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ORIGINAL ARTICLE

Changes in the prevalence of synthetic cannabinoids and cathinone derivatives in Japan until early 2012

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Abstract The changes in the prevalence of designer drugs and their legal status in Japan were investigated on the basis of the analyses of 686 different products containing synthetic cannabinoids and/or cathinone derivatives obtained from 2009 to February 2012. In the early stages of distribution of herbal-type products containing synthetic cannabinoids, cyclohexylphenols and naphthoylindoles were mostly found in the products. In November 2009, however, cannabicyclohexanol, CP-47,497 and JWH-018 were controlled as "designated substances" under the Pharmaceutical Affairs Law in Japan, and the cyclohexylphenols have since disappeared from the illegal drug market and been replaced by various analogs of the naphthoylindoles, phenylacetylindoles and benzoylindoles. These compounds, which have high affinities for the cannabinoid CB_1 receptor, have become very popular, and the number of emergency hospitalizations associated with their use has dramatically increased from 2011. Other synthetic compounds with different structures and pharmacological effects, such as cathinone derivatives, have been detected together with the synthetic cannabinoids in herbal-type products since 2011. Moreover, many new types of synthetic cannabinoids, different from the four typical structures described, have also begun to appear since 2011. In addition to the synthetic cannabinoids, liquid or powdery-type products containing cathinone derivatives have been widely distributed recently. In 2009, the most popular cathinone derivative was 4-methylmethcathinone. After this compound was controlled as a designated substance in November 2009, cathinone derivatives, which have a pyrrolidine structure at the nitrogen atom and a 3,4-methylenedioxy structure, or analogs of 4-methylmethcathinone, became popular. In the present analysis, tryptamines were also detected in 31 % of the products containing cathinone derivatives. Local anesthetics such as procaine, lidocaine, benzocaine and dimethocaine were also frequently detected. In total, we identified at least 35 synthetic cannabinoids and 22 cathinone derivatives during this survey.

Keywords Designer drugs · Synthetic cannabinoids · Cathinone derivatives · Designated substances · Prevalence changes

Introduction

In recent years, many analogs of narcotics have been widely distributed as easily available psychotropic substances and have become a serious problem in Japan. To counter the spread of these designer drugs, the Pharmaceutical Affairs Law in Japan was amended in 2006 to establish a new category, "designated substances," to more strictly control these drugs. Since 31 compounds and 1 plant were first controlled as designated substances in April 2007, 77 substances (13 tryptamines, 17 phenethylamines, 11 cathinone derivatives, 4 piperazines, 23 synthetic cannabinoids, 6 alkyl nitrites and 3 other compounds) and 1 plant (*Salvia divinorum*) have been listed in this category (data from July 2012). However, simultaneously with the control of these designer drugs, new analogs of the controlled substances began to appear one after another on the illegal drug market, and the identification and control of

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these compounds are rapidly devolving into a cat and mouse game. In particular, the recent spread of products containing various analogs of synthetic cannabinoids and/or cathinone derivatives has been a matter of great concern in Japan [1].

Before 2007, the major compounds distributed in the illegal drug market were tryptamines, phenethylamines and piperazines [1–11]. Alkyl nitrites, such as isobutyl nitrite and isopentyl nitrite, were also widely distributed [9, 12]. After they were listed as narcotics or designated substances in 2007, these compounds, especially the tryptamines, quickly disappeared from the market. In their place, various analogs of cathinone derivatives in the forms of liquid or powdery products, called "legal drugs" or "aroma liquids," have been widely distributed, as well as different phenethylamines and piperazines [1, 2, 13–17]. Since 2008, herbal-type products containing various synthetic cannabinoids have appeared in Japan under names such as "legal herbs" and "incense" [1, 2, 18, 19]. These synthetic cannabinoids had been originally synthesized by medicinal chemistry during the development of new medicines affecting the central nervous system. They have been reported to have high affinity actions on cannabinoid CB_1 and/or CB_2 receptors [20, 21]. At present, the synthetic cannabinoids and cathinone derivatives are the most popular designer drugs sold on the illegal drug market in Japan [1, 2, 22–34]. Among the 27 designated substances that have been controlled since 2011, 89 % of the compounds were either synthetic cannabinoids (18 compounds) or cathinone derivatives (6 compounds).

In this study, we analyzed two types of products, the herbal-type products sold as "legal herbs" or "incense" and the liquid/powdery-type products sold as "legal drugs" or "aroma liquids" on the Internet during the last 3 years, and the changes in the prevalence of these designer drugs and their legal status in Japan were investigated.

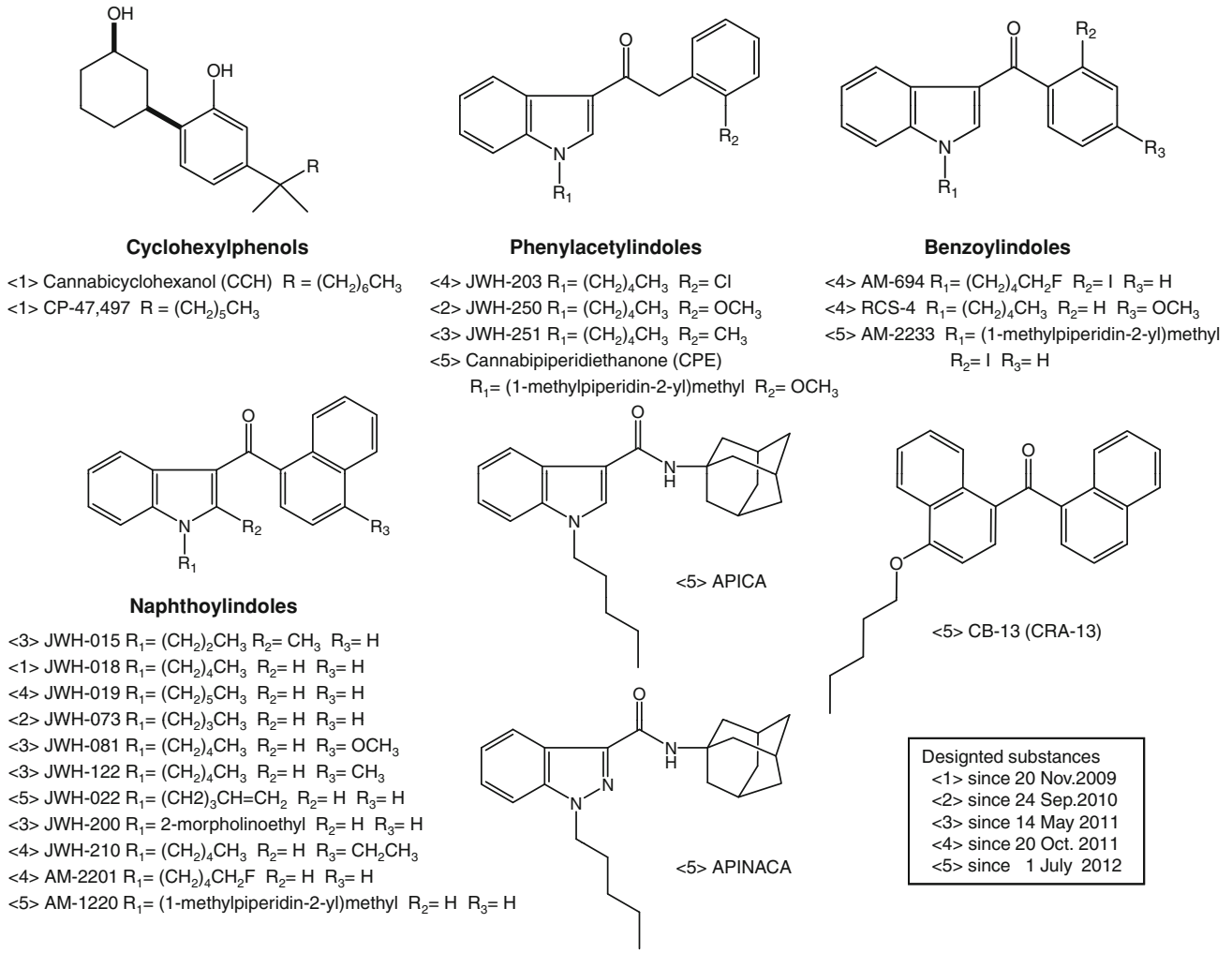


Fig. 1 Structures of synthetic cannabinoids controlled as designated substances in Japan (as of July 2012)

Materials and methods

Materials

Five hundred sixty-two different herbal-type products, sold as "legal herbs" or "incense" for their expected cannabis-like effects in Japan, were purchased via the Internet from January 2009 to February 2012. Most of them contained mixtures of dried cutting leaves, although some of the products contained powders or resin-like solids without herbal mixtures. In addition to herbal-type products, 124 different liquid or powdery-type products, sold as "legal drugs" or "aroma liquids," were also purchased via the Internet from September 2009 to February 2012.

Chemicals and reagents

Most of the authentic synthetic cannabinoids and cathinone derivatives were purchased from Cayman Chemical (Ann Arbor, MI, USA), LGC standards (Luckenwalde, Germany) and Sigma-Aldrich Co., LLC (St. Louis, MO, USA). Other authentic compounds were isolated from products and identified as described in our previous studies [18, 19, 27, 31]. All other common chemicals and solvents were of analytical reagent grade or HPLC grade.

Sample extraction procedures

The products consisting of a mixture of dried cutting leaves (10 mg) were crushed into powder and extracted with 1 ml of methanol under ultrasonication for 10 min. The powdery product (2 mg) or liquid product (20 μl) was dissolved with 1 ml of methanol. After centrifugation (5 min at 3,000 rpm), the supernatant solution was passed through a centrifugal filter (Millex LG filter, 0.45-μm; Merck Millipore, Darmstadt, Germany). When necessary, the solution was diluted with methanol to a suitable concentration before instrumental analyses.

Instrumental analyses

The methanol extracts were analyzed by gas chromatography-mass spectrometry in the electron ionization mode (GC-EI-MS) and by ultra-performance liquid chromatography-electrospray ionization–mass spectrometry (UPLC-ESI-MS). The identification of unknown compounds was mainly carried out by nuclear magnetic resonance (NMR) analysis and by direct analysis in real time (DART) ion source coupled to a time-of-flight mass spectrometer (TOF–MS). The analytical conditions were described in detail in our previous report [33].

Table 1 Specification of 562 herbal-type products purchased via the Internet from January 2009 to February 2012

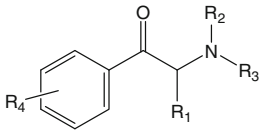
	Years				Total
	2009	2010	2011	2012[a]	
Total numbers of products purchased for the testing	67	80	365	50	562
in the form of dried cutting leaves	66	64	344	48	522
in the form of powders	0	12	21	2	35
in the form of resin-like solids	1	4	0	0	5
Total numbers of products in which synthetic cannabinoids were detected	62	79	365	50	556
without other synthetic compounds[b]	60	78	311	33	482
with cathinone derivatives[b]	0	0	27	5	32
with tryptamines[b]	0	0	12	10	22
with local anesthetics[b]	0	0	7	2	9
with other synthetic compounds except the above compounds[b, c]	2 (caffeine)	1 (caffeine)	38	3 (caffeine)	38
with constituents of psychotropic plants[b]	4	2	1	0	7
Total numbers of products in which synthetic cannabinoids were not detected	5	1	0	0	6
without other synthetic compounds[b]	5	1	0	0	6
with constituents of psychotropic plants[b]	1	0	0	0	1
Average numbers of synthetic compounds detected in one product	2.0	1.9	2.9	2.2	2.6

[a] During January and February in 2012

[b] Data were partially overlapped with those of other compounds

[c] α-Tocopherol and flavoring agents were excluded

Table 2 Non-controlled and controlled cathinone derivatives detected in this survey and our other studies



Common name	R_1	R_2	R_3	R_4	Regulation category in Japan (as of July 2012)
Cathinone[a]	CH_3	H	H	H	Narcotic
Methcathinone (ephedrone)[a]	CH_3	CH_3	H	H	Narcotic
3,4-Dimethylmethcathinone	CH_3	CH_3	H	3,4-Dimethyl	Designated substance (since 1 July 2012)
Ethcathinone	CH_3	CH_2CH_3	H	H	Designated substance (since 16 Jan 2009)
Amfepramone (diethylpropion)[a]	CH_3	CH_2CH_3	CH_2CH_3	H	Psychotropic
4-Methylmethcathinone (mephedrone)	CH_3	CH_3	H	4-CH_3	Designated substance (since 20 Nov 2009)
4-Methylethcathinone	CH_3	CH_2CH_3	H	4-CH_3	Designated substance (since 20 Oct 2011)
3-Fluoromethcathinone	CH_3	CH_3	H	3-F	Designated substance (since 14 May 2011)
4-Fluoromethcathinone (flephedrone)	CH_3	CH_3	H	4-F	Designated substance (since 20 Oct 2011)
4-Methoxymethcathinone (methedrone)	CH_3	CH_3	H	4-OCH_3	Designated substance (since 14 May 2011)
4-Methoxy-*N*,*N*-dimethylcathinone[b]	CH_3	CH_3	CH_3	4-OCH_3	
Buphedrone	CH_2CH_3	CH_3	H	H	
4-Methylbuphedrone[b]	CH_2CH_3	CH_3	H	4-CH_3	
4-Methyl-*N*-methylbuphedrone	CH_2CH_3	CH_3	CH_3	4-CH_3	
N-Ethylbuphedrone (NEB)	CH_2CH_3	CH_2CH_3	H	H	
Pentedrone	$CH_2CH_2CH_3$	CH_3	H	H	
Methylone (bk-MDMA)	CH_3	CH_3	H	3,4-Methylenedioxy	Narcotic (since 3 Feb 2007)
Ethylone (bk-MDEA)[c]	CH_3	CH_2CH_3	H	3,4-Methylenedioxy	Designated substance (since 11 Jan 2008)
Butylone (bk-MBDB)[c]	CH_2CH_3	CH_3	H	3,4-Methylenedioxy	Designated substance (since 11 Jan 2008)
Pentylone	$CH_2CH_2CH_3$	CH_3	H	3,4-Methylenedioxy	
α-PBP	CH_2CH_3	Pyrrolidinyl		H	
α-PVP	$CH_2CH_2CH_3$	Pyrrolidinyl		H	
4-MePPP	CH_3	Pyrrolidinyl		4-CH_3	
Pyrovalerone	$CH_2CH_2CH_3$	Pyrrolidinyl		4-CH_3	Psychotropic
MDPBP	CH_2CH_3	Pyrrolidinyl		3,4-Methylenedioxy	
MDPV	$CH_2CH_2CH_3$	Pyrrolidinyl		3,4-Methylenedioxy	Designated substance (since 16 Jan 2009)
Naphyrone	$CH_2CH_2CH_3$	Pyrrolidinyl		(Naphthyl structure)	Designated substance (since 20 Oct 2011)

α-PBP 1-phenyl-2-(pyrrolidin-1-yl)butan-1-one, *α-PVP* 1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one, *4-MePPP* 1-(4-methylphenyl)-2-(pyrrolidin-1-yl)propan-1-one, *MDPBP* 1-(3,4-methylenedioxyphenyl)-2-(pyrrolidin-1-yl)butan-1-one, *MDPV* 1-(3,4-methylenedioxyphenyl)-2-(pyrrolidin-1-yl)pentan-1-one

[a] Cathinone, methcathinone and amphepramone were never detected in our survey

[b] These compounds were not detected in this survey, although we detected them in the second quarter of 2012 [32]

[c] These compounds were not detected in this survey, although we detected them in our previous survey [10]

Results and discussion

Survey of herbal-type products sold as "legal herbs" or "incense"

In the last 3 years, synthetic cannabinoids described as "legal highs" or "synthetic marijuana" have been the most popular non-controlled designer drugs in the world. In July 2012, 23 synthetic cannabinoids were controlled as designated substances in Japan, as shown in Fig. 1. Table 1 shows the summary of our survey of 562 different herbal-type products purchased via the Internet under the descriptions "legal herbs" or "incense" from January 2009 to February 2012. Most of these products were in the form of dried cutting leaves (522 products), although some of them were in the forms of powders (35 products) or resin-like solids (5 products) without herbal mixtures, as shown in Table 1. The synthetic cannabinoids were detected in

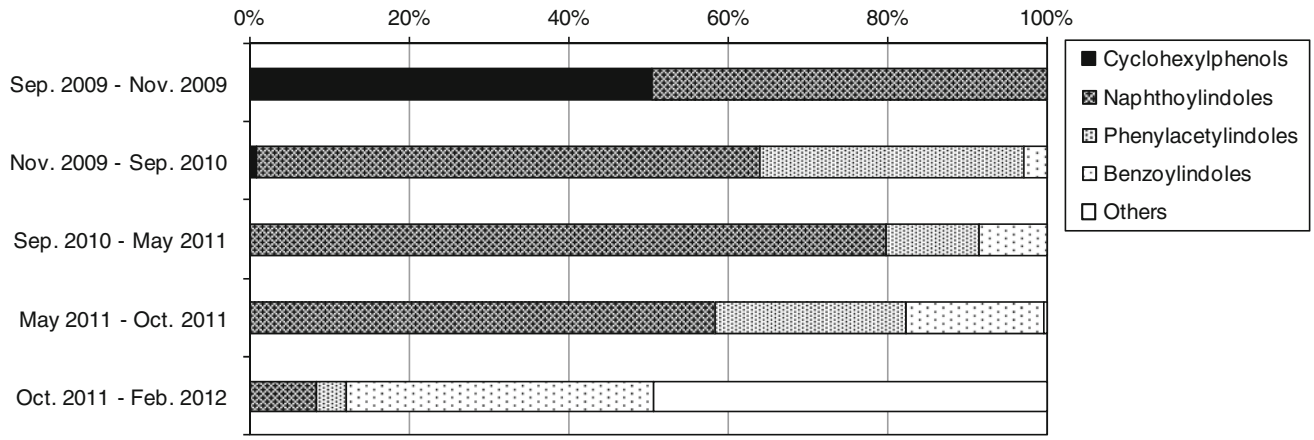


Fig. 2 Changes in the rates of various types of synthetic cannabinoids, i.e., cyclohexylphenols, naphthoylindoles, phenylacetylindoles, benzoylindoles and others, detected in 562 herbal-type products that were sold as "legal herbs" or "incense" on the Internet between January 2009 and February 2012

556 of the 562 products. The other six products, which were purchased in 2009 and 2010, contained no synthetic compounds, and one of them contained some active constituents derived from typical psychotropic cacti and plants. Typical constituents of marijuana (*Cannabis sativa*), Δ^9-tetrahydrocannabinol, cannabidiol and cannabinol, were detected together with the synthetic cannabinoids in an herbal product in 2009. Before 2011, there was no product that contained other types of synthetic compounds except caffeine. However, cathinone derivatives [e.g., 1-(4-methylphenyl)-2-(pyrrolidin-1-yl)propan-1-one (4-MePPP), 4-methylethcathinone, 1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one (α-PVP), ethcathinone, *N*-ethylbuphedrone (NEB), 1-(3,4-methylenedioxyphenyl)-2-(pyrrolidin-1-yl)pentan-1-one (MDPV) and pyrovalerone; the structures are shown in Table 2], tryptamines [e.g., α-methyltryptamine (AMT), which has been controlled as a narcotic in Japan since 2005; *N*,*N*-diallyl-5-methoxytryptamine (5-MeO-DALT), which has been controlled as a designated substance since 2007; and *N*,*N*-diethyl-4-hydroxytryptamine (4-OH-DET)], and local anesthetics (e.g., lidocaine, procaine and dimethocaine) have been detected together with the synthetic cannabinoids from 2011. Methoxetamine (a derivative of ketamine), 2-diphenylmethylpyrrolidine and some phenethylamines were also found in the products in 2011. Overall, the average number of synthetic compounds detected per product was 2.6 over the 3 years. In 2009 and 2010, most products contained only one or two synthetic compounds, except caffeine and a *trans*-form of cannabicyclohexanol, which was mostly detected together with cannabicyclohexanol [25]. However, the numbers of the synthetic compounds detected in the products dramatically increased in 2011, with one of the products containing as many as ten synthetic compounds.

The synthetic cannabinoids detected in Japan were divided mainly into four groups, cyclohexylphenols, naphthoylindoles, phenylacetylindoles and benzoylindoles, as shown in Fig. 1. The changes in the rates of these four types and other types of synthetic cannabinoids, detected in the herbal-type products purchased from January 2009 to February 2012, are shown in Fig. 2. In the earliest stage, only cyclohexylphenols and naphthoylindoles were found in the products. However, following the control of cannabicyclohexanol, CP-47,497 and JWH-018 in November 2009, the cyclohexylphenols disappeared from the illegal drug market, and various analogs of naphthoylindoles, phenylacetylindoles and benzoylindoles were widely distributed. Furthermore, in 2011, various compounds began to appear that had structures different from those of the four groups described above.

Figure 3 shows the changes in the detailed prevalence of each synthetic cannabinoid and their legal status on the basis of our survey of the 562 herbal-type products sold as "legal herbs" or "incense" during the last 3 years. We identified at least 35 synthetic cannabinoids in the products during this survey. As described above, cannabicyclohexanol, CP-47,497 and JWH-018 were the most frequently detected until November 2009. After these three compounds were listed as designated substances in that month, the synthetic cannabinoids in herbal products were quickly replaced by JWH-073 and JWH-250. After the prohibition of these two compounds in September 2010, various analogs, such as JWH-081, JWH-122 and JWH-210, began to be widely distributed. At that time, the analogs, structures of which featured the introduction of a halogen substituent, appeared on the drug market; these included JWH-203, AM-2201 and AM-694. Compounds having higher affinities to the cannabinoid CB_1 receptors, such as JWH-122

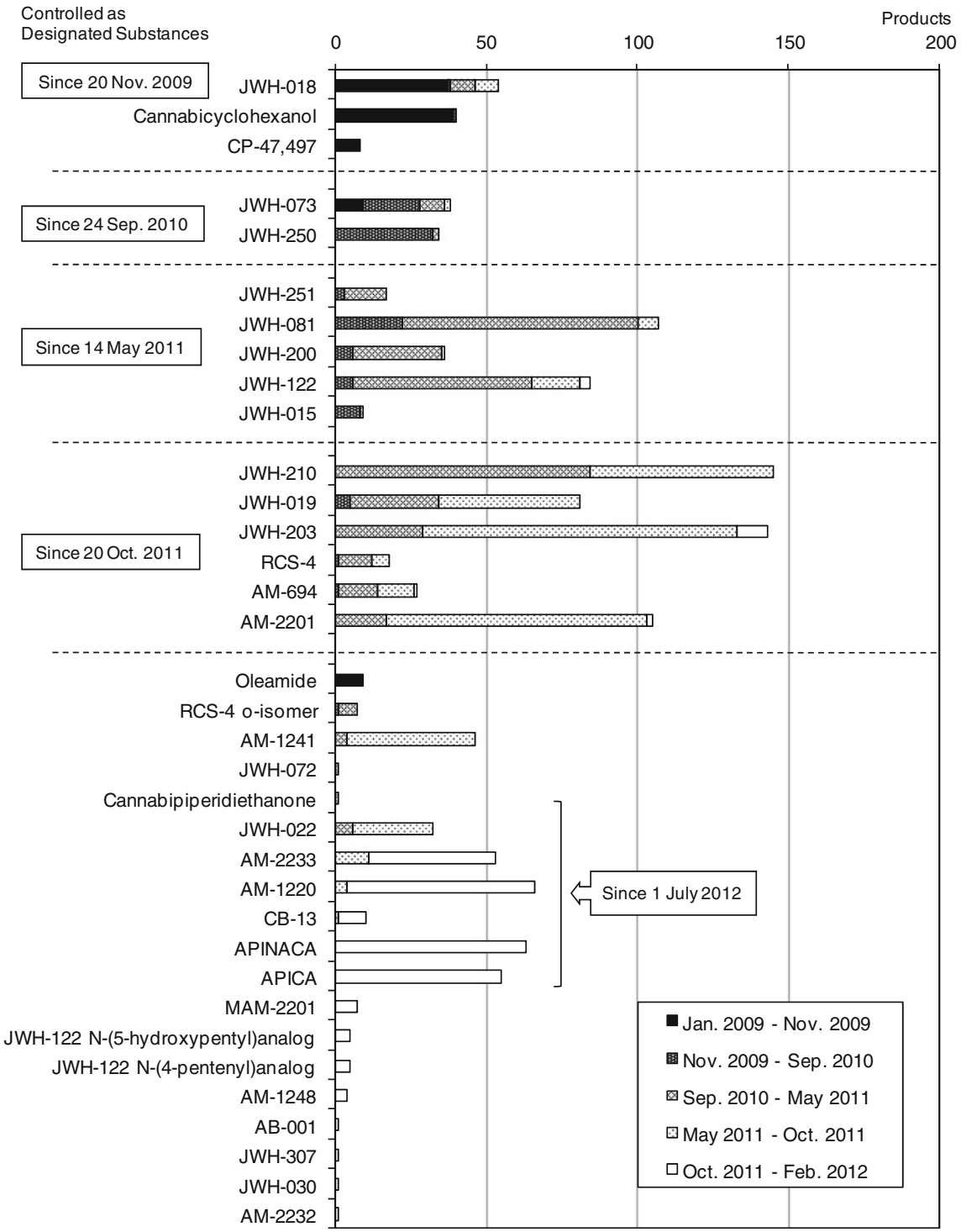


Fig. 3 Changes in the prevalence of synthetic cannabinoids and their legal status on the basis of our survey of 562 herbal-type products sold as "legal herbs" or "incense" on the Internet between January 2009 and February 2012. *The horizontal axis* shows the number of products. ■: products purchased from January 2009 to November 2009; ▩: from November 2009 to September 2010; ▨: from September 2010 to May 2011; ⊡: from May 2011 to October 2011; □: from October 2011 to February 2012

(the K_i value for binding the CB_1 receptor was 0.69 nM) [35], JWH-210 (0.46 nM) [21] and AM-694 (0.08 nM) [36], have also become popular, and the number of emergency hospitalizations associated with the products containing these synthetic cannabinoids has increased since 2011.

Table 3 Specification of 124 liquid or powdery-type products purchased via the Internet from September 2009 to February 2012

	Years			Total
	2009[a]/2010	2011	2012[b]	
Total numbers of products purchased for the testing	34	75	15	124
in the form of liquids	28	70	13	111
in the form of powders	6	5	2	13
Total numbers of products in which cathinone derivatives were detected	34	75	15	124
without other types of compounds	29	37	6	72
with tryptamines[c]	1	32	6	39
with local anesthetics[c]	0	16	6	22
with other synthetic compounds[c]	5	8	2	15
Average numbers of synthetic compounds detected in one product	2.0	2.7	3.1	2.6

[a] From September to December in 2009

[b] During January and February in 2012

[c] Data were partially overlapped with those of other compounds

In 2011, a total of 11 synthetic cannabinoids were added to the designated substance list in May and October. However, new synthetic cannabinoids were simultaneously emerging throughout Japan. After the six synthetic cannabinoids were listed in October 2011 (Fig. 3), new compounds, such as APICA and APINACA, appeared on the illegal drug market [31]. Many of the synthetic cannabinoids have a 3-carbonyl indole moiety, while these compounds belong to a new type of synthetic cannabinoids having each adamantylcarboxamide structure. APINACA additionally has an indazole group in place of an indole group. The adamantyl groups are also found in the structures of AB-001 and AM-1248, which have been distributed since 2011 [31, 33]. AM-1220 and AM-2233 were the most popular synthetic cannabinoids together with APICA and APINACA at the beginning of 2012. AM-1220 and AM-2233 have a (1-piperidin-2-yl)methyl structure at the nitrogen atom in an indole structure [31]. AM-1248, AM-1241 and cannabipiperidiethanone also have this structure and were also found in some products. Moreover, CB-13, JWH-030 and JWH-307 do not have an indole group and are newly found compounds [31, 33]. Although the data are not shown in this study, we also identified UR-144 and XLR-11 (having a tetramethylcyclopropyl structure), [1-(5-fluoropentyl)-1*H*-indol-3-yl](pyridin-3-yl)methanone and URB754 (which was originally reported to be a potent inhibitor of monoacylglycerol lipase [37]) as synthetic cannabinoids having novel structures distinct from those described above in the second quarter of 2012 [33]. As shown in Fig. 2, after October 2011, about 50 % of the synthetic cannabinoids consisted of new types that do not belong to the typical four types of structures mentioned above. Seven synthetic cannabinoids, APICA, APINACA, AM-1220, AM-2233, CB-13, JWH-022 and cannabipiperidiethanone, were controlled as designated substances in July 2012. Additionally, cannabicyclohexanol and JWH-018 will be changed from designated substances to narcotics in August 2012 in Japan.

Survey of liquid or powdery-type products sold as "legal drugs" or "aroma liquids"

In addition to synthetic cannabinoids, the products containing cathinone derivatives have also been widely distributed throughout the world, often under the names "legal highs" or "bath salts." In Japan, cathinone, methcathinone and methylone are controlled as narcotics, and pyrovalerone and amfepramone are controlled as psychotropics under the Narcotics and Psychotropics Control Law. As of July 2012, 11 cathinone derivatives had been controlled as designated substances in Japan (Table 2). Two of these derivatives, 4-methylmethcathinone and MDPV, will be changed from designated substances to narcotics in August 2012, together with cannabicyclohexanol and JWH-018.

Table 3 shows the summary of our survey of 124 different liquid or powdery-type products (111 liquid and 13 powdery-type products) purchased via the Internet from September 2009 to February 2012, all of which were sold as "legal drugs" or "aroma liquids." We detected cathinone derivatives in all 124 products. These products also contained various kinds of synthetic compounds having different pharmacological effects. A few powdery products contained both synthetic cannabinoids and cathinone derivatives, although synthetic cannabinoids have never been detected in liquid products. The failure to detect synthetic cannabinoids in these products may be due to their high hydrophobicities, which would prevent their dissolution in liquids. Tryptamines such as AMT, 5-MeO-DALT and 4-OH-DET were detected in 31 % of the products together with cathinone derivatives. In particular, in 2011, 32 of the 75 products contained tryptamines. In addition to tryptamines, local anesthetics such as procaine, lidocaine, benzocaine and dimethocaine were frequently detected in the liquid or powdery-type products from 2011. Caffeine, methoxetamine, methiopropamine (an analog of methamphetamine), 2-diphenylmethylpyrrolidine and other compounds have also been found together with the cathinone derivatives in these products. Since 2010, the average number of synthetic compounds detected in these products has risen steadily from 2.0 to 3.1, as shown in Table 3. In this survey, 48 of the 124 products contained only one

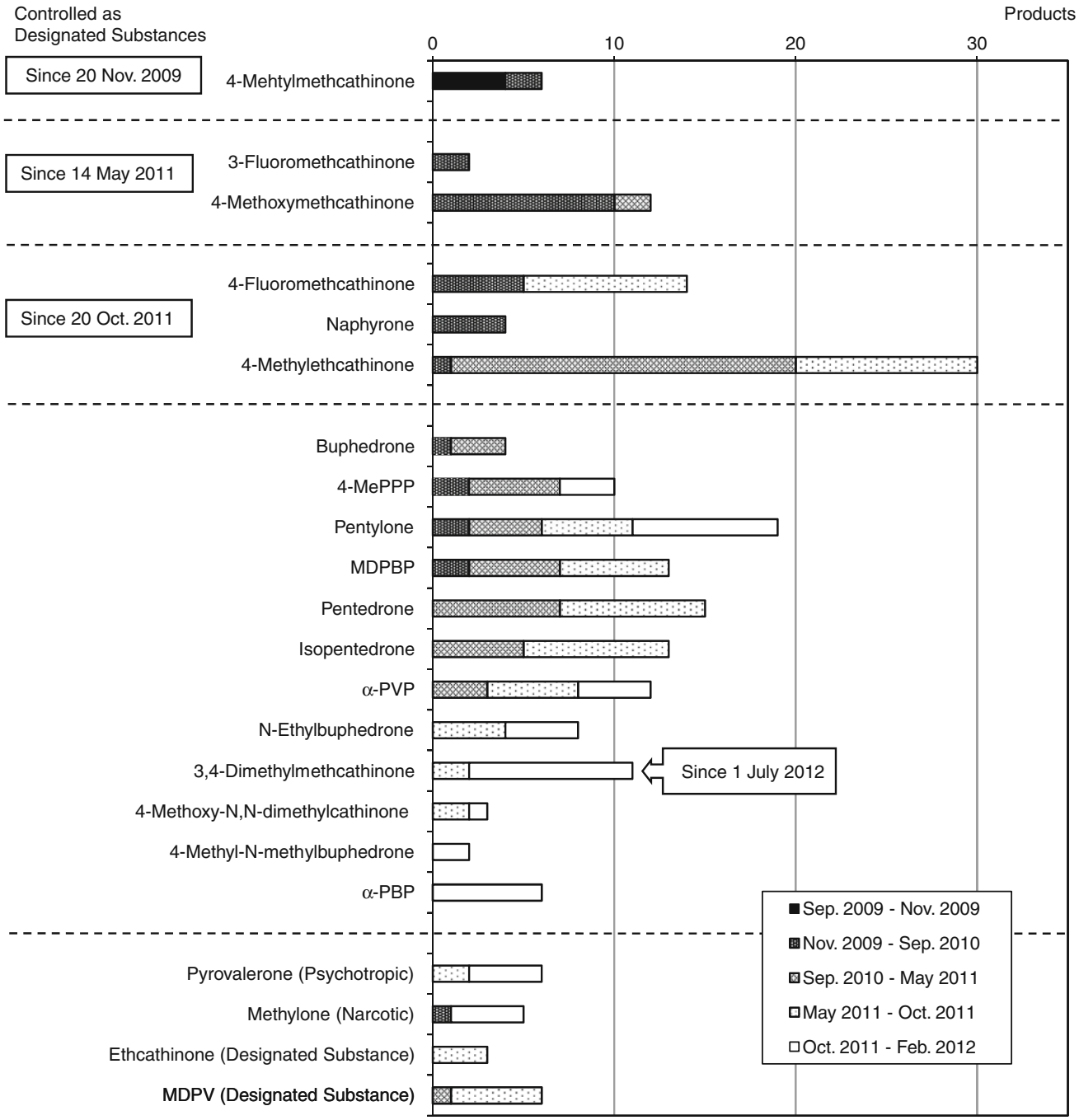


Fig. 4 Changes in the prevalence of cathinone derivatives and their legal status on the basis of our survey of 124 liquid or powdery-type products sold as "legal drugs" or "aroma liquid" on the Internet between September 2009 and February 2012. *The horizontal axis* shows the number of products. ■: products purchased from September 2009 to November 2009; ▩: from November 2009 to September 2010, ▨: from September 2010 to May 2011; ▫: from May 2011 to October 2011; □: from October 2011 to February 2012; *4-MePPP* 1-(4-methylphenyl)-2-(pyrrolidin-1-yl)propan-1-one, *MDPBP* 1-(3,4-methylenedioxyphenyl)-2-(pyrrolidin-1-yl)butan-1-one, *α-PVP* 1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one, *α-PBP* 1-phenyl-2-(pyrrolidin-1-yl) butan-1-one, *MDPV* 1-(3,4-methylenedioxyphenyl)-2-(pyrrolidin-1-yl) pentan-1-one

compound, while there was a liquid product containing as many as eight synthetic compounds (data not shown).

Figure 4 shows the changes in the prevalence of cathinone derivatives and their legal status on the basis of our survey of the 124 liquid or powdery-type products sold as "legal drugs" or "aroma liquids" during the last 3 years. We have identified 22 cathinone derivatives [including isopentedrone: 1-(methylamino)-1-phenylpentan-2-one] in

this survey. Table 2 shows non-controlled and controlled cathinone derivatives detected in this survey as well as those detected in our other studies [11, 33]. In 2009, the most popular cathinone derivative was 4-methylmethcathinone (mephedrone). After this compound was listed as a designated substance in September 2010, the cathinone derivative in the products was replaced by its analogs, 4-methoxymethcathinone (methedrone) and 4-methylethcathinone, in addition to 3- and 4-fluoromethcathinone (flephedrone). Following the control of these compounds in 2011, cathinone derivatives, which have a pyrrolidine structure at the nitrogen atom [such as α-PVP and 1-phenyl-2-(pyrrolidin-1-yl)butan-1-one (α-PBP)], a 3,4-methylenedioxy structure (such as pentylone), and analogs of 4-methylmethcathinone (such as 3,4-dimethylmethcathinone) have become popular. Methylone (narcotic), pyrovalerone (psychotropic), ethcathinone and MDPV (designated substances), which were controlled before September 2009, were also detected in this survey.

Conclusions

After the introduction of the category "designated substances" into the Pharmaceutical Affairs Law in 2007, the conventional designer drugs (such as tryptamines and piperazines) disappeared from the illegal drug market in Japan, and the active entries of various synthetic cannabinoids dramatically changed the situation in the market. These compounds were originally invented in medicinal chemistry. Until now, their numerous analogs have been synthesized during the development of new medicines affecting the central nervous system, and only some of these analogs have appeared as designer drugs in the illegal drug market. Therefore, we are sure that other analogs that have strong activities will appear one after another. In fact, the actual composition in terms of synthetic additives in the products is dynamically changing and rapidly responding to the newly implemented control measures. This fact makes it difficult to control these compounds using the existing systems. The number of emergency hospitalizations associated with synthetic cannabinoid use has increased dramatically from 2011. There have been some fatal cases, which are possibly related to the smoking of these products. Another group of designer drugs extensively appearing on the illegal drug market in Japan is cathinone derivatives; we have detected as many as 22 kinds of this group in this survey. To avoid health problems caused by these new designer drugs, we have to continuously monitor the distribution of these dubious products.

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