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# **Executive Summary**

The rise in cannabis-related disorders seems to be influenced by the proliferation of cannabis-derived products (tinctures, edibles, gummies) with a higher concentration of THC, making them a high-risk substance above all for children. However, future research is necessary to confirm this association. 1,2

Synthetic cannabinoids are emerging as substances whose use is increasing globally. Their wide variety and the appearance of new substances complicate the context surrounding these substances.

There is limited information regarding the use of synthetic cannabinoids in Latin America and the Caribbean, possibly explained by these substances not being included in population surveys, as well as a lack of surveys having been carried out in several countries of the region over the last decade. Furthermore, the issue of underreporting is a problem, which is a result of some countries limited analytical capacity for biological detection as well as difficulty with chemical analysis of seized substances.

A decrease in seizures of some synthetic cannabinoids in the region in recent years does not necessarily mean a decrease in use, although the two countries in the Americas with up-to-date prevalence data for this substance—Chile and the United States—show decreases in use. Its powerful agonist effect on the cannabinoid system has led to sometimes-lethal cases of acute intoxication in which synthetic cannabinoids have been detected in the context of polydrug use, in some cases even reported as the cause of death.

Synthetic cannabinoids are used in association with other risky behaviors, such as driving under the influence of these substances, increases morbidity and mortality. The spread of these substances to at-risk populations should be considered a matter of great concern.

United Nations Office on Drugs and Crime (UNODC). World Drug Report, 2022. United Nations, June 2022.
 Doonan SM., Laramie O., & Johnson JK. (2021, October). "High Tetrahydrocannabinol (THC) Cannabis and Effects on the Human Body—More Research Needed. A Legislative Report and Considerations for Research and Policy." Worcester, MA: Massachusetts Cannabis Control Commission.

#### Information Bulletin

Cannabis with a High Concentration of Tetrahydrocannabinol (THC) and Synthetic Cannabinoids in Latin America and the Caribbean

# 1. Introduction

Cannabis is the most widely produced psychoactive plant in the world. In Latin America and the Caribbean, the largest producing countries are Brazil, Colombia, and Paraguay (South America); Costa Rica, Guatemala, and Honduras (Central America); and Jamaica and Trinidad and Tobago (Caribbean). Since 2010, the potency of cannabis-derived products has quadrupled at the same time adolescents' perception of risk or harms associated with use has dropped to 40%, despite growing evidence that these products pose a greater risk to users, particularly young people.<sup>3</sup>

During the last decade, two types of substances have emerged that act more powerfully on the cannabinoid system, significantly increasing the risk of impacts to user health: high concentration tetrahydrocannabinol (THC) cannabis and synthetic cannabinoids.<sup>4,5</sup> The risk of acute or chronic complications associated with cannabinoids depends on dosage, use over time, THC concentration and potency.<sup>6</sup> The existence of forms of high THC cannabis and synthetic cannabinoids<sup>7</sup> creates a scenario of high risk and great concern to public health in OAS member states.

Under the auspices of the Inter-American Drug Abuse Control Commission (CICAD, by its Spanish-language acronym) through its Inter-American Observatory on Drugs (OID, by its Spanish-language acronym), the Early Warning System of the Americas (SATA, by its Spanish-language acronym) compiles and disseminates the information available from the member states on these and other emerging drugs to alert them of the potential health and public security risks posed. CICAD-OID provides technical assistance and training on the implementation of early warning systems (EWS) and on establishing national drug information networks (DINs) to facilitate quick, effective, and reliable data collection.

<sup>3.</sup> United Nations Office on Drugs and Crime (UNODC). World Drug Report 2022 (United Nations publication).

<sup>4.</sup> Stuyt E. The problem with the current high potency THC marijuana from the perspective of an Addiction Psychiatrist. Missouri Medicine 2018: 482: 115-6.

<sup>5.</sup> Fattore L, Fratta W. Beyond THC: the new generation of cannabinoid designer drugs. Front Behav Neurosci 2011; 5:60. doi: 10.3389/fnbeh.2011.00060

<sup>6.</sup> Fernández Ruíz J, Lorenzo Fernández J, Leza Cerro JC. "Cannabis (I). Farmacología." Págs. 303–327. En: Lorenzo P, Ladero JM, Leza JC, Lizasoain I. Drogodependencias. 3ra Edición 2009. Médica Panamericana, Madrid.

<sup>7.</sup> Synthetic cannabinoids are also referred to as synthetic cannabinoid receptor agonists (SCRAs) and are internationally recognized as a new psychoactive substance (NPS). Source: https://www.unodc.org/documents/scientific/Synthetic\_Cannabinoids\_Sp.pdf

# 2. Cannabis with a High Concentration of Tetrahydrocannabinol (THC)

# **2.1.**Preparations, forms of presentation, and modes of use

In 2020, there were an estimated 209 million cannabis users worldwide, equivalent to 4% of the population between 15 and 64 years of age. Trends indicate an increase of 23% in the number of cannabis users in 2010–2020. According to the data provided from all regions, the prevalence of cannabis use in the past year among adolescents (15-16 years) is higher than in the entire population of working age (15-64 years). There is a wide spectrum of cannabis use in the Americas. In the general population, the proportion of people who used cannabis in the last year ranges from 0.5% to almost 16%. The range is even wider among secondary school students, from (0.9% to 32.8%). In addition to its high prevalence use, cannabis and its derivatives are among the most seized substances worldwide (table 1).

Table 1: Global cannabis seizures in 2020.

Source: UNODC, World Drug Report 2022

<u>Cannabis and derivatives</u>	Tons seized in 2020
Plants	15,173
Herbal (derived from the plant)	4,707
Resin	2,190
Oil	7

<sup>8.</sup> United Nations Office on Drugs and Crime (UNODC). World Drug Report 2022 (United Nations publication).

<sup>9.</sup> Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). Report on Drug Use in the Americas 2019. Washington, D.C., 2019.

OAS member states' data indicate that trends in cannabis seizures by sub-region appear to be changing. Historically, North America has reported larger total seizures of cannabis, driven mainly by seizures in the United States; however, between 2016 and 2020, cannabis seizures fell in this sub-region. In contrast, seizures increased notably in South America and slightly in Central America and the Caribbean. Marijuana, cocaine, and synthetic drugs head the online sales list of illicit substances, which is a thriving business in the region and expected to continue to grow.

For more than a decade in Latin America and the Caribbean, the use of smokeable marijuana has most frequently been associated with forms of cigarette use, whose concentration of psychoactive components (different subtypes of THC, ranged between 2% and 5% (low concentrations). Above 10% is considered a high concentration of THC.<sup>12</sup>

A variety of sources have reported cannabis or marijuana preparations with high concentrations of THC (greater than 15%), for example, national drug observatories have reported seizures to national authorities as well as to CICAD. The data is sourced from their DINs and early warning systems (EWSs) in member states, cases in scientific literature, and, information disseminated by the users themselves.<sup>13</sup>

Some South American countries, including Chile and Colombia, have seen reports of use and a significant increase in seizures of a type of cannabis called "creepy," "cripy," or "kreepy" since 2013. This strain is genetically modified marijuana with a high concentration of cannabinoids with psychoactive effects. "Qualitative data from Chile and Peru mentioned that "creepy" was appearing in domestic markets and, in some cases, displacing the longstanding domination of Paraguayan-sourced cannabis. Guyana also highlighted the appearance of a strain of cannabis from Venezuela, known locally as "poppy" or "creppy," that was becoming very popular in the local market. 15

<sup>10.</sup> Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). Report on Drug Supply in the Americas 2022. Washington, D.C., 2022.

<sup>11.</sup> United Nations Office on Drugs and Crime (UNODC). In Focus: Cannabis legalization - World Drug Report 2020. (United Nations publication).

<sup>12.</sup> Negrin A, Albano L, Laborde A, Pronczuk J. Cannabis sativa "Marihuana." P. 53-59. In: Laborde A, Pronczuk J, Fernandez S. Plantas silvestres y de cultivo. *Manejo y prevención. Intoxicaciones accidentales. Consumo inapropiado.* Toxicology Department. Universidad de la República, Uruguay, 2007.

<sup>13.</sup> National Service for the Prevention and Rehabilitation of Drug and Alcohol Consumption (SENDA). National Drug Observatory. "Informe de resultados: Estudio análisis químico del cannabis incautado en Chile." Ministry for Interior Affairs and Public Security, Government of Chile, Santiago, Chile. October 2021.

<sup>14.</sup> Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). Information Bulletin of the Early Warning System of the Americas 2022. Washington, D.C., December 2022.

<sup>15.</sup> Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). Report on Drug Supply in the Americas 2022. Washington, D.C., 2022.

The Chilean Government Prosecutor's Office, through its Drug Trafficking Observatory, revealed a 700% increase in 'creepy' marijuana seizures in 2017-2020. Data are shown in table 2.

## <u>Table 2:</u> "Creepy" marijuana and total cannabis seized in Chile between 2017 and 2020.

Source: Drug Trafficking Observatory, Office of the Public Prosecutor of the Government of Chile (2020 Report). NA: Data not available.

<u>Year</u>	Amount of "creepy" marijuana seized (in kilograms)	Amount of cannabis seized [in kilograms]
2017	700	31,291
2018	4,400	38,440
2019	ND	15,267
2020	5,500	ND

This new form of cannabis is trafficked by sea on a large scale from Colombia, following the Colombia-Ecuador-Peru-Chile route. This also led to a clear reduction in seizures of pressed cannabis of Paraguayan origin, as well as a downturn in marijuana trafficking from that country.<sup>17</sup>

In 2021, the Chilean National Drug Observatory published a qualitative and quantitative analysis of 490 seized cannabis samples. The average THC concentration was 17%, reaching 80% in 14 samples. These high concentrations can be explained by genetic manipulation of the plant and changes in pressing methods. 19

In 2019, the presence of "creepy" marijuana and presentations in wax or oil for vaping was reported in Colombia. "Creepy" is a pressed form of cannabis, mainly smokeable, while "wax" is consumed through vaporizers. In both substances, the THC concentrations in previous Colombian studies (2017) ranged from 18-19% to 42%.<sup>20</sup>

<sup>16.</sup> Chilean Public Prosecutor. Specialized Unit for Illicit Traffic in Narcotic Drugs and Psychotropic Substances. Drug Trafficking Observatory: Report 2020. May 2020.

<sup>17.</sup> Chilean Public Prosecutor. Specialized Unit for Illicit Traffic in Narcotic Drugs and Psychotropic Substances. Drug Trafficking Observatory: Report 2022. December 2022.

18. National Service for the Prevention and Rehabilitation of Drug and Alcohol Consumption (SENDA). National Drug Observatory. "Informe de resultados: Estudio análisis químico del cannabis incautado en Chile." Ministry for Interior Affairs and Public Security, Government of Chile, Santiago, Chile. October 2021.

<sup>19.</sup> Negrin A, Albano L, Laborde A, Pronczuk J. Cannabis sativa "Marihuana." Pgs. 53-59. In: Laborde A, Pronczuk J, Fernandez S. Plantas silvestres y de cultivo. Manejo y prevención. Intoxicaciones accidentales.

<sup>20.</sup> Ministry of Justice and Law. Colombian Drug Observatory. "Alerta informativa sobre efectos en salud de algunas variedades de cannabis." December 2019.

THC concentrations range from 40% to 80% in cannabis wax extracted from the flower of the plant. Furthermore, THC concentrations of up to 99% are reported to have been found in some preparations.<sup>21</sup>
This type of cannabis is generally used through inhalation following evaporation through exposure of the substance to heat. It can be smokeable or vaporized in devices that contain solvents or other additives to achieve this effect.<sup>22</sup>

Initially used experimentally and by chronic users of smokeable cannabis, over the last decade, cannabis derivatives have become a form of use that raises concern from the toxicological point of view. The use of a variety of edibles (brownies, cookies, cakes and sweets, candies and beverages), containing variable amounts of psychoactive cannabinoids, has become increasingly widespread in countries like the United States, particularly in states that have modified laws regulating cannabis.<sup>23,24</sup>

There have been a number of clinical case reports and reviews of acute intoxications from ingested cannabis (edible cannabis products) published in scientific literature<sup>25,26</sup> that occurred in the context of recreational use, and of unintentional use by children.<sup>27,28,29,30,31</sup> In the context of recreational use, ingested cannabis involves exposure to high doses of THC; however, the psychoactive effects are delayed compared to smokeable cannabis, so the user continues eating the cannabis product(s), frequently experiencing digestive, neuropsychiatric, and cardiovascular symptoms, and causing acute cannabis intoxication. Ingested cannabis also produces longer lasting effects compared to smokeable cannabis.<sup>32</sup>

<sup>21.</sup> Oxford Treatment Center. The Potential Dangers of Highly- Concentrated Marijuana Wax. May 2022.

<sup>22.</sup> Cannabis Concentration and Health Risks. A report for the Washington State. Prevention Research Subcommittee (PRSC). November 2020.

<sup>23.</sup> Wang GS. Pediatric Concerns Due to Expanded Cannabis Use: Unintended Consequences of Legalization. J Med Toxicol. 2017; 13(1):99-105.

<sup>24.</sup> Vo KT, Horng H, Li K, Ho RY, Wu AHB, Lynch KL et al. Cannabis Intoxication Case Series: The Dangers of Edibles Containing Tetrahydrocannabinol. Ann Emerg Med. 2018;71:306-31.

<sup>25.</sup> Cao D, Srisuma S, Bronstein AC, Hoyte CO. "Characterization of edible marijuana product exposures reported to United States poison centers." Clinical Toxicology, (Philadelphia) 2016; 54:840.

**<sup>26.</sup>** B. Lewis B, Judge B, Riley B, Fleeger T, Ambrose, Jones JS. Acute Toxicity Associated with Cannabis Edibles Following Decriminalization of Marijuana in Michigan. Annals of Emergency Medicine 2020; 76: S30. https://doi.org/10.1016/j.annemergmed.2020.09.085

<sup>27.</sup> Claudet I, Mouvier S, Labadie M, Manin C, Michard-Lenoir AP, Didier Eyer D et al. Unintentional Cannabis Intoxication in Toddlers. Pediatrics. 2017; 140(3):e20170017.

<sup>28.</sup> Claudet I, Le Breton M, Bréhin C, Franchitto N. A 10-year review of cannabis exposure in children under 3-years of age: do we need a more global approach? Eur J Pediatr 2017; 176[4]:553-556.

<sup>29.</sup> Lovecchio F, Heise CH. Accidental pediatric ingestions of medical marijuana: a 4-year poison center experience. Am J Emerg Med 2015;33(6):844-5.

<sup>30.</sup> Richards JR, Smith NE, Moulin AK. Unintentional Cannabis Ingestion in Children: A Systematic Review. J Pediatr 2017;190:142-52.

<sup>31.</sup> Noroya N, Urgoiti M, del Cioppo F, Juanena C, Pascale A, Negrin A, et al. "Exposición no intencional a cannabis en niños en el marco de la Regulación del Mercado en Uruguay. Reporte de casos asistidos en el Departamento de Emergencia del Hospital Pereira Rossell entre marzo y junio de 2017." Archivos de Pediatría del Uruguay 2018; 89(5): 329-336.

32. Cao D, and others. Op. cit

## 2.2.

# Health risks from the use of cannabis concentrates

There is an increased risk of acute intoxication when using cannabis with high concentrations of THC. Likewise, the use of "creepy" marijuana and other cannabis concentrates increase the risk of associated chronic complications.<sup>33</sup>

#### **2.2.1.**

## Acute complications related to the use of cannabis concentrates

The use of cannabis preparations, such as "creepy" marijuana or concentrates in the form of waxes or oils pose a greater risk to the health of users.<sup>34</sup>

Acute complications are mainly neuropsychiatric in nature (dysphoria, anxiety, depersonalization, acute psychotic symptoms). These acute events are dependent on dose, frequency of use, and THC concentration.<sup>35</sup> The effects also depend on individual factors (e.g., psychiatric comorbidities such as anxiety, depression, and psychosis) and environmental factors (e.g., environment and social context in which the substance is used).<sup>36</sup>

Cannabis use affects the cognitive and motor skills used for driving and operating machinery, doubling the risk of traffic accidents<sup>37</sup> and increasing the risk of an occupational accident. The risk to chronic cannabis users persists for longer, as demonstrated by the presence of psychomotor effects and THC levels in blood and urine up to three to four weeks after the last use. The higher the concentration of THC, the higher the concentration in the body and the slower the elimination rate.<sup>38</sup>

<sup>33.</sup> United States, Centers for Disease Control and Prevention. Increases in Availability of Cannabis Products Containing Delta-8 THC and Reported Cases of Adverse Events. September 2021.

<sup>34.</sup> National Institute on Drug Abuse (NIDA). Cannabis (Marijuana) Concentrates DrugFacts. June 2020.

<sup>35.</sup> Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. N Engl J Med 2014;370[23]:2219-27.

**<sup>36.</sup>** Bidwell CL, Ellingson JM, Karoly HC, York Williams SL, Hitchcock LN, Tracy BL et al. Association of Naturalistic Administration of Cannabis Flower and Concentrates with Intoxication and Impairment. AMA Psychiatry. 2020;77(8):787-796.

<sup>37.</sup> Brands B, Mann RE, Wickens CM, Sproule B, Stoduto G, Sayer GS et al. Acute and residual effects of smoked cannabis: Impact on driving speed and lateral control, heart rate, and self-reported drug effects. Drug Alcohol Depend. 2019; 205:107641. doi: 10.1016/j.drugalcdep.2019.107641.

<sup>38.</sup> Huestis MA. Deterring driving under the influence of cannabis. Addiction 2015; 110: 1697–1698.

Research shows that in some countries, where the cannabis market has been legalized and/or regulated, there has been an increase in acute, unintentional, or involuntary intoxication by cannabis and its derivatives in children under the age of six. Such intoxication is most frequent via ingestion of plant parts, of food (edibles or gummies with high THC concentrations), or of tinctures made from cannabis.<sup>39</sup> Other potential sources of exposure include secondhand smokeable inhalation and breastfeeding.<sup>40</sup> A higher concentration of cannabinoids such as THC can produce greater acute toxicity in children who are exposed to it.

#### 2.2.2.

# Chronic complications related to the use of cannabis concentrates

The chronic effects that are harmful to health are linked to the age at which use begins, as well as frequency and dose. There is evidence that cannabis use can have a negative impact on neurodevelopment. Adolescence is a critical period during which cannabis use can affect brain maturation. Greater impact is related to how early use started, along with frequency and dose. When it comes to dose, a higher concentration of THC has a greater impact on learning, memory, and attention span. Some cognitive impacts can persist in the long term.<sup>41</sup> Chronic cannabis use has been associated with impacts on verbal expression, working memory, learning, and attention span.

Regular cannabis use is associated with an increased risk of developing symptoms of psychosis and schizophrenia in genetically-predisposed individuals, or accelerating the onset of the disease. Other factors that can increase risk are how early use begins, higher THC concentrations in preparations, 42 and, individual and environmental factors. Regular cannabis use can aggravate the course of schizophrenia, leading to a higher relapse rate. 43

<sup>39.</sup> Wang GS, Le Lait MC, Deakyne SJ, Bronstein AC, Bajaj L, Roosevelt G. Unintentional Pediatric Exposures to Marijuana in Colorado, 2009-2015. JAMA Pediatr.2016;170(9):e160971.doi:10.1001/jamapediatrics.2016.0971.

**<sup>40.</sup>** Noroya N, Urgoiti M, del Cioppo F, Juanena C, Pascale A, Negrin A, et al. Exposición no intencional a cannabis en niños en el marco de la Regulación del Mercado en Uruguay. Reporte de casos asistidos en el Departamento de Emergencia del Hospital Pereira Rossell entre marzo y junio de 2017. Arch Pediatr Urug 2018; 89(5): 329-336. **41.** Jacobus J, Tapert SF. Effects of cannabis on the adolescent brain. Curr Pharm Des 2014; 20(13):2186-93.

**<sup>42.</sup>** Di Forti M, Quattrone D, Freeman TP, Tripoli G, Gayer-Anderson C, Quigley H. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. Lancet Psychiatry 2019. http://dx.doi.org/10.1016/ S2215-0366(19)30048-3.

<sup>43.</sup> Cardeillac V. "Cannabis y esquizofrenia. Revisión de la literatura de los últimos quince años." Revista de Psiquiatría del Uruguay, 2016; 80[1]:33-44.

The use of cannabis and its derivatives during pregnancy has been associated with impacts on fetal growth and neuro-behavioral disorders during the prenatal period, early childhood, and adolescence. Some mechanisms involved in developing these complications are related to dose and to concentration of psychoactive cannabinoids during the prenatal stage.<sup>44</sup>

Regular and frequent use of smokeable cannabis is related to a higher prevalence of respiratory disease in the form of inflammation of the bronchial mucosa, chronic bronchitis, and greater susceptibility to respiratory infections. For vaping, solvents are used, and the devices contain additives like propylene glycol, polyethylene glycol, glycerin, and terpenes. These substances—the cannabis as well as the solvents and additives in the devices—are harmful to the respiratory system, leading to lung disease. The presence of vitamin E acetate has been reported as the cause of numerous cases of serious pulmonary complications, including death.<sup>45</sup>

<sup>44.</sup> Pascale A, Laborde A. "Efectos del consumo de cannabis durante el embarazo y la lactancia." Archivos de Pediatría del Uruguay 2019; 90 (3):161-168.
45. United States, Centers for Disease Control and Prevention. Outbreak of lung injury associated with the use of e-cigarette, or vaping, products. February 2020.

# 3. Synthetic cannabinoidss

3.1. General concept

As their name implies, synthetic cannabinoids are not natural in origin, meaning they are not derived from plants from the Cannabaceae family, which includes marijuana. There is a growing and global illegal market for producing, trafficking, and using these substances for recreational purposes.<sup>46</sup>

Synthetic cannabinoids are known by different names, including "Spice," K2," and variants thereof: "Spice Silver," "Spice Gold," "Spice Diamond," "Yucatán Fire," and "Smoke." Since the 1990s, synthetic cannabinoids have been available over the Internet and in "headshops" that sell cannabis-related products (pipes and accessories for smoking cannabis, T-shirts with cannabis designs) and tobacco products. Numerous reports indicate that this substance is sold as plant-based cannabis.<sup>47</sup>

Synthetic cannabinoids take the form of solid powder mixes with herbs or incense. They also take liquid forms. Some presentations are for use in vape pens. A single product may contain one to two or more different types of synthetic cannabinoid. They are used via smoking (more frequent), inhalation (through incense), and ingestion (through infusions). They can be use on their own, but are frequently associated with other drugs.<sup>48</sup>

<sup>46.</sup> Tai S, Fantegrossi WE. Pharmacological and Toxicological Effects of Synthetic Cannabinoids and Their Metabolites. Curr Top Behav Neurosci. 2017; 32:249-262. doi:10.1007/7854 2016 60

<sup>47.</sup> Nelson M, Bryant S, Aks S. Emerging Drugs of Abuse. Emerg Med Clin N Am 2014; 32: 1-28.

<sup>48.</sup> Junta Nacional de Drogas de Uruguay. Uruguayan Drug Observatory (OUD). SAT Drogas. Special Report: Synthetic Cannabinoids. Abril 2017.

Synthetic cannabinoids contain two to 100 times more active THC than natural cannabis. The high affinity of CB1 and CB2 receptors<sup>49</sup> and the high potency of their metabolites would explain the potential severity of acute intoxication and the greater risk of complications, compared to the use of cannabis of natural origin.<sup>50</sup> Because synthetic cannabinoid effects are stronger, the risk of acute intoxication is greater.<sup>51</sup>

Table 3 illustrates the location of the cannabinoid receptors. CB1 receptors modulate functions related to memory, emotional responses, cognition, motivation, and motor coordination. CB2 receptors regulate the immune system and modulate functions in the digestive tract, liver, heart, muscles, skin, and reproductive organs.

<u>Table 3:</u> Cannabinoid receptors and their location.

	CB1 receptors	CB2 receptors
<u>Location</u>	Central nervous system (hippocampus, gray basal nuclei, cerebellum, cerebral cortex, and spinal cord)	Immune system cells Retina
	Peripheral nerve endings	Central nervous system (some neurons, reactive astrocytes, and activated microglia)
	Testes, vascular endothelium,	
	adipose tissue, muscle, pancreatic	
	islets, retina	

**<sup>49.</sup>** CB1 y CB2 son los dos receptores endocannabinoides primarios. Los receptores CB1 se encuentran principalmente en el sistema nervioso central. Los receptores CB2 se encuentran principalmente en el sistema nervioso periférico, especialmente en las células inmunitarias. Estos receptores se activan en el cuerpo cuando este produce endocannabinoides, que son neurotransmisores que envían mensajes por todo el organismo, similares a la serotonina o la dopamina.

**<sup>50.</sup>** United Nations Office on Drugs and Crime (UNODC). Global SMART Update, Synthetic cannabinoids: Key facts about the largest and most dynamic group of NPS. Volume 13. March, 2015.

<sup>51.</sup> Pan American Health Organization. Efectos sociales y para la salud del consumo de cannabis sin fines médicos. Washington, D.C. 2018

# **3.2.**Situation in Latin America and the Caribbean

As of 2019, 36 synthetic cannabinoids had been identified in Latin America and the Caribbean, the vast majority before 2016. Starting that year, those identified as first generation (called JWH) were being replaced by new cannabinoids, such as 5F-MDMB-PINACA, detected in seizures in Argentina and Brazil, among other countries.<sup>52</sup>

Information on the extent of use of these substances in the region is limited. Between 0.5% of university students in Peru and 4.2% in Colombia have used synthetic cannabinoids at some point in their lives. <sup>53,54</sup> In Chile, the first seizures of first-generation synthetic cannabinoids date back to 2008 brought in bags labeled as aromatic products. In July 2017, the discovery of the synthetic cannabinoid XLR-11 was confirmed. <sup>55</sup> Chile saw use rates in the general population increase from 0.5% (2014) to 1.1% (2018), reaching 3.9% in young people between the ages of 19 and 25. <sup>56</sup> However, data from the 2020 general population survey in Chile show a drop in the annual consumption rate to 0.6%, observed in both men and women and in all age groups, with a decrease as well among young people between the ages of 19 and 25, to a rate of 1.8%. <sup>57</sup>

Other countries in Latin America—including Argentina, Brazil, Costa Rica, Mexico, Panama, and Uruguay—have detected the presence of synthetic cannabinoids, but do not have data on use rates. First-generation synthetic cannabinoids (JWH-248, JWH-208) were detected in 7% of the 28 urine samples taken from 5,000 electronic music party attendees in Uruguay in 2019, while second-generation synthetic cannabinoids—like UR-144/XLR -11—were detected in 11%. A prior similar study from 2016 detected JWH-250.

cocaína en muestras de orina obtenidas en una fiesta musical en el área metropolitana." May 2020.

<sup>52.</sup> United Nations Office on Drugs and Crime (UNODC). Synthetic Drugs and New Psychoactive Substances in Latin America and the Caribbean - 2021. September 2021.

**<sup>53.</sup>** United Nations Office on Drugs and Crime (UNODC). III Andean epidemiological study on drug use in the university population, Regional Report 2016. June 2017.

<sup>54.</sup> Inter-American Drug Abuse Control Commission (CICAD), Organization of American States (OAS). Report on Drug Use in the Americas 2019. Washington, D.C., 2019. 55. Government of Chile, Ministry for Interior Affairs and Public Security. National Roundtable on New Psychoactive Substances. Synthetic cannabinoids. Report num. 3. December 2017.

**<sup>56.</sup>** National Service for the Prevention and Rehabilitation of Drug and Alcohol Consumption (SENDA). National Drug Observatory. Thirteenth National Study of Drugs in the General Population of Chile, 2018. Santiago de Chile, 2019.

**<sup>57.</sup>** National Service for the Prevention and Rehabilitation of Drug and Alcohol Consumption (SENDA). National Drug Observatory. Fourteenth National Study of Drugs in the General Population of Chile, 2020. Santiago, Chile, 2021.

<sup>58.</sup> United Nations Office on Drugs and Crime (UNODC). Synthetic Drugs and New Psychoactive Substances in Latin America and the Caribbean - 2021. September 2021.
59. Environment, Drugs, and Doping Unit, Pando Technological Institute, School of Chemistry – UdelaR. Final report: "Screening de nuevas sustancias psicoactivas, THC y

**<sup>60.</sup>** Junta Nacional de Drogas de Uruguay. Uruguayan Drug Observatory (OUD), Early Warning System. Alert 20-002. Synthetic Cannabinoids JWH-208 and JWH-248 are identified using gas chromatography coupled with mass spectrometry (GC/MS). June 2020.

In other countries outside the region, the use of synthetic cannabinoids is observed in at-risk populations, including homeless persons or persons deprived of liberty. In this latter population, using synthetic cannabinoids gives an advantage because it is difficult to detect using rapid drug tests. 61,62,63 A recent paper describes the seizure of synthetic cannabinoids in prisons in São Paulo, Brazil. 64 The impact of the use of this type of substance—which is highly toxic and can lead to dependency—poses a public health problem in these social contexts.

# **3.3.** Health effects

The most frequent complications in acute intoxication and health effects of synthetic cannabinoid use are shown in Figure 1.

<u>Figure 1:</u> Acute complications and health effects of synthetic cannabinoid use (adapted from Nelson et al., 2014).

Nausea and vomiting.

Neuropsychiatric effects: agitation, confusion, violent behavior, psychosis, seizures.

Cardiovascular effects: tachycardia, arterial hypertension, myocardial infarction, cardiac arrhythmias.

Hypoglycemia, hypokalemia.

Rhabdomyolysis, acute kidney damage.

**<sup>61.</sup>** Ellsworth JT. Spice, vulnerability, and victimization: Synthetic cannabinoids and interpersonal crime victimization among homeless adults. Subst Abus. 2019; 7:1-7. doi: 10.1080/08897077.2019.1686725.

**<sup>62.</sup>** European Monitoring Centre for Drugs and Drug Addiction (2018). New psychoactive substances in prison, EMCDDA Rapid Communication, Publications Office of the European Union, Luxembourg.

<sup>63.</sup> United Nations Office on Drugs and Crime (UNODC). World Drug Report, 2022. United Nations, June 2022.

**<sup>64.</sup>** Rodríguez TB, Souza MP, de Melo Barbosa, L, de Carvalho Ponce J, Neves Júnior LF, Mauricio Yonamine M et al. Synthetic cannabinoid receptor agonists profile in infused papers seized in Brazilian prisons. Forensic Toxicol 2022; 40: 119–124. https://doi.org/10.1007/s11419-021-00586-7.

International reports indicate that using some types of synthetic cannabinoids can lead to dependence and withdrawal syndrome, characterized by agitation, increased heart rate, irritability, anxiety and mood swings.<sup>65,66</sup>

Conventional immunoassay or screening techniques do not detect synthetic cannabinoid metabolites in urine, making diagnostic confirmation difficult for emergency care services in Latin America and the Caribbean, which do not have more accurate tests available.<sup>67</sup>

**<sup>65.</sup>** Nelson M, Bryant S, Aks S. Emerging Drugs of Abuse. Emerg Med Clin N Am 2014; 32: 1–28.

**<sup>66.</sup>** Tait RJ, Caldicott D, Mountain D, Hill SL, Lenton S. A systematic review of adverse events arising from the use of synthetic cannabinoids and their associated treatment. Clin Toxicol (Phila). 2016;54(1):1-13. doi: 10.3109/15563650.2015.1110590.

<sup>67.</sup> Junta Nacional de Drogas de Uruguay. Uruguayan Drug Observatory (OUD). SAT Drogas. Special Report: Synthetic Cannabinoids. Abril 2017.



INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION (CICAD)

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