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Original Article

Characterization of Ephedrine as Illegal Methamphetamine Precursors Based on $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ Isotopes: Their Application for Methamphetamine Profiling in Indonesia

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ABSTRACT

Objectives: The $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ profile of the ephedrine as a methamphetamine precursor is a fingerprint to describing its origin. The origin of the precursor is one of the supporting data in methamphetamine profiling. In this research, the isotope profiles of natural, synthetic, and semi-synthetic clusters of ephedrine were established. These clusters were applied to predict the origin ephedrine from seized methamphetamine samples in Indonesia. **Methods:** The isotope profiles of methamphetamine and its precursor were clustered in two steps. Initially, ephedrine and pseudoephedrine from various of the origin were prepared, and then the methamphetamines were synthesized from 4 samples ephedrine of known origin using *Emde* and *Moscow* routes. Emde is a method mostly found in Indonesia, and also Moscow as a comparison. Elemental Analyzer-IRMS were used to analyze isotope abundance ratio in order to establish the natural, synthetic, and semi-synthetic clusters. This study was carried out to a total of 20 methamphetamine samples to identified the origin of precursors. **Results:** The results showed that the isotope profiles of ephedrine and pseudoephedrine formed groups based on the origin. And the isotope profiles of methamphetamine were similar to those of the precursors. **Conclusion:** The $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ isotope clusters of ephedrine/pseudoephedrine can be applied to seized methamphetamine samples to characterize the origin of the precursor.

Key words: Ephedrine isotope clustering, Isotope Ratio Mass Spectrometry, Precursor of methamphetamine, Ephedrine natural, Ephedrine semi-synthetics, Ephedrine syntetics.

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INTRODUCTION

The use of ephedrine as an illegal methamphetamine precursor in several countries until now is still rampant. Although that precursor has been strictly regulated globally, there are still many illegal laboratories that use ephedrine in producing methamphetamine. According to *World Drug Report 2020* released by United Nations Office on Drugs and Crime (UNODC), the number of methamphetamine seized in the world in 2018 was reported to be 228 tonnes.[1] During 2014–2018, UNODC received reports of the dismantling of nearly 30,000 illegal laboratories used in the manufacture of a*mphetamine type stimulants* (ATS), about 95 percent of these laboratories produced methamphetamine dominant in the regions of North America, East and Southeast Asia, South Asia, and Oceania. There are significant geographic differences from the methamphetamine starting material. The majority of methamphetamine produced in Asia, Oceania, Africa, and parts of Europe uses ephedrine or pseudoephedrine as the starting material. Meanwhile, the precursor phenyl-2-propanone (P2P) dominates in North America and Western Europe.[1] In Indonesia, the methamphetamine abuse ranks second in the top after Marijuana. The methamphetamine seizures in Indonesia is thought to have originated from the illegal laboratory synthesis in Indonesia and also smuggled from abroad.[2]

During 2018 to 2020, The Center of Drug Testing Laboratory, National Narcotics Board (NNB) Republic Indonesia had conducted the profiling analysis of 303 methamphetamine crystal samples seized by the investigators sent for drug signature analysis. Of this number, it was revealed that 63.70% of the profiling samples came from ephedrine and 61.72% of those were made through Emde route. Therefore, it could be concluded that the ephedrine and Emde pathway are the predominant precursors and synthesis method for illicit methamphetamine in Indonesia (narcotics profiling report. The Center of Drug Testing Laboratory of BNN).

The $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ isotope profiles of ephedrine or pseudoephedrine can be fingerprinted describing the origin of ephedrine or pseudoephedrine.[3] There have been many studies revealing the correlation between the isotope ratio profile of methamphetamine with the isotope ratio profile of ephedrine/pseudoephedrine as a precursor. Therefore, by analyzing the $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ isotope profiles of methamphetamine, the origin of the ephedrine or pseudoephedrine as a precursor used can be traced, whether they come from natural ephedrine, semi-synthesis, or fully-synthesis.[4] The abundance of $\delta^{15}N$ and $\delta^{13}C$ isotope ratios in ephedrine reflected in the isotope profile of methamphetamine. That is not modified during the synthesis reactions.[5] Meanwhile, the H isotope ratio profile apart from being derived from the precursor, it is also affected during the reaction.[6]

Unfortunately, methamphetamine profiling analysis in Indonesia has not included the characterization of isotope profile. Nowadays, in Indonesia there is no data on the isotope profile of ephedrine and also

pseudoephedrine to trace the source of the smuggling of precursors of methamphetamine narcotics. So far, the intelligence information regarding the origin of precursor sources is only based on the results of field investigations. Considering that the data from the acquisition source of precursors can be useful complementary data for narcotics investigators, it is necessary to conduct research to characterize the isotope values of ephedrine and pseudoephedrine which are precursors of methamphetamine illegal in Indonesia.

The aim of this work was to establish isotope profile from three clusters ephedrine to classify seized methamphetamine samples. The isotope $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ profile presented from natural, semi-synthetic, and fully-synthetic of ephedrine/pseudoephedrine and also methamphetamine from ephedrine or pseudoephedrine precursor with known sources. The methamphetamine synthesis used the method mostly found in Indonesia, that is the Emde route and also the Moscow route as a comparison. The isotope cluster formed were then used to map the origin of the precursor from 20 seized methamphetamine samples sent to The Center of Drug Testing Laboratory NNB on February 2020 - February 2021.

MATERIALS AND METHODS

Materials

All certified reference materials, and standards were obtained from the reference collection of The Center of Drug Testing Laboratory NNB, they are d-methamphetamine (Lipomed, Switzerland), l-ephedrine (Lipomed, Switzerland), d-pseudoephedrine (Lipomed, Switzerland), d-pseudoephedrine (Malladi, India), caffeine (IAEA-600, Austria), calcite (IAEA-603, Austria), and polyethylene (IAEA-CH-7, Austria). Dried Ephedra was obtained from the market. Twenty methamphetamine samples were samples from The Center of Drug Testing Laboratory NNB for between February 2020 and February 2021.

Analytical grade of toluene (Merck, Germany), hydrochloric acid 37% (Merck, Germany), copper sulfate (Merck, Germany), chloroform (Merck, Germany), diethyl ether (Merck, Germany), thionyl chloride/ $SOCl_2$ (Merck, Germany), palladium on barium sulfate/PdBaSO4 (Merck, Germany), red phosphor (Merck, Germany), iodine (Merck, Germany).

METHODS

Extraction natural ephedrine from Ephedra plant

Natural ephedrine was obtained from the dry and crushed Ephedra plant. A total of 250 g of Ephedra was washed with petroleum ether twice, then macerated with methanol for 24 h, the solution is filtered and evaporated until a thick extract is obtained. The thick extract was then dissolved in water and acidified with hydrochloric acid until it reached pH 2. Then the mixture was heated at 60°C for 1 h. The filtrate was extracted with 100 ml diethyl ether, the ether layer was then removed. The sodium hydroxide solution was used to basified the water layer and the mixture extracted again with diethyl ether. The diethyl ether was removed leaving an oil.[7]

The oil was then crystallized with 2-propanol (6 ml) and acidified until it reached pH 1 with hydrochloric acid (concentrate). Diethyl ether (12 ml) was then added to form a white solid crystal. Furthermore, the white crystal was separated from the mixture and purified with acetone and dried.

Synthesis of methamphetamine

Methamphetamine was prepared by Emde and Moscow routes. Four samples ephedrine and pseudoephedrine used. The result of synthesis giving crystals confirmed as methamphetamine be compared by of Gas Chromatography-Mass Spectrometry retention time and mass of spectrum with the certified reference material. Ultra High Performance Liquid Chromatography was used to analize the purity and chirality of the methamphetamine.

Emde Method

In this reaction, chloroephedrine / chloropseudoephedrine was synthesized first. The ephedrine/pseudoephedrine was slowly dissolved in 15 ml chloroform and $SOCl_2$ (10 ml), the reaction took place in the ice bath coating and stirred for several hours. The mixture layered with diethyl ether and causing precipitation of crystal immediate. The crystal formed was separated from the mixture and purified with a 50:50 solution of chloroform and diethyl ether.[8]

The formed chloroephedrine / chloropseudoephedrine crystals were reacted with $Pd/BaSO_4$ as a catalyst. The mixture attached to a hydrogenator apparatus and flushed with hydrogen gas in a vacuum system for several times. After the reaction was complete, the catalyst was filtered off. Diethyl ether was used to extract the filtrate and then the diethyl ether was evaporated after being alkalized with sodium hydroxide. The residue was obtained and then crystallized with 2-propanol solution and acidified until it reached pH 1 with hydrochloric acid (concentrate). The solution was then added with diethyl ether to form a white solid crystal. The white crystal was separated from the mixture and purified with chloroform and diethyl ether and dried.[8]

Moscow Method

Ephedrine/pseudoephedrine with 0.6 g of red phosphorus, 4 g of iodine, and 2 ml of distilled water were refluxed for 24 h and allowed to cool. After the process was complete, the mixture was filtered to remove red phosphorus. Diethyl ether was used to extract the filtrate and then the diethyl ether was evaporated after being alkalized with sodium hydroxide. Methamphetamine residue was obtained and then crystallized with 2-propanol solution and acidified until it reached pH 1 with hydrochloric acid (concentrate). The solution was then added with diethyl ether to form a white solid crystal. Additionally, the white crystal was separated from the mixture and purified with chloroform and diethyl ether and dried.[9]

Elemental Analyzer-Isotope Ratio Mass Spectrometry Analysis

Determination of the $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ values of all samples and standards by the elemental analyzer Isolink with dual combustion and thermal conversion (TC), connected with Conflo IV interface and Delta V Advantage (Thermo Scientific, Bremen, Germany). Data was collected and processed using Isodat software (Thermo Scientific, Bremen, Germany) and data interpretation was plotted using SigmaPlot (Systat Software Inc., USA).

Sample preparation

Approximately 300 µg of samples were placed into a tinfoil capsule for $\delta^{15}N$ and $\delta^{13}C$ analysis, and 200 µg of samples were weighed into a silver-foil capsule for $\delta^{2}H$ analysis. The sample was then packed in the foil by folding it until it was solid and circular with a diameter of 2-3 mm.

$\delta^{15}N$ and $\delta^{13}C$ analysis by Elemental Analyzer-Isotope Ratio Mass Spectrometry

The folded tinfoil capsules containing certified reference material caffeine (IAEA-600, $\delta^{13}C$: -27,771 ± 0,043 ‰ VPDB and $\delta^{15}N$: +1,0 ± 0,2 ‰ N_2) was the first analysis perform in a sequence to calibrate high-purity CO_2 and NO_2 gas. The tin capsule containing sample material burned by flash combustion in an elemental analyzer. The gases passed through a quartz reactor packed with Cr_2O_3 on alumina and Co_3O_4/Ag, separated in a GC column, and then into IRMS to obtain the ratios of

$^{13}C/^{12}C$ and $^{15}N/^{14}N$. Measured $\delta^{13}C$ values reported as a per mile (‰) deviations from the Vienna Pee Dee Belemnite (VPDB) and $\delta^{15}N$ values are expressed relative to the conventional standard material for nitrogen.

Analysis of δ2H by Termal Combustion-Isotope Ratio Mass Spectrometry

Sample materials contained in silver-foil were pyrolyzed in TC furnace to afford H_2 and CO in a ceramic reactor packed with glassy carbon granulate and silver wool packing at 1420°C. Gas samples separated in GC column and then into IRMS to obtain the $^{2}H/^{1}H$ ratios. Measured $\delta^{2}H$ values reported as a per mille (‰) deviations from the Vienna Standard Mean Ocean Water (VSMOW). Sample values were measured relative to ultra-high purity H_2 gas calibrated against certified reference material polyethylene (IAEA-CH_2, $\delta^{2}H$: -100,3±2,0 ‰VSMOW)

RESULTS

In this present study, the certified materials of ephedrine and pseudoephedrine with the method of fully-synthesis manufacture was analyzed for isotopic measurement. Furthermore, ephedrine and pseudoephedrine from the origin is known semi-synthetic also ephedrine plan-based was analyzed for isotopic measurement and for synthesis of methamphetamine. Thus, the profile isotope from various sources are available. Table 1 presents the isotope profile data from ephedrine and pseudoephedrine various sources.

Methamphetamine was prepared from 4 samples ephedrine and pseudoephedrine, which isotope profile were known, and using two different synthetic routes, Emde and Moscow route. The Emde method was chosen based on the data stated that it is rampant in Indonesia. The data are presented in Table 2. The methamphetamine and it is precursor were analyzed for nitrogen, carbon, and hydrogen isotopes using an elemental analyzer-IRMS. And further the measurement results of isotope abundance were then clustered using Sigma Plot based on the K-means clustering algorithm.

The total of 20 seized methamphetamine samples collected by The Center of Drug Testing Laboratory NNB. Analysis of purity, chirality, and identification of impurities on 20 seized methamphetamine samples has been carried out. The samples were classified and clustered using EA/TC-IRMS for the $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ isotope profiles. As a result, it was possible to conclude the acquisition source of the precursor.

DISCUSSION

The $\delta^{13}C$, $\delta^{15}N$, and $\delta^{2}H$ values of ephedrine from various sources

Measured values of carbon and nitrogen isotope ratios were very useful in identifying the origin of ephedrine, even though it is challenging to distinguish methamphetamine based on the impurity profile.[10] From the data in Table 1, it could be seen that each acquisition source had its own fingerprint. The $\delta^{15}N$ values in natural was very different than synthetic ephedrine, so it could be the difference between those. The nitrogen source in the synthetic ephedrine was from methylamine, whereas in the natural ephedrine, it was nitrate or ammonia from the soil.[11]

Table 1: The isotope profile of ephedrine from various origin measured by EA-IRMS.

Sample	$\delta^{15}N$ (‰)	$\delta^{13}C$ (‰)	$\delta^{2}H$ (‰)
Synthetic ephedrine	−9.11 to −6.05	−28.26 to −26.06	−100.86 to −50.39
Semi-synthetic ephedrine	3.31 to 9.08	−26.21 to −25.38	50.05 to 130.13
Nature ephedrine	5.36	−28.36	−150.75

Table 2: $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ values for Emde and Moscow synthesized methamphetamine.

Precursors	Methamphetamine product			
	Synthesis pathway	$\delta^{15}N$ (‰)	$\delta^{13}C$ (‰)	$\delta^{2}H$ (‰)
Ephedrine sample-1	Emde route	9.92	−25.84	75.94
$\delta^{15}N$ = 9.08 ‰				
$\delta^{13}C$ = −26.21 ‰	Moscow route	9.11	−26.42	80.2
$\delta^{2}H$ = 130.13 ‰				
Pseudoephedrine sample-2	Emde route	5.79	−26.1	70.97
$\delta^{15}N$ = 5.92 ‰				
$\delta^{13}C$ = −25.43 ‰	Moscow route	4.92	−24.78	70.3
$\delta^{2}H$ = 91.33 ‰				
Pseudoephedrine sample-3	Emde route	3.84	−24.85	32.2
$\delta^{15}N$ = 3.31 ‰				
$\delta^{13}C$ = −25.38 ‰	Moscow route	3.03	−22.38	30.13
$\delta^{2}H$ = 50.05 ‰				
Ephedrine sample-4	Emde route	4.75	−29.37	−180.31
$\delta^{15}N$ = 5.36 ‰				
$\delta^{13}C$ = −28.36 ‰	Moscow route	4.95	−29.89	−201.21
$\delta^{2}H$ = −150.75 ‰				

Furthermore, Makino *et al.* stated that the $\delta^{13}C$ value of the ephedrine plant-based ranged from -31.1‰ to -26.0‰ and pseudoephedrine semi synthetic usually derived from the ephedrine produced by acid isomerization gave the $\delta^{13}C$ value ranging from -27‰ to -22‰.[10] The values from this study were consistent with previous observations, which is $\delta^{13}C$ from the Ephedra plant is -28.36‰, fully-synthetic are ranging from -28.26‰ to -26.06‰, and semi-synthetic are ranging from -26.21‰ to -25.38‰.

Comprehensive classification not only be achieved from $\delta^{13}C$ and δ15N values. The measurement $\delta^{2}H$ would be a useful method for characterizing of the source of ephedrines. Makino *et al.*[10] stated that natural ephedrine had $\delta^{2}H$ values of -193‰ to -151‰, those for synthetic ones were -73% to -30%, and semi-synthetic ephedrine had $\delta^{2}H$ values widely, -73‰ to 243‰. The values from this study were consistent with the previous observations. From this study, it was interesting to observe that the ephedrine/pseudoephedrine from the fermentation process had increased $\delta^{2}H$ values compared to fully-synthetic ephedrine and natural ephedrine, that is 50.05‰ to 130.13‰. It is known that semi-synthetic ephedrine is made using benzaldehyde. The industrial benzaldehyde is generally produced by the catalytic oxidation of toluene, which results in $\delta^{2}H$ values up to 700‰, it is assumed.[12]

The $\delta^{13}C$, $\delta^{15}N$, and $\delta^{2}H$ values of methamphetamine synthesized from known ephedrine/pseudoephedrine and its precursor

The Emde route is a methamphetamine synthesis method which is thought to have been widely revealed in Indonesia. It was involving chloroephedrine and chloropseudoephedrine as intermediate compound, and reduction reaction using hydrogen gas and Palladium as a catalyst. While the Moscow method used red phosphorus, iodine, and water to

forming hydriodic acid *in situ*. The hydriodic acid is thought to protonate the hydroxy groups of ephedrine / pseudoephedrine to form aziridine compounds which have reduced to methamphetamine.[13]

From the data obtained in Table 2, it could be seen that $\delta^{15}N$ and $\delta^{13}C$ isotope values of the precursor and the product did not significantly change. It was caused reduction ephedrine/pseudoephedrine to methamphetamine difference only in the benzylic hydroxyl group. So, it is possible that the $\delta^{15}N$ and $\delta^{13}C$ values will remain largely unchanged. The $\delta^{2}H$ isotopic shift between ephedrine/pseudoephedrine and methamphetamine occurred. It was caused the hydroxyl group of ephedrine was released and replaced with hydrogen atom, so it affected the hydrogen isotope profile of the product. The decrease of $\delta^{2}H$ values indicates that the hydrogen isotope profile of methamphetamine's benzylic hydroxyl group is much lower than the hydrogen isotope profile of ephedrine's benzylic hydroxyl group.

Differences in the Emde and Moscow routes are shown in $\delta^{2}H$ isotopic composition observed for the methamphetamine of either route. Methamphetamine synthesized by the Moscow route produced more negative $\delta^{2}H$ values compared to the Emde route.

The isotope profile analysis is a reliable tool to identify different sources of precursors from the product, although it is prepared in the same clandestine facility, by the same or different synthetic route.[13] Meanwhile, based on this study, the clustering results illustrated the closeness of the isotope profiles between precursor and methamphetamine as the product. The natural, semi-synthetic, and fully-synthetic cluster had unique fingerprints for nitrogen and carbon isotope ratios.[14] The $\delta^{15}N$ values of the synthetic cluster were more negative in the value range of -9.11‰ to -0.17‰ than the other clusters. On the other hand, for the natural and semi-synthetic clusters, fingerprints were in $\delta^{13}C$ profile. The natural cluster had the $\delta^{13}C$ value which is more negative than the semi-synthetic cluster, in the value range of -29.89 ‰ to -28.36‰. Meanwhile, the semisynthetic cluster had a carbon isotope profile in the value range of -26,42‰ to -22,38‰ and a nitrogen isotope profile of 3.03‰ to 9.92‰.

From hydrogen isotope profiles, it could also be seen that the grouping of the three clusters. The natural cluster gave the most negative value compared to the other two clusters, ranging from -201,21‰ to -150.75‰. For the synthetic cluster, the $\delta^{2}H$ value ranged from -100.86‰ to -50.39‰, while the semi-synthetic clusters provided a wide range of $\delta^{2}H$ values, from 30.13‰ to 130.13‰ (Figure 1). Based on Makino's work, believed that the $\delta^{2}H$ values from the semi-synthetic cluster were also positive.[10]

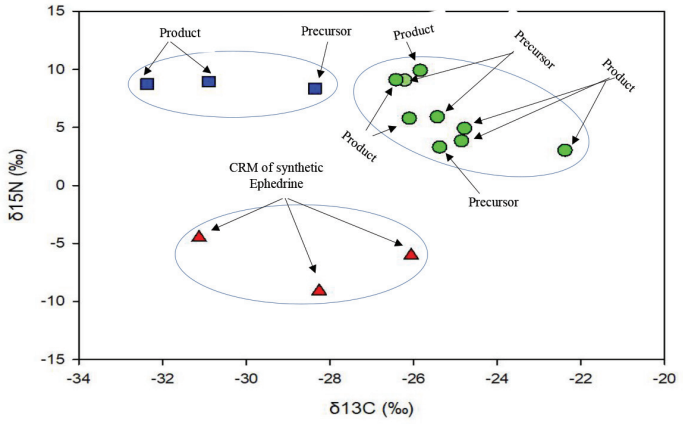

Figure 1: The $\delta^{13}C$, $\delta^{15}N$, and $\delta^{2}H$ values for ephedrine and methamphetamine synthesized by Emde and Moscow route : (▲) synthetic cluster; (■) natural cluster; (●) semi-synthetic cluster

The $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ values isotope of 20 seized methamphetamine samples

Table 3 showed the characterization of isotope profile of 20 seized methamphetamine samples and the presumed origin of precursors. The

Table 3: The Isotop values of synthetic cluster, semi-synthetic cluster, and natural cluster.

Cluster type	Samples	Isotope values		
		$\delta^{15}N$ (‰)	$\delta^{13}C$ (‰)	$\delta^{2}H$ (‰)
Synthetic cluster	Pseudoephedrine CRM	−6.05	−26.06	−100.86
	Ephedrine CRM	−9.11	−28.26	−50.39
	Meth CRM	−4.50	−31.13	−75.84
	Sample−1	−2.95	−27.59	−124.48
	Sample−2	−2.79	−27.58	−129.12
	Sample−3	−2.95	−27.74	−123.71
	Sample−4	−2.42	−29.84	−137.57
	Sample−5	−0.17	−32.61	−113.87
	Sample−6	−5.10	−29.36	−136.29
	Sample−7	−4.19	−28.96	−124.11
	Sample−8	−1.37	−29.18	−129.53
	Sample−9	−3.30	−29.51	−104.56
	Sample−10	−4.23	−29.76	−80.15
Semi−synthetic cluster	Ephedrine_01	9.08	−26.21	130.13
	PE−01	5.92	−25.43	91.33
	PE−02	3.31	−25.38	50.05
	Meth−E−01.1	9.92	−25.84	75.94
	Meth−E−01.2	9.11	−26.42	80.20
	Meth−PE−01.1	5.79	−26.10	70.97
	Meth−PE−01.2	4.92	−24.78	70.30
	Meth−PE−02.1	3.84	−24.85	32.20
	Meth−PE−02.2	3.03	−22.38	30.13
Natural cluster	Ephedrine_03	5.36	−28.36	−150.75
	Meth−E−03.1	4.75	−29.37	−180.31
	Meth−E−03.2	4.95	−29.89	−201.21
	Sample−11	2.87	−28.27	−189.11
	Sample−12	3.64	−28.31	−192.41
	Sample−13	3.16	−28.30	−193.67
	Sample−14	3.01	−28.23	−190.06
	Sample−15	3.76	−30.32	−188.53
	Sample−16	3.75	−28.37	−191.75
	Sample−17	3.84	−28.85	−189.11
	Sample−18	3.05	−30.05	−189.30
	Sample−19	3.65	−27.65	−193.91
	Sample−20	3.62	−27.89	−190.70

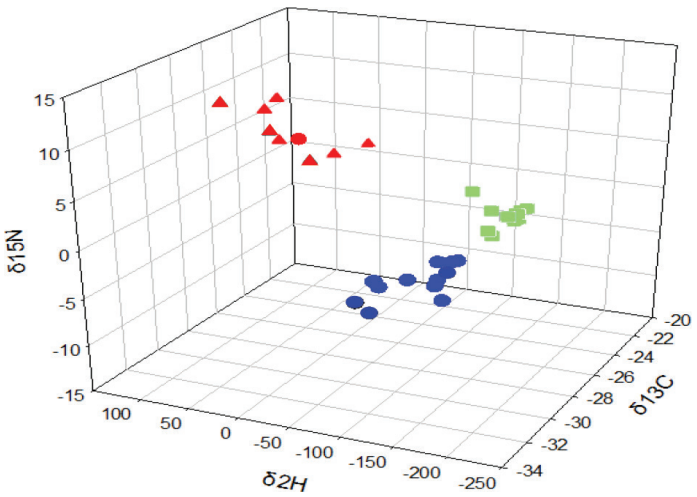

Figure 2: Scatter plots of $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ values from 20 seized methamphetamine samples: (●) synthetic cluster; (▲) semisynthetic cluster; (■) natural cluster.

$\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ values isotope values from 20 methamphetamine samples were then clustered based on synthetic, semi-synthetic, and natural cluster data that had been previously obtained. Of the 20 samples, it is suspected that 10 samples were synthesized using synthetic ephedrine / pseudoephedrine and 10 samples of methamphetamine derived from natural ephedrine / pseudoephedrine.

Figure 2 shows the result of K-means clustering on the $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ values of 17 seized methamphetamine samples, plus methamphetamine and its precursor, and also certified standard materials. Ternary isotope plots of $\delta^{2}H$, $\delta^{13}C$ and $\delta^{15}N$ in three-dimensions presented a graphical illustration of the determination of ephedrines. The data analysis results illustrated the isotope profile from the seized methamphetamine samples were -5.10‰ to 3.84‰ for $\delta^{15}N$ values, -32.61‰ to -27.58‰ for $\delta^{13}C$ values and also -193.91‰ to -80.15‰ for $\delta^{2}H$ values. Based on the isotope clustering criteria, 10 samples were identified to be synthetic origin, 10 samples were classified to be natural cluster, and no sample was identified as semi-synthetic origin.

CONCLUSION

The $\delta^{15}N$, $\delta^{13}C$, and $\delta^{2}H$ isotope profile from ephedrine and pseudoephedrine with known origin sources was performed. The result gives the values for fully-synthetic cluster were $\delta^{15}N$: -9.11‰ to -0.17‰; $\delta^{13}C$: -32.61‰ to -26.06‰; $\delta^{2}H$: -137.57‰ to -50.39‰. Additionally, the values for semi-synthetic cluster were $\delta^{15}N$: 3,03 ‰ to 9,92‰; $\delta^{13}C$: -26,42‰ to -22,38‰; $\delta^{2}H$: 30.13‰ to 130.13‰. Moreover, the values for natural cluster were $\delta^{15}N$: 2.87‰ to 5.36‰; $\delta^{13}C$: -30.32‰ to -27.65‰; δ2H: -201.21‰ to -150.75‰.

The nitrogen and carbon isotope profiles of the synthesized methamphetamine were similar to the ephedrine precursor it used. Meanwhile, the isotope value of hydrogen experienced a shift in values in the range of 13 ± 17‰. It could be said that this was because there was no fractionation of nitrogen and carbon isotopes during the synthesis process. The different synthesis methods did not have a significant effect on the isotope profile. Hence, it could be concluded that it was possible to trace the acquisition sources of ephedrine precursor via the isotopic profile of methamphetamine by using EA-IRMS analysis.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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