



Letter to the Editor

A report of novel psychoactive substances in forensic autopsy cases and a review of fatal cases in the literature

*Dear Editor*

Novel psychoactive substances (NPSs), which include synthetic cannabinoids, synthetic cathinones, phenethylamine derivatives and others, continue to be an increasing problem in Japan and all over the world [1]. By the end of 2015, over 700 NPSs had been reported [2]. These compounds are referred to as “legal highs” because they are often developed and abused before laws can be passed to make them illegal. This is a challenge for healthcare professionals, law enforcement, and forensic scientists, who must deal with the negative effects of these drugs on the public.

Information on the toxicity of NPSs is limited. In 2016, Chung et al. reported on the trend of NPSs and discussed the reported levels from fatal cases in the literature [3]. Another review article by Zawilska and Wajcieszak that has been published online but at the time of this writing is not in print discusses the rapid increase in designer cathinones being abused [4]. The purpose of this letter is to summarize and supplement these findings and provide concentrations of NPSs determined from cases analyzed at the Department of Forensic Medicine of Fukuoka University, many of which contained the synthetic cathinone α -PHP, a NPS that has been rarely reported on.

Data from the Chung et al. review article, Zawilska and Wajcieszak’s review article, and several cases not included in those articles are shown in Table 1 [5–47]. In summary, 84 fatal cases from reports published from 2010 to 2016 where NPSs were detected from postmortem blood and/or urine are shown. Thirty-three different NPSs were detected, consisting of 16 cathinone derivatives, 10 synthetic cannabinoids, and 7 phenethylamine derivatives. The cause of death in 38 of the 84 cases was determined to be acute drug intoxication (45%). Twenty-two of the 84 cases listed a cause of death other than acute intoxication (26%), and 24 of the 84 cases did not report a cause of death (29%).

Data from fatal cases where NPSs were detected that were analyzed at Fukuoka University, Faculty of Medicine, Department of Forensic Medicine are shown in Table 2. In summary, 12 different NPSs were detected from 10 cases. Five cathinone derivatives, 4 synthetic cannabinoids, and 3 phenethylamine derivatives were confirmed. Five of the 10 cases contained the cathinone derivative α -PHP. The cause of death in 8 of the 10 cases was determined to be acute drug intoxication. In the 2 cases not determined to be from acute drug intoxication, one was a suicide by hanging (Case 1) and the other was a fall from a height (Case 2). In the remaining 8 cases, other than brain edema, pulmonary edema and congestion, there were no remarkable injuries, diseases, or other findings by gross and microscopic examination that could explain the death. Thus, these cases were all considered acute drug intoxication.

In a previous report, we reported LC-MS/MS and GC-PCI-MS/MS databases covering 104 NPSs and their MS/MS transition and collision energy data [47]. Screening was performed by GC-MS and LC-MS/MS using protein precipitation with acetonitrile and solid-phase extraction. Quantitation was carried out by LC-MS/MS using a simple protein precipitation with acetonitrile and lipid removal by filtration. A detailed procedure of both the GC-MS and LC-MS/MS processing methods and instrument settings can be found in a previous report [48].

In this letter, we report on the presence of NPS compounds in 10 forensic autopsy cases analyzed at Fukuoka University, Faculty of Medicine, Department of Forensic Medicine. A total of 94 cases, including the 10 from our autopsy cases, have reported NPSs in samples from autopsy specimens. These cases included 41 different NPSs (Table 3). Acute drug intoxication was determined to be the sole cause of death in 46 of the 94 cases reviewed (49%). Of the 10 cases analyzed at Fukuoka University, Department of Forensic Medicine, 5 were found to contain α -PHP, and these are the only fatal cases in the literature to date that included this compound. Also, in all 5 α -PHP cases, acute drug intoxication was determined to be the cause of death. Therefore, we believe these findings are a strong argument for the importance of testing for the presence of NPSs and reporting their quantitation data for the forensic medicine and toxicology communities.

Table 1
Fatal cases involving Novel Psychoactive Substances as reported in the literature.

Case	NPS	Drug Class	Blood Concentration (µg/mL)	Urine Concentration (µg/mL)	Other Drugs[blood conc.](µg/mL)	Cause of Death (if provided)	Primary Author	Year Report Published	Reference
1	Methedrone	Phenethylamines	8.4		Diazepam (0.05) Midazolam (0.02) Lidocaine (0.6)	Intoxication	Wikstrom	2010	5
2	Methedrone	Phenethylamines	9.6			Intoxication			
3	Mephedrone	Phenethylamines	22		Diazepam (< 0.1) nordiazepam (< 0.1) Amphetamine (0.34)		Torrance	2010	6
4	Mephedrone	Phenethylamines	3.3	> 0.5		Intoxication			
5	Mephedrone	Phenethylamines	5.7						
6	Mephedrone	Phenethylamines	1.2			Stabbing			
7	Mephedrone	Phenethylamines	5.1	186	Cocaine (0.007) MDMA (0.011) Oxazepam (< 0.01) Midazolam (0.006) Dextromethorphan (< 0.02)	Intoxication	Lusthof	2011	7
8	Methylone	Phenethylamines	1.000		Lamotrigine (2.5) Midazolam (0.02) Lorazepam (0.029) Fentanyl (0.0021) Clonazepam (0.0055)	Intoxication	Pearson	2012	8
9	Methylone	Phenethylamines	3.300			Intoxication			
10	Methylone	Phenethylamines	0.580			Intoxication			
11	JWH-018	Synthetic cannabinoids	0.199		7-aminoclonazepam (0.0566) Methadone (0.887) EDDP (0.115) Morphine (0.122) Pregabalin (1.8) Topiramate (4.1)	Intoxication	Shanks	2012	9
12	JWH-018	Synthetic cannabinoids	0.0196			Intoxication			
	JWH-073	Synthetic cannabinoids	0.0683						
13	JWH-018	Synthetic cannabinoids	0.0833			Suicide by exsanguination			
14	JWH-018	Synthetic cannabinoids	0.0002						
	JWH-073	Synthetic cannabinoids	0.0002						
15	JWH-018	Synthetic cannabinoids	0.0001						
16	JWH-018	Synthetic cannabinoids	0.0008						
	JWH-073	Synthetic cannabinoids	0.0003						
17	JWH-018	Synthetic cannabinoids	0.001						
	JWH-073	Synthetic cannabinoids	0.0003						
18	JWH-018	Synthetic cannabinoids	0.0022						
19	JWH-018	Synthetic cannabinoids	0.0012						
	JWH-073	Synthetic cannabinoids	0.0004						
20	JWH-018	Synthetic cannabinoids	0.0005						
	JWH-073	Synthetic cannabinoids	0.0003						
21	JWH-018	Synthetic cannabinoids	0.0006						
22	JWH-018	Synthetic cannabinoids	0.0001						
	JWH-073	Synthetic cannabinoids	0.0001						
23	JWH-018	Synthetic cannabinoids	0.0004						
	JWH-073	Synthetic cannabinoids	0.0002						
24	JWH-018	Synthetic cannabinoids	0.0003						
25	JWH-018	Synthetic	0.0001						

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