IDENTIFICATION OF SYNTHETIC CANNABINOIDS 5F-ADB AND XLR-11 IN SEIZED SAMPLE IN PENANG, MALAYSIA

Choon Hiang Ng*, Siti Aishah Che Ani, Khairuzzaman Mustafa, Shaari Desa, Maimonah Sulaiman

Forensic Division, Chemistry Department of Malaysia, Jalan Tull, 10450 Pulau Pinang.

* *Forensic Division, Chemistry Department of Malaysia, Jalan Tull, 10450 Pulau Pinang; Email: chng@kimia.gov.my*

ABSTRACT: Eight herbal samples were seized by police agency in Penang State, Malaysia. A simple and rapid gas chromatography-mass spectrometry (GC-MS) method was used to identify active ingredients in the samples seized by police agency. As a result of the analysis, two species of synthetic cannabinoids were identified as main active ingredient, which are 5F-ADB (n=1), and XLR-11 (n=7). This is the first report to identify synthetic cannabinoid 5F-ADB and XLR-11 as designer drug in Penang State, Malaysia.

Keywords: Synthetic cannabinoids, New Psychoactive Substances, Gas chromatography–mass spectrometry, 5F-ADB, XLR-11.

Introduction

In the past decades, the recreational use of New Psychoactive Substances (NPS) has grown in popularity throughout the world. Based on a report released by United Nations Office on Drugs and Crimes in March 2018, there were 779 NPS registered up to December 2017 [1]. 250 out of 779 NPS identified were synthetic cannabinoids, a group of psychoactive compounds that mimic the effect of cannabis. Some synthetic cannabinoids were also marketed as “Legal High” because these products were not banned by the authorities compared to the regulated cannabis.

The “earlier generations” of synthetic cannabinoids are mostly chemical structural similar to the Δ9-tetrahydrocannabinol (THC), the main psychoactive compound in cannabis. The synthetic cannabinoids that have emerged recently show greater structural diversity, it is believed that these newer compounds were designated to bypass the legislative action that had been put in place to counter the earlier generations of synthetic cannabinoids [2]. Although synthetic cannabinoids can mimic the effect of THC, many of them are actually several times more potent than Δ9-THC [3].

The production of herbal product is carried out by dissolving synthetic cannabinoids in organic solvent and spraying the solution onto some commercially available plant materials. The spiked plant materials are then dried and smoked in the same way as smoking cannabis. A study on the quantitation of synthetic cannabinoids in dried leaves without homogenisation showed that the synthetic cannabinoids were actually unevenly distributed [4]. The high variation of synthetic cannabinoids content may be due to unevenly spraying technique during the manufacturing process and this can cause high toxic effect among drug abusers.

In this paper, we report two different cases from Penang, Malaysia which suspected to be containing cannabis. However, gas chromatography mass spectrometric (GC-MS) analysis of the herbal products confirmed the presence of the two synthetic cannabinoids: 5F-ADB and XLR-11. The following case histories provide some case information on seized samples.

Case Report

Case 1: Marshmallow Leave

A packet of dried leaves (Sample 1), as demonstrated in Figure 1, was submitted to Narcotic Section, Department of Chemistry Malaysia, Pulau Pinang in August 2018. According to the label on the plastic, the name of this dried leaves was “WILD LEAF #8 Marshmallow” and the weight was 100 gram per packet. The packet label claimed that the ingredients were made up of dried marshmallow leaves and could be used as tea, tonic recipes and cosmetic bath. This sample was submitted because it was suspected as cannabis. However, from physical and microscopic examination, we found out it was different from cannabis leaves.

Figure 1: Wild Leaf # 8 Marshmallow (Sample 1).

Case 2: Cigarette

Seven seized cigarettes (Sample 2 to Sample 8) suspected to be containing cannabis as in Figure 2, were submitted to our laboratory for analysis. However, from physical and microscopic examination, it was found out that the content in all the cigarettes were made up from same unknown dried leaves.

Figure 2: Seven Cigarettes (Sample 2 to Sample 8).

Materials and Method

Materials

Eight herbal samples were seized in Penang Island from August to December of year 2018 by Royal Malaysia Police. The seized samples were sent to the Department of Chemistry in the course of investigation and were used in this study. All chemicals and solvents used were of analytical reagent grade.

Microscopic examination

In this study, a LEICA M205C Microscope was used for microscopic examination. A Manta G504C camera was fixed to capture image developed by microscope.

Isolation of synthetic cannabinoids

For analysis of synthetic cannabinoids in plants material, approximately 40 mg of plant material was sonicated in 10.0 mL of chloroform for 10 minutes. The chloroform extract was filtered and used for GC-MS analysis.

Gas Chromatography - Mass Spectrometry (GC-MS) condition

The synthetic cannabinoids were analysed using an Agilent 7890A gas chromatograph equipped with an Agilent 5975C mass selective detector and an DB-5MS capillary column (30 m×0.25 mm×0.25 μm film thickness). The injector was operated in split mode (30:1) at 280°C. The injection volume was set at 1 μL. Helium gas was used as carrier gas at a flow rate of 0.9 mL/min. The oven temperature was initially held at 80°C for 3 minutes, then increased to 300°C at a heating rate of 40°C/min, and held at that temperature for 25 minutes. The MS was operated in scan mode, and the acquisition range was set to 35–480 m/z. For identification of synthetic cannabinoids, the mass spectrum of sample was compared with NIST 2014 and SWGDRUG MS Version 3.4 Library.

Results

Microscopic Examination

All the eight samples submitted to Narcotic Laboratory were suspected to be containing cannabis or cannabis mixture because one of the common ways to use cannabis was mixing cannabis together with tobacco leaves and repacking as commercial cigarettes. Therefore, the first step of analysis was to identify cannabis leaves inside the samples. Microscopic examination for the presence of cystolith hairs is significant for the identification of cannabis as it is the most characteristic feature found in the microscopic examination of cannabis.

Physical and microscopic examination of Sample 1 showed that it was made up of same green dried leaves. The light microscope photographs of sample 1 showed the presence of simple hairs, but absence of cystolith hair (Figure 3). The contents in the cigarettes (Sample 2 to Sample 8) were made up by dark brownish dried herbal products. The light microscope photographs of herbal products in Sample 8 showed the surface of herbal products did not contain any trichome (Figure 4). Microscopic examination showed all the eight samples did not contain any cannabis.

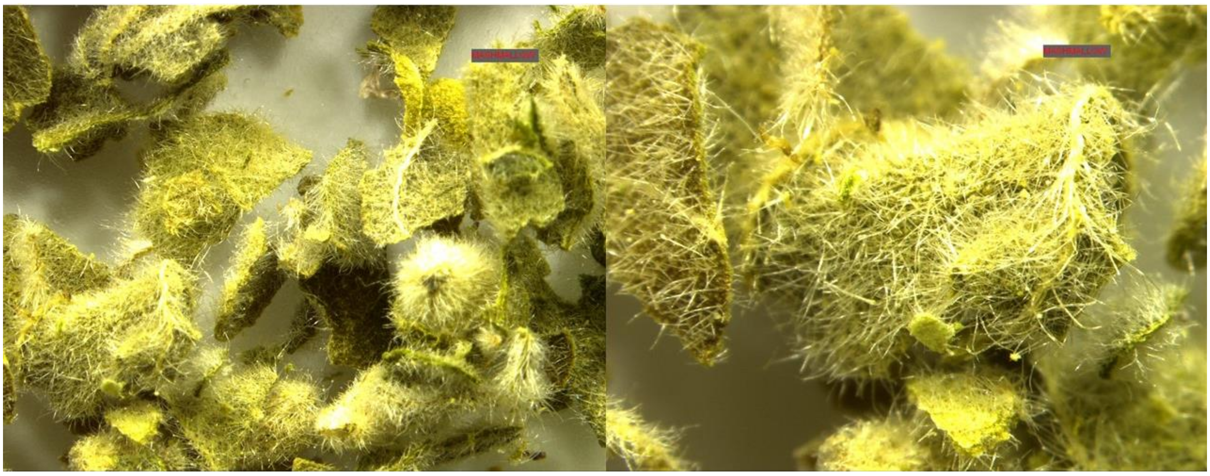


Figure 3: Light microscope (LM) photographs of Sample 1.

Figure 4: Light microscope (LM) photographs of sample 8.

Gas Chromatography-Mass Spectrometry

A total of eight seized samples were analysed for the presence of synthetic cannabinoids using the GCMS technique described above. In this study, two species of synthetic cannabinoids have been identified in the herbal products.

5F-ADB (also known as 5F-MDMB-PINACA or Methyl (2S)-2-{[1-(5-fluoropentyl)-1H-indazole-3-carbonyl] amino}-3,3-dimethylbutanoate) was identified in Sample 1. A few unknown peaks were detected along with 5F-ADB. Figure 5 shows the GC-MS total ion chromatogram (TIC) and mass spectrum obtained from herbal products extract of sample 1. GC-MS peak of 5F-ADB was detected at 9.790 min showed a mass spectrum with ion peaks at m/z 233, 289 and 321.

XLR-11 (also known as 5”-fluoro-UR-144) with the chemical name 1-(5-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl) methanone was detected in Sample 2 to Sample 8. A few unknown peaks were detected along with XLR-11. Figure 6 shows the GC-MS total ion chromatogram and mass spectrum obtained from the herbal product extract of Sample 8. The retention time for XLR-11 was 10.240 min, with a mass spectrum carrying major abundance at m/z 232, 314 and 329.

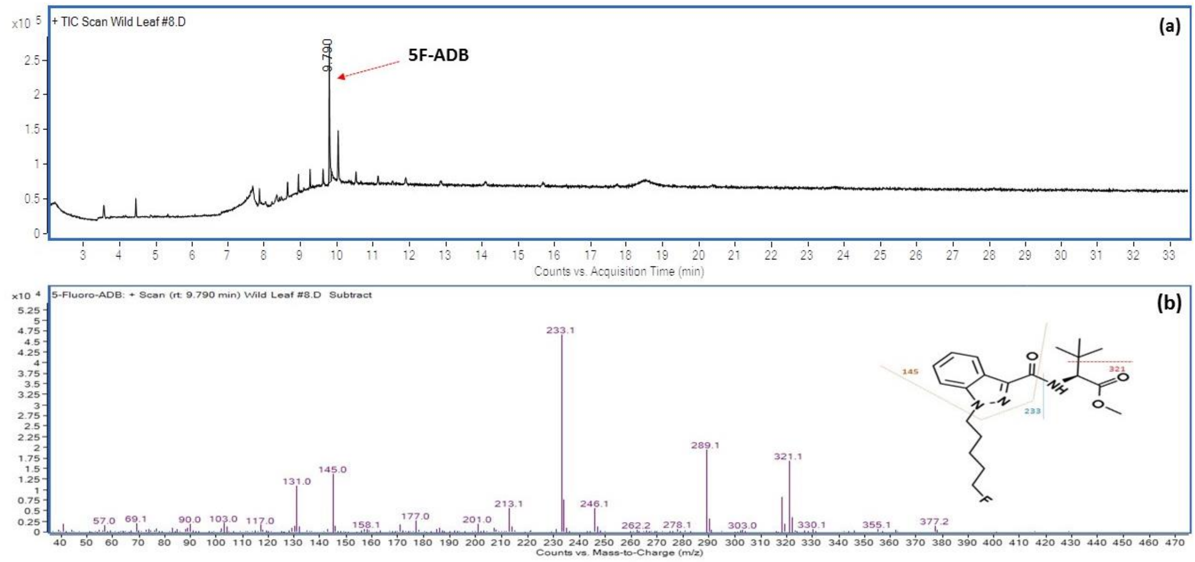


Figure 5: (a) Total ion chromatogram (TIC) of dried leaves extract containing 5F-ADB; (b) the mass spectrum of 5F-ADB.

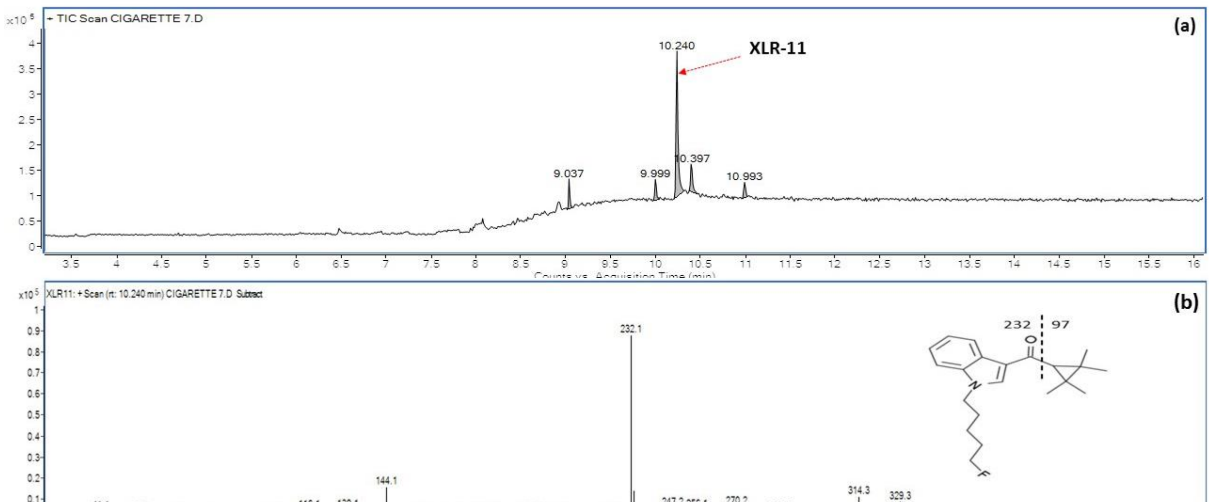
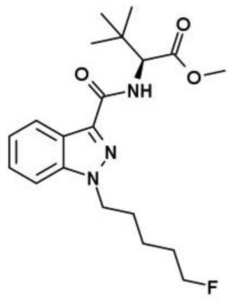


Figure 6: (a) Total ion chromatogram of dried leaves extract containing XLR-11; (b) the mass spectrum of XLR-11.

Discussion

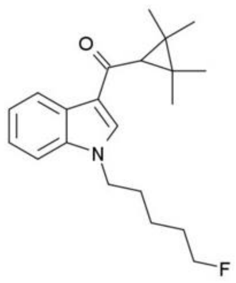
Sample 1 and Samples 2-8, respectively, were made up by two different plant materials which varied in colour and physical characteristics. This indicates that the manufacturing of herbal products was done by dissolving synthetic cannabinoids into solvent and then sprayed onto dried leaves. The variation of herbal products appearance posed difficulty to law enforcement agency to identify if it is of controlled substances, especially when they marketed as cigarette. Furthermore, the online market has provided an easy platform for the drug dealers to circulate new drugs effectively. Although some of the synthetic cannabinoids were sold via internet as research chemical and classified as not for human consumption, but it was still being abused as recreation drugs. Figure 7 shows the molecular structires of synthetic cannabinoids detected in the samples.

(a)



5F-ADB
5F-MDMB-PINACA
Methyl (2S)-2-{[1-(5-fluoropentyl)-1H-indazole-3-carbonyl] amino}-3,3-dimethylbutanoate

(b)



XLR-11
5-fluoro-UR-144
(1-(5-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl) methanone

Figure 7: Molecular structure of synthetic cannabinoids detected in samples.

5F-ADB is a synthetic cannabinoid that first appeared in the United States in late 2014. Consumption of 5F-ADB has been linked to sevaral cases of fatal intoxication and impaired driving [5]. In Japan, ten fatality cases reported in Japan as a result of smoking 5F-ADB. Therefore, 5F-ADB is considered as one of the most dangerous synthetic cannabinoids [6].

Synthetic cannabinoid XLR-11 is the fluorinated analog of UR-144. XLR-11 was first identified in herbal products in Japan in 2012. In 2013, the first case report of driving under influences of XLR-11 where the driver blood specimen was found to be containing only XLR-11. An evaluation of driver by drug recognition expert found the symptoms of low body temperature, rigid muscle tone, normal pulse, lacks of horizontal and vertical gaze nystagmus, nonconvergence of the eyes, dilated pupil size, and normal papillary reaction to light [7].

The number of synthetic cannabinoids is increasing rapidly either with appearance of new compounds or fluorinated modification of existing compounds. Those new synthetic cannabinoids are novel compound with less or no toxicological information and most of the available side effects and fatal intoxication caused by synthetic cannabinoids are from forensic cases. Pharmacological or toxicological studies have not been conducted on most of the synthetic cannabinoids as forensic laboratories having hard time keeping up with the emergence of new compounds into market. Therefore, improper abuse can caused overdose and unexpected side effects.

In Malaysia, synthetic cannabinoids AB-CHMINAGA, AB-PINAGA, 5F-ADB, UR-144 and 5F-PB-22 were controlled under the First Schedule of Dangerous Drug Act as of January 2019. One of the synthetic cannabinoids detected in this study, 5F-ADB was controlled under the First Schedule Dangerous Drug Act 1952 started 10th January 2019. However, XLR-11 is still not regulated under any Malaysia regulations, it is hoped that this study could provide useful information for Malaysia legislation authorities in making decision on its control in the future.

To date, Malaysia currently regulated only particular synthetic cannabinoids structure, but their possible analogs are not regulated. Modification especially fluorinated of existing synthetic cannabinoids has become a common synthetic cannabinoids evolution trend to avoid worldwide drugs regulation. Thus, the legal authority should consider to regulate synthetic cannabinoids compound together with their possible analogs.

Conclusion

The drug trend shows that the synthetic drugs have entered the drug market faster than they can be restricted. Identification of new psychoactive substances in herbal products represent a major challenge to forensic chemists. This study hopes to facilitate collective efforts from various departments to continue monitoring new psychoactive substances in drug samples to prevent abuse of these substances.

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