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Something New about Something Old: A 10-Year Follow-Up on Classical and New Psychoactive Tryptamines and Results of Analysis

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ABSTRACT

New psychoactive tryptamines may be a public health risk since they intend to mimic the hallucinogenic effects of regulated psychoactive drugs. Few studies describe uses and clinical effects of unregulated new psychoactive tryptamines. This study aims (1) to explore the presence of tryptamines classified as NPS among the substances delivered for analysis to a harm-reduction organization; (2) to describe the substances found in the samples after analysis; and (3) to compare analytical results of regulated vs. non-regulated tryptamines. Samples delivered and analyzed by gas chromatography-mass spectrometry from 2006 to 2015 were included. A descriptive study of results was conducted. From 25,296 samples that were delivered, 436 were tryptamines; from these 232 (53.21%) were non-regulated. The most delivered non-regulated tryptamine was 4-AcO-DMT. A search of the PubMed database in July 2016 revealed that no studies in humans have ever been carried out with 4-AcO-DMT. Unregulated tryptamines likely contained one unadulterated substance ($p \leq 0.001$). The number of samples submitted which contained tryptamines increased during the course of the study, with significant differences in client expectations vs. analysis results between the controlled and uncontrolled groups. There is a need for further research in order to prevent the potential health risks associated with their use.

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Hallucinogens; new psychoactive substances; substituted tryptamines; tryptamines

Tryptamine is a monoamine alkaloid that can be synthesized by decarboxylation of the aminoacid tryptophan and is naturally found in plants, fungi, and animals. Psychedelic tryptamines are substituted tryptamines (organic compounds derived from tryptamine) that act as hallucinogens, primarily as agonists of the serotonergic receptor 5-HT_{2A}. They require low doses to produce psychotropic phenomena such as changes in perception, mood, and thought (Araújo et al. 2015; Tittarelli et al. 2015). Substituted tryptamines are one of the seven groups into which new psychoactive substances (NPS) are divided (EMCDDA 2015; UNODC 2013).

The United Nations Office on Drugs and Crime (UNODC) defines NPS as: "substances of abuse, either in a pure form or a preparation, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat" (UNODC 2013). During 2014, the EU Early Warning System reported a total of 101 new substances, raising the number of

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substances currently monitored to more than 450 and maintaining the unprecedented increase in the number, type, and availability of NPS (EMCDDA 2015).

The effects of unregulated tryptamines are expected to be similar to those of the controlled tryptamines such as psilocybin or DMT (Farré, Galindo, and Torrens 2015), and are offered as a non-illegal alternative (Tittarelli et al. 2015). The UNODC lists 25 different molecules as unregulated tryptamines (UNODC 2013). However, information available mainly from Internet forums points towards significant differences among the molecules: alpha methylation of 5-MeO-a-MT and α-MT confers a stimulant activity compared to the unmethylated analogues (Hill and Thomas 2015; Lessin, Long, and Parkes 1965), and substitution in position 5 of the indole ring is considered to increase the potency compared to the parent drug (Tittarelli et al. 2015).

Psilocin (4-HO-DMT), psilocybin (4-PO-DMT), N,N-diethyltryptamine (DET or T-9), N,N-dimethyltryptamine (DMT), and α-ethyltryptamine (etryptamine or α-ET) are the only tryptamines internationally controlled under the 1971 International Drug Control Convention, where they are listed as schedule I compounds (UNODC 2013). These are the only tryptamines that are regulated in Spain (BOE 2015). DMT is present in natural preparations like ayahuasca or *Psychotria viridis*, and psilocybin and psilocin are the main components of hallucinogenic psilocybes mushrooms (Farré, Galindo, and Torrens 2015).

The EDADES survey conducted in Spain (Ministerio de Sanidad Asuntos Sociales e Igualdad 2015) does not explore the epidemiology of the different tryptamines which are included in the more general category of hallucinogens. International surveys like Maxwell's (2014) do not explore the prevalence of different tryptamines and do not differentiate between regulated and unregulated tryptamines.

Tryptamines are not routinely detected in screening panels used in emergency departments and are not included in routine analysis, which can lead to misinterpretation of symptoms presented by users. Given their potential threat and risks, it is important to organize the information to which professionals have access. For the time being, the Internet is the main source of information for clinicians and researchers interested in tryptamines (Tittarelli et al. 2015).

Consequently, current resources do not provide validated data about the actual use and distribution of new psychoactive tryptamines, either locally or internationally. To our knowledge, there have been no previous studies which discuss individual tryptamines and compare the substance expected by service users to the identity of the substance. Therefore, the aim of this study is threefold: firstly, to explore the presence of new psychoactive tryptamines among the samples delivered to the harm-reduction service "Energy Control" to provide a clearer perspective of the prevalence of tryptamines. Secondly, to evaluate the composition of these samples and the agreement between the substance expected and the substance found. And finally, to compare these results with the prevalence of internationally controlled tryptamines.

Materials and methods

Samples

All samples delivered to Energy Control from 2006 to 2015 containing or expected to contain one of the aforementioned tryptamine compounds were studied. Energy Control (http://energycontrol.org) is a harm-reduction service that provides information and counseling to people intending to use psychoactive substances. It offers a free and anonymous drug-checking service to Spanish nationals, and charges a fee when samples come from international deliverers. Spanish nationals can bring their samples to one of the four Energy Control headquarters (in Madrid, Catalonia, the Balearic Islands, or Andalucía), send them by mail, or submit them during outreach work in nightlife settings, such as at music festivals, clubs, and underground raves where Energy Control will often have a presence.

Method of analysis

To analyze the substances delivered, gas chromatography/coupled mass spectrometry (GC/MS) was performed at the IMIM (Institut de Recerca Hospital del Mar—Parc de Salut Mar, Barcelona). From 2006 to 2012, GC/MS analysis was done in an Agilent 5890 series II gas chromatograph coupled to a 5971A quadruple mass spectrometer detector (Agilent). The gas chromatograph was fitted with a 6890 auto sampler injector. Samples were injected in splitless mode into a 12 m × 0.2 mm i.d., 0.33 μm film thickness, 5% phenylmethylsilicone column (ULTRA-2, Agilent Technologies). The oven temperature was initially maintained at 90°C for 2 min and programmed to reach 300°C at 20°C per min. It was finally maintained at 300°C for 4 min, resulting in a total run time of 14.5 min. Insert liners packed with silanized glass wool were used. The injector and the interface were operated at 280°C. Helium was used as carrier gas at a flow rate of 0.48 mL/min. The mass spectrometer was operated in electron impact ionization mode at 70 eV. To confirm the mass spectra, the 2007 Wiley-VCH Verlag GmbH & Co. KgaA., Weinheim, and the Searchable Mass Spectral Library NIST/EPA/NIH Mass Spectral Library, Data Version: NIST 08 Version 2.3

(http://www.swgdrug.org/ms.htm) were used (Caudevilla-Gálligo et al. 2012; Giné, Espinosa, and Vilamala 2014). From 2012 to 2015, an Agilent 7890B gas chromatograph coupled to a 5977A quadrupole mass spectrometer detector (Agilent; Santa Clara, CA, USA) was used. The gas chromatograph was fitted with a G4513A auto sampler injector. Samples were injected in split mode (1:10) into a 30 m 0.25 mm i.d., 0.25 µm film thickness, 5% phenyl-methylsilicone column (HP-5MS, Agilent Technologies). The oven temperature was initially maintained at 90°C for 2 min and programmed to reach 320°C at 20°C per min. It was finally maintained at 320°C for 9.5 min, for a total run time of 21.5 min. Insert liners packed with silanized glass-wool were used. The injector and the interface were operated at 280°C. Helium was used as carrier gas at a flow rate of 1 mL/min. The mass spectrometer was operated in electron impact ionization mode at 70 eV. In order to confirm the mass spectra, four libraries were used: the Searchable Mass Spectral Library NIST/EPA/NIH Mass Spectral Library, Data Version: NIST 14; Searchable Mass Spectral Library Version 2.3 (http://www.swgdrug.org/ms.htm); Searchable Mass Spectral Library Cayman Spectral Library (CSL) (https://www.caymanchem.com/app/template/SpectralLibrary.vm); and a proprietary Mass Spectral Library developed by Energy Control.

A descriptive study of the samples was then conducted. Statistical analysis and bivariate analysis were performed using SPSS software (SPSS Inc., Chicago, IL).

Results

From a total of 25,296 samples delivered during the studied period, 436 (1.72%) were expected to be hallucinogenic tryptamines. From these, 232 (53.21%) were expected to be unregulated tryptamines and 204 (46.79%) regulated tryptamines. The mean age of subjects delivering unregulated tryptamines was 30 years old (±5.84 SD) with males making up 90.55% of the sample. For the group submitting uncontrolled samples, the mean age was 29.4 years old (±8.53 SD) and the percentage of males was 88.07%.

Samples delivered as unregulated tryptamines were expected to be one of 21 different compounds, from which 18 are listed by the UNODC as new psychoactive tryptamines. The three not previously listed were MiPT, 5-MeO-EIPT, and 4-AcO-DALT. One sample of each of these molecules was submitted (Table 1). No samples were delivered as 4-AcO-DPT, 4-AcO-DET, 4-HO-DPT, 5-HTP, 5-MeO-DPT, 5-MeO-MET, which are listed in the UNODC documentation. Apart from these, 5-HO-DMT was identified in three samples presented as animal or fungi derivatives and 5-MeO-DiPT was found in three samples delivered as an unspecified tryptamine.

Internationally controlled tryptamines were delivered in different preparations supposedly containing DMT, psilocin, or psilocybin (Table 2). No substances were expected to be DET or α-etryptamine; however, one sample delivered as DMT was found to contain DET. Apart from these, DMT, harmine, harmaline, THH, and carbolines were found in four samples delivered as "Changa."

4-Aco-DMT was the most commonly expected unregulated psychoactive tryptamine, representing 13.3% of all the tryptamines delivered. In the regulated tryptamine group, DMT was the most prevalent substance, representing 34.17% of all the tryptamines submitted.

After substance analysis, tryptamines were found in 14 samples which the submitter did not expect to contain tryptamines or substances structurally related to tryptamines. These substances were delivered as unknown substances (n = 4) containing a-MT (n = 1), 5-MeO-a-MT (n = 1), 5-MeO-DMT and 4-HO-DMT plus 4-AcO-DMT (n = 1), respectively; pills (n = 3) containing all 5-MeO-MiPT; legal highs (n = 2) containing both 5-MeO-DALT plus caffeine; 2-CB (n = 2) containing 5-MeO-MiPT and a-MT plus 5-MeO-a-MT, respectively; MDA (n = 1) containing 5-MeO-DiPT; cocaine (n = 1) containing cocaine plus 4-HO-DiPT plus 4-AcO-DiPT, and ADB-FUBINACA (n = 1) containing 5-MeO-DALT.

There was a progressive increase in the number of samples expected to be tryptamines over the duration of the study. However, the percentage of samples delivered per year between 2010 and 2015 did not show a statistically significant change. The low total number of samples submitted from 2006 to 2009 might give a skewed view of the first years (Figure 1).

Among the samples delivered as new psychoactive tryptamines, 150 (64.7%) contained the expected substance and 57 (24.6%) contained the expected substance plus another psychoactive tryptamine. In five samples (2.2%), other substances different from tryptamines were found, and in five samples (2.2%), no active substance was found.

Among the samples delivered as classical tryptamines, 128 (62.7%) contained the expected substance and 43 (21.1%) contained the expected substance plus another psychoactive tryptamine or natural contaminants. In seven samples (3.4%), other non-tryptamine substances were found, and in 22 samples (10.8%) no active substance was found.

Samples expected to be unregulated tryptamines were predominantly submitted from Spain (73.27% of the group; n = 170), with the remainder from EU countries (18.10% of the group; n = 42) and non-EU countries (5.6% of the group; n = 13). Among samples delivered as

Table 1. Substances submitted to EC as non-regulated tryptamines and the result of their analysis

Substances delivered (N = 232)		Substances found	
Molecules	N (%)	Molecules	N (%)*
4-Aco-DMT	58 (25)	4-AcO-DMT	15 (25.86)
		4-AcO-DMT + 4-HO-DMT	40 (68.97)
		Other psychoactive tryptamines	2 (3.45)
		Caffeine + Amphetamine	1 (1.72)
a-MT	38 (16.38)	a-MT	34 (89.48)
		a-MT + THH	2 (5.26)
		5-APB	1 (2.63)
		2C-B	1 (2.63)
5-Meo-DMT	31 (13.36)	5-Meo-DMT	22 (70.97)
		Other psychoactive tryptamines	6 (19.35)
		2C-I	1 (3.23)
		No active substance	2 (6.45)
4-HO-MET	19 (8.19)	4-HO-MET	17 (89.48)
		4-HO-DET	1 (5.26)
		No active substance	1 (5.26)
4-AcO-DiPT	16 (6.9)	4-AcO-DiPT	8 (50)
		4-AcO-DiPT + 4-HO-DiPT	7 (43.75)
		5-MeO-DiPT	1 (6.25)
5-MeO-DALT	12 (5.17)	5-MeO-DALT	12 (100)
5-Meo-MiPT	11 (4.74)	5-MeO-MiPT	10 (90.91)
		No active substance	1 (9.09)
5-MeO-DiPT	7 (3.01)	5-MeO-DiPT	4 (57.14)
		5-MeO-DiPT + 5-MeO-MiPT	1 (14.29)
		Other psychoactive tryptamines	2 (28.57)
4-HO-DiPT	6 (2.59)	4-HO-DiPT	6 (100)
5-MeO-AMT	6 (2.59)	5-MeO-AMT	4 (66.66)
		a-MT	1 (16.67)
		a-MT + DMT	1 (16.67)
DPT	6 (2.59)	DPT	6 (100)
4-HO-MiPT	5 (2.16)	4-HO-MiPT	5 (100)
4-HO-DET	4 (1.72)	4-HO-DET	4 (100)
DiPT	4 (1.72)	DiPT	2 (50)
		DiPT + 4-HO-DiPT	1 (25)
		DiPT + 5-MeO-DiPT	1 (25)
4-AcO-MET	2 (0.86)	4-HO-MET	1 (50)
		4-AcO-MET + 4-HO-MET	1 (50)
5-MeO-MALT	2 (0.86)	5-MeO-MALT	1 (50)
		5-MeO-MALT + 25C-NBOMe	1 (50)
4-AcO-MiPT	1 (0.43)	4-AcO-MiPT + 4-HO-MiPT	1 (100)
5-HO-DMT	1 (0.43)	No active substance	1 (100)
Other new psychoactive tryptamines	3 (1.29)	One unadulterated psychoactive substance	3 (100)

*Percentages on the fourth column are calculated over the samples of each individual substance as shown in the second column. The "other new psychoactive tryptamines" delivered were: 4-AcO-DALT, MiPT, and 5-MeO-EIPT.

regulated tryptamines, submissions from Spain were also more common (88.72% of the group; n = 181), with the remainder from EU countries (1.96% of the group; n = 4) and non-EU countries (7.35% of the group; n = 15), again represented to a lesser degree.

The agreement between expected substance and analyzed substance, as well the origin of the sample, showed a statistically significant difference for the controlled and uncontrolled groups (Table 3).

Discussion

This is the first study analyzing the presence of tryptamines within a 10-year perspective. Each tryptamine delivered was considered independently and the information was compared with the results of the analysis.

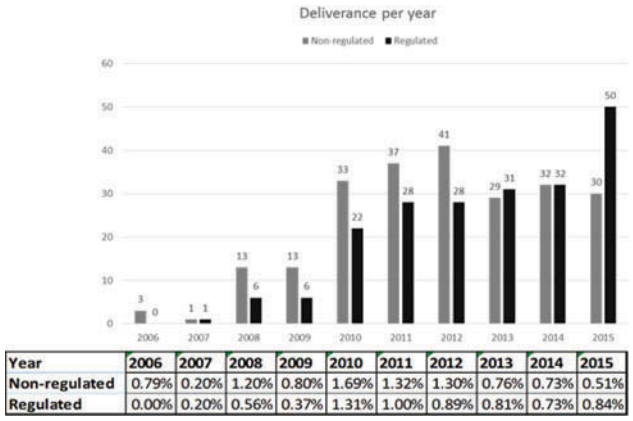
The results show a significant incidence of psychoactive tryptamines being delivered to Energy Control. Sociodemographic data from submitters did not completely agree with a previous study (Maxwell 2014) in the mean age of the tryptamine users, as the mean age obtained in this study was over 10 years older. However, the mean age of our study did agree with results for research chemicals users' mean age found in a previous Spanish study (González et al. 2013). The percentage of male users from the present study was closer to Maxwell's study. In all studies, age and gender were not different for submitters of unregulated and regulated tryptamines.

In the U.S., very few national surveys ask about independent tryptamines molecules as NPS (Palamar et al. 2015). The National Survey of Drug Use and Health asks specifically for three molecules: DMT, α-MT, and 5-MeO-DiPT. Tryptamines were the most prevalent group of NPS used according to Palamar's

Table 2. Substances submitted to EC as regulated tryptamines and the result of their analysis.

Substances delivered (N = 204)		Substances found	
Molecules	N (%)	Molecules	N (%)*
DMT	149 (73.04)	DMT	94 (63.09)
		DMT + beta-carbolines	31 (20.81)
		DMT + NMT + beta-carbolines	1 (0.67)
		DMT + NMT	10 (6.71)
		DMT + 3-methylquinoline	1 (0.67)
		5-MeO-DMT	1 (0.67)
		DET + lidocaine	1 (0.67)
		Beta-carbolines	3 (2.01)
		Cannabinoids	3 (2.01)
		Mephedrone	1 (0.67)
		Scopoletin	1 (0.67)
		No active substance	2 (1.35)
Mushrooms	26 (12.75)	4-HO-DMT	10 (38.46)
		Psilocybin	2 (7.69)
		No active substance	14 (53.85)
Ayahuasca	15 (7.35)	Beta-carbolines	9 (60)
		Beta-carbolines + DMT	1 (6.67)
		Nicotine	1 (6.67)
		No active substance	4 (26.67)
Psychotria viridis	9 (4.41)	DMT	9 (100)
Psilocybin	3 (1.47)	Psilocybin	1 (33.33)
		No active substance	2 (66.67)
4-HO-DMT	2 (0.98)	4-HO-DMT	1 (50)
		4-HO-DMT + 4-AcO-DMT	1 (50)

*Percentages on the fourth column are calculated over the samples of each individual substance as shown in the second column.



Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Non-regulated	0.79%	0.20%	1.20%	0.80%	1.69%	1.32%	1.30%	0.76%	0.73%	0.51%
Regulated	0.00%	0.20%	0.56%	0.37%	1.31%	1.00%	0.89%	0.81%	0.73%	0.84%

Figure 1. Submissions per year of non-regulated and regulated tryptamines; percentages are calculated over the whole number of samples submitted per year.

study (86.1% out of all NPS users and 1% out of the whole surveyed sample). However, it is not possible to know the use of each independent tryptamine. Another North American study identified different molecules of tryptamines, also reporting DMT as the most common tryptamine used (88% of lifetime use among their sample), followed by α-MT (31% of lifetime use). This ranking is consistent with the results of the present study (Sanders et al. 2008). Our results are also consistent with a study conducted in Australia on NPS use by ecstasy users (Bruno et al. 2012) DMT was the most prevalent tryptamine among the psychedelic group (13% of lifetime use). The other substituted tryptamine molecule considered by that study was 5-MeO-DMT (2% of lifetime use).

Most of the new psychoactive tryptamines included in the UNODC list (UNODC 2013) were present among the samples delivered to Energy Control. In addition, three unregulated psychoactive tryptamines were found among the substances delivered (which analyzed as expected by the submitters). These were MiPT, 5-MeO-EIPT, and 4-AcO-DALT. Further submission of these substances should also be monitored.

Table 3. Bivariate comparison.

		Non-regulated**	Regulated**	Total**	Significance
Result of the analysis	One single unadulterated substance	150 (64.7%)	128 (10.8%)	278 (63.8%)	$p \leq 0.001$
	Substance delivered plus another psychoactive tryptamine	57 (24.6%)	43 (21.1%)	100 (22.9%)	
	Other psychoactive tryptamines	15 (6.5%)	4 (2.0%)	19 (4.4%)	
	Other psychoactive substances	5 (2.2%)	7 (3.4%)	12 (2.8%)	
	No active substance	5 (2.2%)	22 (10.8%)	27 (6.2%)	
Origin of the sample	National	170 (75.56%)	181 (90.5%)	351 (82.59%)	$p \leq 0.001$
	EU	42 (18.67%)	4 (2.0%)	46 (10.82%)	
	Non-EU	13 (5.78%)	15 (7.5%)	28 (6.59%)	

**Percentages are calculated according to the total samples of the columns. Samples of unknown origin have not been taken into account for the bivariate comparison.

It would be interesting to conduct further studies on these three substances in order to check whether they meet the criteria to be included in the UNODC unregulated tryptamines' list.

The most prevalent new psychoactive tryptamine in this study was 4-AcO-DMT. According to a PubMed database search in 2016, there have been no human studies conducted on 4-AcO-DMT, despite its apparent prevalence.

The second most delivered substance was α-MT, a tryptamine initially developed as an antidepressant, but withdrawn because of its toxicity (Kamour et al. 2014; Tittarelli et al. 2015). Therefore, the possibility of self-medication should be considered when discussing its recreational use.

Both substances were the most prevalent tryptamines used as research chemicals in a previous Spanish study that analyzed the pattern of use of NPS (González et al. 2013). A significant number of submissions of these substances was received between 2010 and 2012, and high purity was common. Since α-MT was prohibited after being commercialized as an antidepressant due to its toxicity (Kamour et al. 2014), the possibility of self-medication should be considered when discussing its recreational use.

The third most delivered substance was 5-MeO-DMT, a substance with a higher reported history of recreational use and on which more scientific information is available (Sogawa et al. 2007).

Other substances about which more information is known based on case reports, such as 5-MeO-DiPT or 5-HO-DMT (Shen et al. 2010; Tanaka et al. 2006; Weil and Davis 1994; Wilson et al. 2005), are only scarcely prevalent in this study.

Unregulated tryptamines were slightly more likely to contain the substance as which they were presented. The percentage of samples containing only the expected compound was comparable to a previous study conducted on other NPS (Caudevilla-Gálligo et al. 2013).

Interestingly, very few substances expected to be tryptamines were found to contain substances from other classes. This suggests that the sources of psychoactive tryptamines are reliable at correctly labelling the substances sold. Unregulated tryptamines were more likely to contain only the expected substance. Samples containing no substance were also more frequent in the regulated group than in the non-regulated. Both facts suggest the higher reliability of new psychoactive tryptamine sources.

In samples where more than one substance was found, the minor constituent was often chemically very similar to the expected substance. Examples include 4-HO-DMT, found in samples also containing 4-AcO-DMT, and 4-HO-DiPT, found in samples also containing 4-AcO-DiPT. 4-Acetoxy substituted tryptamines are thought to be metabolized into the 4-HO substituted equivalents in the human body, but no scientific evidence of this assumption has been found (Erowid 4-Acetoxy-DET Vault 2016; Erowid 4-Acetoxy-DiPT Vault 2016; Erowid 4-Acetoxy-DMT Vault 2016; Erowid 4-Acetoxy-MiPT Vault 2016). Whether the presence of possible hydrolysis products in samples of esters is a result of adulteration, degradation, or an analytical artefact should be considered.

A remarkable finding was the presence of 25C-NBOMe in one of the two samples delivered as 5-MeO-MALT in 2015. 25C-NBOMe is a hallucinogen active at microgram doses (Bersani et al. 2014), while tryptamines are usually active at milligram doses (Araújo et al. 2015). The confusion of the two classes of substances may represent a life-threatening situation.

During the period of study, the submission of samples of new psychoactive tryptamines slightly exceeded that of regulated tryptamines. This suggests a higher risk, since less evidence is available on these newer substances. However, there is a decreasing trend in the submission of unregulated tryptamines over the last year, while the submission of regulated tryptamines has continued an increasing trend with samples of controlled tryptamines exceeding those of uncontrolled tryptamines since 2013 (Figure 1). The most submissions from unregulated tryptamines took place from 2010 to 2012, while the peak deliverance of regulated tryptamines was registered in 2015. Further research could help to uncover the reasons for the variability in the samples submitted as regulated and unregulated tryptamines.

It is hard to compare this data with the data provided by Spanish surveys, since there is no specific category for the use of hallucinogenic tryptamines and different tryptamines are not considered independently. The results of this study are more consistent with other Spanish studies conducted with targeted sampling techniques (Caudevilla-Gálligo et al. 2013; González et al. 2013) than with surveys conducted on the general population regarding the use of NPS.

The high prevalence of DMT samples found in this study is consistent with international surveys that explore the use of hallucinogens (Winstock, Kaar, and Borschmann 2014). It is also interesting to point out that the increase in regulated tryptamines delivered was mostly at the expense of the increase in DMT samples. Monitoring of sample submission should be maintained to check whether this trend continues over the next few years.

The presence of tryptamines as adulterants was rare in samples submitted as non-tryptamine substances. Other Spanish and international studies have found a higher prevalence of NPS as adulterants of controlled substances (Giné, Espinosa, and Vilamala 2014; Honderbrink et al. 2015) than is found for controlled tryptamines. This might be due to the more careful nature of tryptamine users, who may be more concerned about purity and plan their consumption more clearly.

When considering the prevalence of regulated tryptamines, it is interesting to discuss their ritual use in ancient civilizations and their current use as adjuvants in diverse psychotherapeutic procedures and in dishabituation therapies (Bogenschutz 2013; Young 2013; De Osório et al. 2015; Johnson et al. 2014; Sessa and Johnson 2015; Winkelman 2014). This ritualistic and medical background might have influenced the user profile of these substances and the patterns of distribution within the market. The fact that regulated hallucinogenic tryptamines might have therapeutic effects contradicts the claims of danger (Araújo et al. 2015), despite the evidence of fatal outcomes related to their use (Corkery et al. 2012; Morano et al. 1993; Sklerov et al. 2005; Tittarelli et al. 2015). These fatal outcomes might not be inherently associated with the use of tryptamines, but, instead, with an excessive dosage and their combination with other psychoactive substances. Due to the potential risks, extreme care should be taken in dosing and planning of consumptions. However, it would be interesting to study whether the therapeutic properties of psychoactive tryptamines are also shared by the unregulated molecules, since there are no studies fn this according to a PubMed search in July 2016.

The appearance of pills containing psychoactive tryptamines distributed during 2015 represents a new trend not detected previously. Even though the number of pills delivered containing new psychoactive tryptamines is low, the fact that it is such a recent phenomenon and that it affects a group of substances from which there was no precedent in the past of their use as adulterants should spark concern. Moreover, the submission of new psychoactive tryptamines as "legal highs" sets a precedent in the submission of tryptamines. This phenomenon should be closely monitored to establish whether it is an emerging trend in the market. Due to the fact that tryptamines act at higher doses than other hallucinogens (Tittarelli et al. 2015), the presence of tryptamines marketed as pills and "legal highs" might have clinical implications. This phenomenon is especially relevant taking into account that it had not been systematically registered prior to 2015.

Limitations include a potential selection bias, since the submission was voluntary and anonymous. This may mean that there is a bias towards more cautious drug users who will want to have their substances analyzed by Energy Control before consumption, and therefore a bias towards users who select more reliable sources of tryptamines in the first place.

Equally, epidemiological data for gender and age might be influenced by the fact that information on these fields was not always available, and this may affect the possible agreement with the results of other surveys.

On the whole, tryptamines have a significant incidence among recreational users. The possibility of self-treatment and apparent safety might be pointed out as potential reasons for this prevalence and the high levels of purity among tryptamine samples. Further and wider studies should be conducted about psychoactive tryptamines, not only to determine patterns of consumption and distribution, but also to establish a more accurate understanding of the potential consequences of human consumption.

Further studies analyzing the pharmacokinetics and pharmacodynamics as well as the clinical effects on humans of the new psychoactive tryptamines would be useful to researchers and clinicians interested in NPS as well as the clinical distinctions between the different molecules. The prevalence of other tryptamines not listed by the 2013 UNODC report should also be explored. Until further research is carried out on these new substances, extreme caution should be advised and awareness should be raised in order to prevent the potential health risks associated with their use.

Abbreviations and IUPAC name

25C-NBOMe	2-(4-chloro-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine
4-AcO-DALT	3-{2-[Di(prop-2-en-1-yl)amino]ethyl}-1H-indol-4-yl acetate
4-AcO-DiPT	3-[2-(Diisopropylamino)ethyl]-1H-indol-4-yl acetate
4-Aco-DMT	3-[2-(Dimethylamino)ethyl]-1H-indol-4-yl acetate
4-HO-DiPT	3-[2-(diisopropylamino)ethyl]-1H-indol-4-ol
4-HO-DMT	3-[2-(Dimethylamino)ethyl]-4-indolol
5-HO-DMT	3-(2-Dimethylaminoethyl)-1H-indol-5-ol
5-MeO-α-MT	1-(5-methoxy-1H-indol-3-yl)propan-2-amine
5-MeO-DALT	N-allyl-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]prop-2-en-1-amine
5-MeO-DiPT	3-[2-(Diisopropylamino)ethyl]-5-methoxyindole
5-Meo-DMT	2-(5-methoxy-1H-indol-3-yl)-N,N-dimethylethanamine
5-MeO-EIPT	N-ethyl-5-methoxy-N-(1-methylethyl)-1H-indole-3-ethanamine
5-MeO-MALT	N-[2-(5-Methoxy-1H-indol-3-yl)ethyl]-N-methylprop-2-en-1-amine
5-Meo-MiPT	N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-N-methylpropan-2-amine
ADB-FUBINACA	N-(1-Amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1H-indazole-3-carboxamide
α-MT	2-(1H-indol-3-yl)-1-methyl-ethylamine
DET	N,N-diethyl-2-(1H-indol-3-yl)ethanamine
DiPT	3-[2-(diisopropylamino)ethyl]indole
DMT	2-(1H-Indol-3-yl)-N,N-dimethylethanamine
DPT	3-[2-(dipropylamino)ethyl]indole
MDA	(R) 1-(benzo[1,3]dioxol-5-yl)propan-2-amine
MiPT	N-[2-(1H-indol-3-yl)ethyl]-N-methylpropan-2-amine
NMT	2-(1H-Indol-3-yl)-N-methylethanamine

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Declaration of interest

No conflicts of interest are reported.

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