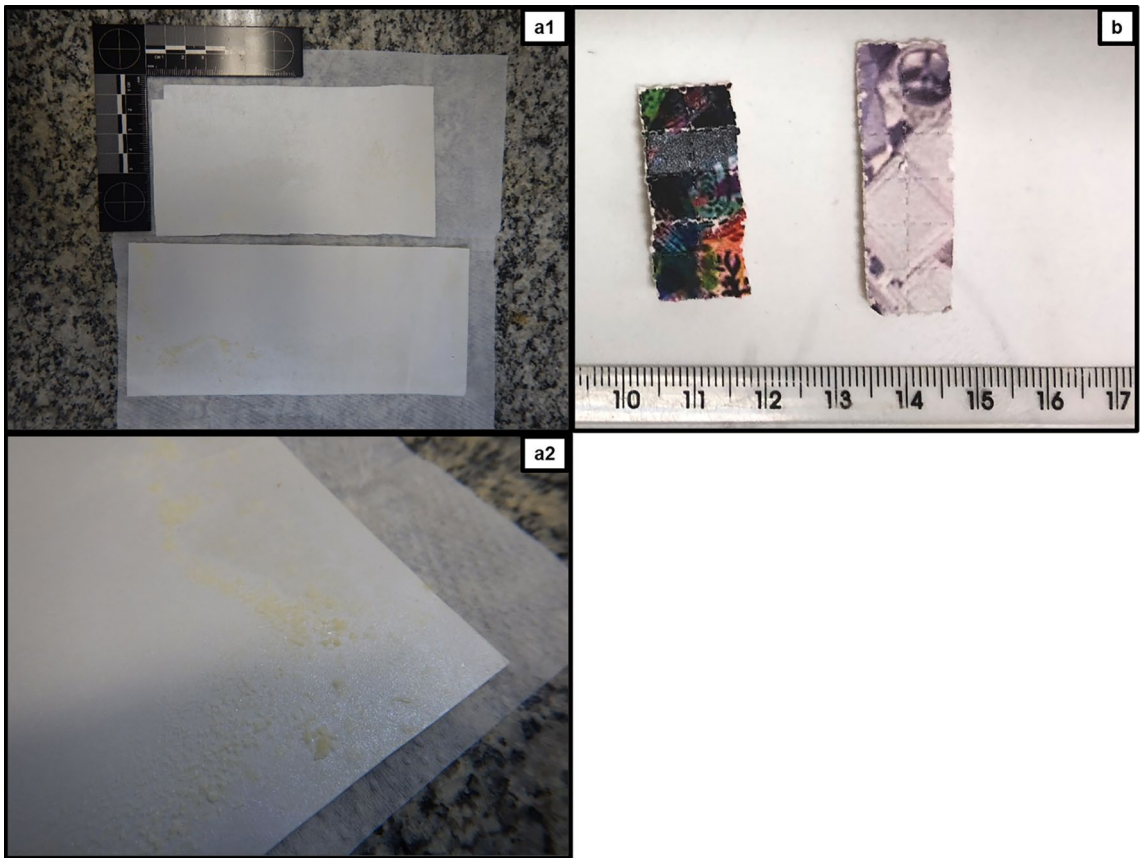

Fig. 2 Infused paper samples seized in a Brazilian prison containing MDMB-4en-PINACA (**a1**), with material crystallized on the surface of the paper sheet (**a2**). Blotter paper ("LSD-like") infused with AMB-FUBINACA (**b**)

Table 1 Synthetic cannabinoid receptor agonists (SCRAs) detected in infused paper samples seized at prisons by Sao Paulo State Police and Brazilian Federal Police (2016–2020)

Substance	Number of seizures	%
4F-MDMB-BINACA	2	3.4
ADB-BUTINACA	2	3.4
AMB-FUBINACA	2	3.4
4F-MDMB-BUTINACA	7	12.1
ADB-FUBINACA	11	19.0
MDMB-4en-PINACA	14	24.1
5F-MDMB-PICA	20	34.5

Discussion

In 2018, approximately 10.7 million people worldwide were held in prisons, corresponding to almost 0.14% of the global population [1]. Although prisons often rely on security systems to detect contraband, NPS are usually colorless and odorless, and are, thus, able to evade standard detection methods. Moreover, there have been reports of SCRAs sprayed onto clothing, letters and even children's drawings sent into prisons, likely to facilitate contraband and in response to the implementation of prison smoking bans in some countries [2, 5]. According to UNODC, in 2019, 53 different NPS were reported to UNODC by countries of South America, Brazil being responsible for approximately 62.2%: SCRAs were the third most reported NPS between 2015 and 2017 [7].

Norman et al. [5, 19] analyzed samples seized by the Scottish Prison Service in 2018–2019 and urine samples from Pennsylvania (US) prisoners in March and July 2019, being 5F-MDMB-PICA also the most prevalent SCRAs. According to EMCDDA [24], between June 2019 and July 2020, almost 15% of police seizures in prisons and correctional houses from six European countries contained MDMB-4en-PINACA. Moreover, by September of 2020, this SCRAs was mostly commonly detected in seizure data from UK and urine samples from German prisoners [19].

Indole and indazole SCRAs have greater potency than THC on activation of both CB_1 and CB_2 receptors, being high efficacy agonists. Activation of CB_1 receptors leads to the psychoactive effects of cannabinoids, and most of these SCRAs show a preference for CB_1 over CB_2 receptors

(1.3–20 times) [25]. The 5F-MDMB-PICA is the most cited SCRAs in UNODC Early Warning Advisory—Tox-Portal, being related to 128-intoxication cases between 2017 and 2020, from 10 different countries. The MDMB-4en-PINACA was related to 36 intoxication cases reported to the Tox-Portal, from 4 different countries (16 cases in the USA), all of them reported in 2020 [26].

Herbal mixtures containing SCRAs are often cited in Brazilian forensic reports; however, the detection of these substances in blotter papers or infused papers, since 2016, has shown a new trend in the use of these NPS [27]. In Brazil, NPS sold as blotter papers were mostly related to phenethylamine (NBOMe and NBOH families) [28–30] and few cases of fentanyl analogs (mostly furanylfentanyl) [31]. However, in Brazilian prisons, SCRAs represent a vast majority of NPS found in infused and blotter paper drugs.

Conclusions

In recent years, the number of SCRAs that have been smuggled into prisons as infused papers [5, 8, 17, 19] is increasing in Europe (Scotland, England, Wales and Germany) and USA (Florida), and close monitoring of these seizures could serve as an early warning for law enforcement, once studies show an alignment between SCRAs detected in prisons and the local market. As observed in Europe and the USA, Brazil also shows the prevalence of indazole-3-carboxamides and indole-3-carboxamides among SCRA seizures in the prison system. These data on the prevalence could help to determine safety, security and health risks for prisoners, staff, and the prison environment, leading to positive effects in this population. To our knowledge, this is the first demonstration of SCRA smuggling into prisons in Latin America.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest associated with this manuscript.

Ethical approval This article does not contain studies with human participants or animals performed by any of the authors.

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