Journal of Substance Use

ISSN: 1465-9891 (Print) 1475-9942 (Online) Journal homepage: http://www.tandfonline.com/loi/ijsu20

Impurity characteristics of street methamphetamine crystals seized in Tehran, Iran

Ahmad Shekari, Maryam Akhgari, Farzaneh Jokar & Zahra Mousavi

To cite this article: Ahmad Shekari, Maryam Akhgari, Farzaneh Jokar & Zahra Mousavi (2016): Impurity characteristics of street methamphetamine crystals seized in Tehran, Iran, Journal of Substance Use, DOI: 10.3109/14659891.2015.1068389

To link to this article: http://dx.doi.org/10.3109/14659891.2015.1068389

Published online: 20 Jan 2016.

Journal of Substance Use

www.tandfonline.com/ijsu
ISSN: 1465-9891 (print), 1475-9942 (electronic)

J Subst Use, 2015, 00(00): 1–5
 DOI: 10.3109/14659891.2015.1068389

Taylor & Francis
Taylor & Francis Group

Impurity characteristics of street methamphetamine crystals seized in Tehran, Iran

Ahmad Shekari[1], Maryam Akhgari[2], Farzaneh Jokar[2], and Zahra Mousavi[1]

[1]*Pharmacology & Toxicology Department, Faculty of Pharmacy, Pharmaceutical Sciences Branch, Islamic Azad University (IAUPS), Tehran, Iran and* [2]*Forensic Toxicology Department, Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran*

Abstract

Background. Methamphetamine (MA) is classified as the most widely abused drug during the last decade and it possesses one of the most domestic markets among other drugs of abuse in Iran. Forensic analysis of MA samples is performed in many countries for the elucidation of synthetic pathways, adulterants, and active pharmaceutical ingredients (APIs) deliberately added to them. However, little is known about APIs in MA samples seized in Iran. The current study aimed to identify APIs, intermediates, and manufacturing by-products in MA samples seized in Iran. *Method*. Analytical study was conducted on 112 MA samples using gas chromatography/mass spectrometry method. *Results*. Results showed that MA samples contained MA, amphetamine, ecstasy, phenmetrazine, chlorpheniramine, dextromethorphan, pseudoephedine, ketamine, heroin, and cannabis derivatives in addition to *N*-acetylmethamphetamine, *N,N*-dimethylamphetamine, acetic acid, and other chemicals. *Conclusion*. We can conclude that illicit MA crystals contained impurities originated from manufacturing processes and APIs deliberately added to them. The main synthetic routes for MA synthesis are Leuckart and Nagai methods in Iran.

Keywords

Forensic analysis, gas chromatography/mass spectrometry, impurity characterization, methamphetamine

History

Received 1 May 2015
Revised 12 June 2015
Accepted 29 June 2015
Published online 21 December 2015

Introduction

Methamphetamine (MA) is one of the most addictive substances from the family of amphetamine-type stimulants (ATS) and had been one of the most abused substances in the world in the past two decades, but it was not available in Iranian drug black market before 2005 (United Nations Office on Drugs and Crime [UNODC], 2007). In 2014, UNODC reported that Iran ranked fifth behind Thailand in MA seizure between 2010 and 2012 (UNODC, 2014). Now, MA is the most common available ATS in Iran and its popularity is growing rapidly (Alam Mehrjerdi et al., 2013). The growing demand for MA encourages drug makers to produce illicit forms of this substance in clandestine laboratories. These laboratories were discovered in Iran since 2008 (UNODC, 2014). The product of these substandard laboratories is a complex mixture of MA, additives (cutting agents or adulterants), together with manufacturing by-products and impurities originated from precursors, incomplete reaction of reagents, and inadequate purification. The most common street names for MA are Shesheh/Shishe (glass), Shabu, Dar Va Panjereh, Gach, Lachaki, Ice, and Crystal in Iran (Alam Mehrjerdi, 2013). MA domestic market and seizure continues to surge as shown by the number of people receiving treatment for MA abuse in Iran (UNODC, 2012). Also there are some reports that indicate an increase in the trend of psychostimulants toxicity in Tehran, Iran (Hassanian-Moghaddam et al., 2014). There is increasing recognition that illicit MA may contain active pharmaceutical and nonpharmaceutical ingredients which can cause severe health consequences for users (Choe et al., 2013). This issue has drawn a great deal of attention with the starting the activity of clandestine laboratories to produce illegal drugs without any control measures. Also analysis of by-products, intermediates, impurities, and other active pharmaceutical ingredients (APIs) in MA samples can help in criminal investigation of drug trafficking routes, common synthetic, or geographical origin between seizures and sources of supply (Lurie et al., 2000; Stojanovska et al., 2013). In spite of dramatic increases in the use of MA in Iran, little attention has been paid to MA seizures containing pharmaceutical and other illegal substances deliberately added to them. Most of the research studies had focused on the manufacturing by-products and MA impurity analysis. Khajeamiri et al. (2012), in a study conducted on 50 samples, found out that 1,2-dimethyl-3-phenylaziridine was the most frequently found impurity in MA samples (Khajeamiri et al., 2012). According to Choe et al. (2013), coingredients of over-the-counter drugs, ephedrine and pseudoephedrine, acetaminophen, ambroxol, and other psychoactive drugs such as barbital and ketamine were found in MA samples (Choe et al., 2013). Evidence from Japan suggests that ephedrine and pseudoephedrine were the

Correspondence: Maryam Akhgari, Assistant Professor of Forensic Toxicology, Department of Forensic Toxicology, Legal Medicine Research Center, Legal Medicine Organization, Old Qom Road, 500 meters after Beheshte Zahra, P.O. Box 1816153141, Tehran, Iran. E-mail: akhgari1349@yahoo.com

most impurities in seized MA samples (Mikuma et al., 2015). The main goal of the current study was to determine active pharmaceutical, nonpharmaceutical, and manufacturing by-products in MA crystal samples. In this concern, a systematic toxicological analysis was performed using gas chromatography/mass spectrometry (GC/MS) method.

Materials and methods

Chloroform, methanol, and isopropanol (HPLC grade) were obtained from Merck Chemical CO. (Darmstadt, Germany). Helium (99.99% purity) was supplied by Roham CO. (Tehran, Iran). All chemicals and solvents were of analytical reagent grade obtained from Merck (Darmstadt, Germany). Standards for drugs were obtained from pharmaceutical companies, Tehran, Iran. MA hydrochloride, amphetamine hydrochloride (AM), methylenedioxymethamphetamine (MDMA) hydrochloride, and pseudoephedrine hydrochloride were obtained from Lipomed Pharmaceutical (Arlesheim, Switzerland).

Qualitative and quantitative analyses were conducted on street MA samples. Included in the present study were 112 MA samples referred to forensic toxicology laboratory, Tehran, Iran, between 2012 and 2013 for systematic toxicological analysis using GC/MS method.

Laboratory analyses of samples were as follows.

Characterization of methamphetamine samples

The first step in MA analysis was the visual inspections of physical characteristics, color, form, and weighing of samples. Laboratory analyses of samples were as follows.

Sample preparation method

Five grams of MA samples were weighted out from each seizure. Samples were crushed well to a fine powder. Fifty milligrams of each sample was mixed in 1 mL of phosphate buffer solution (pH = 10 and 0.1 M) and vortexed for 5 min. Each sample was mixed with 500 μL of ethyl acetate and vortexed for 10 min. The mixture was centrifuged for 5 min at 3,000 rpm. Aqueous phase was freezed in a cooling bath and the organic phase (ethyl acetate) was separated for subsequent analysis. Inert substances, bulking agents, and herbal constituents were not tested due to little interest in this study context.

Residues were analyzed as follows: Methanol (100 μL) was added to residues, and after mixing, 0.2 μL of sample was injected into GC/MS. All of the samples were analyzed qualitatively, except for MA, amphetamine, and MDMA. These three ingredients were analyzed quantitatively. The linearity of the method was evaluated at five concentration levels ranging from 30–1500 ng/mL ($y = 5.54 \times 10^{-2} X + 1.8 \times 10^{-1}$) with $r^2 = 0.9910$ for MA; concentration levels ranging from 30–1500 ng/mL ($y = 3.171 \times 10^{-4} X + 2.33 \times 10^{-3}$) with $r^2 = 0.9954$ for AM; and concentration levels ranging from 40–1500 ng/mL ($y = 1.09 \times 10^{-2} \chi + 1.574 \times 10^{-1}$) with $r^2 = 0.9999$ for MDMA. Limit of detection (LOD) was 10 ng/mL for all three analytes. Limit of quantitation (LOQ) was 30 ng/mL for MA and AM and 40 ng/mL for MDMA.

Gas chromatography/mass spectrometry technique

For chemical characterization and qualitative and quantitative analysis of samples, GC/MS had been used as the mainstays of pharmaceutical analysis. An Agilent model 7890A gas chromatograph (Agilent Technologies, Sdn Bhd, Selangor, Malaysia) fitted with split/splitless injector and an HP5-MS capillary column (cross-linked 5% methyl phenyl silicone, 30 m length × 0.25 mm ID × 0.25 μm film thickness) was used. The capillary column was connected to a mass analyzer (MS 5975C) (Agilent Technologies) operated by electron impact (70 eV) in full scan mode (50–550 m/z) with the following parameters: injector temperature, 250°C; interface temperature, 280°C. The oven temperature was programmed as follows: initial temperature, 60°C; initial hold, 1 min; temperature program rate, 2°C/min; final temperature, 280°C; final hold, 15 min. Helium carrier gas was maintained at a constant flow of 1.5 mL/min. NIST, Wiley, and MPW 2011 libraries were used for identification of precursors, intermediates, final products, and APIs.

Results

To detect pharmaceutical and nonpharmaceutical ingredients, precursors, intermediates, and synthetic by-products in MA samples in Tehran, Iran, we analyzed 112 MA samples using GC/MS technique. Results showed that 98 (87.5%) of samples had white color, 7 were creamy, 3 samples were brown, 2 of them were in pink, and 2 of them were in yellow colors. A total of 106 (94.64%) samples were in crystal form and the shape of the rest of samples was noncrystalline. GC/MS analysis showed that all of the samples contained MA and 106 (94.64%) contained amphetamine. The most frequent impurity in MA samples was *N*-acetylmethamphetamine followed by *N,N*-dimethylamphetamine and acetic acid. Other impurities, frequency of their occurrence in seized samples, and the reason for their presence are shown in Table 1. Quantitative analysis of samples showed that the range of MA, AM, and MDMA contents in street MA samples was 20–73%, 15–30%, and 2–5%, respectively. It is important to say that not all impurities were present in all samples.

Discussion

The purpose of the present study was to characterize the impurities in MA samples seized in Iran. According to the results of the study, most of the samples were in white crystalline form. This result was in agreement with those of Khajeamiri et al. (2012). Our study demonstrated that MA samples contained various types of precursors, intermediates, APIs, and other illicit drugs in combination with amphetamine and MA. Amphetamines can be synthesized by numerous synthetic pathways in clandestine laboratories. A wide variety of reagents and precursors are used in the production of ATS, resulting in the manufacturing of a large number of by-products, intermediates, and impurities (Stojanovska et al., 2013).

Synthetic routes are classified as phosphorous–Iodine (Moscow, Nagai, Hypo), Birch, and metal hydrogenation

Table 1. Impurities, frequency of their occurrence, and the reason for their presence in seized methamphetamine samples, Tehran, Iran.

Impurity found	Frequency of occurrence No (%)	Potential reason for presence as impurity or additive
N-acetylmethamphetamine	108 (96.4)	Product of Nagai method, product of MA precipitation using acetic moiety (Allen and Cantrell, 1989)
N,N-Dimethylamphetamine	107 (95.5)	Cutting agent in the production of ATS (Stojanovska et al., 2013)
Acetic acid	105 (93.8)	Used in the production of MA using P2P (Dayrit & Dumlao, 2004)
N-Formylmethamphetamine	102 (91.1)	Produced as incomplete hydrolysis of MA in Leuckart reaction (Stojanovska et al., 2013)
N-Benzyl 2-methylaziridine	95 (84.8)	An intermediate in MA synthesis procedure from ephedrine and pseudoephedrine by Emde and Nagai methods (Ko et al., 2007)
2,7-Dimethylnaphthalene	88 (78.6)	Route and condition specific by-product in Nagai method (Stojanovska et al., 2013)
Phenmetrazine	76 (67.9)	Mood elevating substance (Wille & Lambert, 2004)
Chlorpheniramine	74 (66.1)	Co-ingredients in cold medicine used as pseudoephedrine source (Choe et al., 2013)
Benzaldehyde	17 (15.2)	Starting material in the synthesis of P2P (Dayrit & Dumlao, 2004)
Dextromethorphan	10 (8.9)	Co-ingredients in cough syrup used as pseudoephedrine source (List of narcotic drugs under control, Iran)
pseudoephedrine	9 (8)	Used as precursor in MA synthesis (Brzeczko et al., 2013)
Pheniramine	6 (5.4)	Co-ingredients in cold medicine used as pseudoephedrine source (Choe et al., 2013)
Ecstasy	6 (5.4)	Overlapping with areas of MA synthesis (Puthaviriyakorn et al., 2002)
Ketamine	4 (3.6)	Added to increase psychoactivity
P2P	2 (1.8)	Intermediate reagent in the production of MA by the Leuckart or reductive amination methods (Stojanovska et al., 2013)
Triprolidine		OTC antihistamine in combination with pseudoephedrine used as source of pseudoephedrine in MA synthesis (Choe et al., 2013)
3,6-Diacetylmorphine (heroin)	1 (0.9)	Overlapping with areas of MA synthesis (Puthaviriyakorn et al., 2002)
6- Acetylmorphine	1 (0.9)	Intermediate reagent in acetylation process of morphine to heroin
Codeine	1 (0.9)	Opioid alkaloid
Acetylcodeine	1 (0.9)	Heroin impurity
Papaverine	1 (0.9)	Opioid alkaloid
Caffeine	1 (0.9)	Stimulant effect similar to but milder than ATS
Lidocaine	1 (0.9)	Enhance numbing effect

MA, methamphetamine.
ATS, amphetamine-type stimulants.
P2P = Phenyl-2-propanone.
OTC = Over the counter.

(Emde), using ephedrine and pseudoephedrine as precursors, and reductive amination from phenyl-2-propanone (P2P) (Stojanovska et al., 2013).

Diagnosing the source of substances in street drugs is a crucial task. It is supposed that some impurities such as *N*-acetylmethamphetamine are produced during manufacturing process, whereas other additives such as APIs (3,6- diacetylmorphine, ecstasy, and ketamine) with different chemical structures are added to the final product.

N-acetylmethamphetamine was found in about 96% of our samples. Precipitating of MA in acidic condition in the presence of acetates as solvent yields *N*-acetylmethamphetamine (Allen & Cantrell, 1989). It can be produced from thermal decomposition of an unknown compound in the injection port of GC too (Sekine & Nakahara, 1990).

More than 95% of our study samples contained *N,N*-dimethylamphetamine (DMA). Li et al. (2006) reported that DMA and amphetamine can be the products of pyrolysis at high temperatures using GC/MS analysis method.

Acetic acid was detected in 93.8% of samples as a precipitating reagent (Allen & Cantrell, 1989). This finding is in agreement with other studies (Dayrit & Dumlao, 2004).

More than 90% of samples in the present study contained *N*-formylmethamphetamine. This intermediate is the key and route-specific substance in the production of MA by the Leuckart method (Stojanovska et al., 2013).

The presence of benzaldehyde in about 15% of samples suggests that it was used as starting material for the production of P2P, which is converted to MA in Leuckart method (Dayrit & Dumlao, 2004). The presence of *N*-formylmethamphetamine, P2P, and benzaldehyde in seized MA samples supports more evidence for the use of Leukart method as one of the most routine ways for the production of MA in Iran.

More than 85% of the current study samples contained aziridine and naphthalene derivatives. This is possibly due to the involvement of Nagai method for the production of MA (Makino et al., 2005).

N-Benzyl-2-methyl aziridine was one of the most frequently found (84.8%) impurities in 112 samples in the present study. Ko et al. concluded that the presence of aziridines in MA samples cannot be a key marker for the differentiation between the involvement of Nagai and Emde methods (Ko et al., 2007).

Naphthalenes are products of heating P2P in the presence of an acid (Stojanovska et al., 2013). The presence of 2,7-dimethylnaphthalene in 88% of samples may be due to the connection to Nagai method. Therefore, Nagai method can be another method for the production of MA in Iran.

There are many studies in other countries indicating routes of MA synthesis in a specific geographic area. As indicated by Collins et al. (2007), the most synthetic routes for MA production in Australia are iodine/phosphorus and Birch reduction methods (Collins et al., 2007). MA is synthesized in USA by one of the two methods, from P2P with the reductive amination method or from the reduction of ephedrine and pseudoephedrine. Leuckart and reductive amination methods are used in Europe for MA synthesis (Aalberg et al., 2005; Andersson et al., 2007; Lock et al., 2007).

Many APIs are added to illicit drugs to make synergistic or antagonistic effects with proposed drugs (Cole et al., 2010).

Dextromethorphan was detected in 10 samples in the present study. Dextromethorphan/pseudoephedrine combination (Dextromethrorphan-P in Iran drug list) is used as cough suppressant and decongestant in Iran ("*List of Narcotic Drugs*", 2011). It can be used as a source of pseudoephedrine for illicit production of MA. Moreover, some of this relates to illicit use of dextromethorphan. Dextromethorphan can cause an individual to feel "high" in high doses (Cooper, 2013). This property explains the reason for adding dextromethorphan to MA samples intentionally.

Pseudoephedrine or ephedrine can be used in its pure form or extracted from medicines called sympathomimetic decongestants used as cold or flu drugs (Brzeczko et al., 2013). Chlorpheniramine, triprolidine, and pheniramine are antihistamines which were detected in 66.1%, 1.8%, and 3.6%, respectively. They are coingredients in cold medicines containing pseudoephedrine used for MA synthesis (Choe et al., 2013). The results of our study was in agreement with those of Choe et al. (2013) in Korea, who reported that two samples out of 609 crystal MA showed positive results for chlorpheniramine, whereas Khajeamiri et al. (2012) stated that 12% of their study samples contained chlorpheniramine (Khajeamiri et al., 2012).

Ketamine was one of the APIs in four of samples in the present study. This result has been observed by Khajeamiri et al. (2012). One possible explanation for this finding is that ketamine's psychoactive effect is considered synergistic when combined with MA.

Methyl and propylparaben were detected in one sample together with pseudoephedrine. This finding provides more evidence for the fact that dextromethorphan-P syrup was used as the source of pseudoephedrine in the present study. Parabens are used as preservatives in syrup formulations to avoid alteration or degeneration of dosage form by microorganisms (Khalil et al., 2011).

Formaldehyde contamination of solvents and high injector temperature in GC can result in the conversion of ephedrine to phenmetrazine (Wille & Lambert, 2004). More than 67% of samples showed positive results for phenmetrazine. According to the UN convention of psychotropic substances, 1971 phenmetrazine is a controlled substance and can be abused for its mood elevating property (Wille & Lambert, 2004) and this can be one of the reasons for adding this substance to MA samples.

The origin of some of the impurities in MA samples in the present study is obscure. Dronabinol and cannabidiol were detected in one of the samples in the present study. This is the first report indicating the presence of dronabinol in illicit MA samples.

In agreement with our study MA tablets seized in Thailand contained diacetylmorphine (Puthaviriyakorn et al., 2002).

Cannabinoids and heroin have different structures in comparison to ATS and cannot be categorized as intermediates and synthetic by-products. One possible explanation for the detection of other illicit drugs in MA samples is the common synthesis place for the production of these substances (Puthaviriyakorn et al., 2002).

In fact, the following points should be emphasized; we recommend further studies on samples obtained from other provinces or different geographic areas in Iran to detect impurities, characterization, and routes of production of illicit MA. As illicit drug manufacturers use different methods and precursors for MA synthesis, it is important to perform continuous analysis of illicit drugs. In addition, other added drugs and adulterants may change at different time intervals.

One limitation to this study was that it was not possible to analyze all APIs quantitatively. However, this limitation did not overshadow our main purpose.

Microbial contamination is considered a common task in drug abusers in Iran; therefore, it is recommended to analyze illicit drugs from a micribiological point of view.

Acknowledgments

The authors wish to thank the kind personnel of the Toxicology Department, Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran, for their cooperation in this study.

Declaration of interest

The authors report no conflicts of interest.

References

Aalberg, L., Andersson, K., Bertler, C., Cole, M. D., Finnon, Y., Huizer, H., et al. (2005). Development of a harmonized method for the profiling of amphetamines. II. Stability of impurities in organic solvents. *Forensic Science International*, 149(2–3), 231–241.

Alam Mehrjerdi, Z. (2013). Crystal in Iran: Methamphetamine or heroin kerack. *Daru Journal of Pharmaceutical Sciences*, 21(1), 22.

Alam Mehrjerdi, Z., Barr, A. M., & Noroozi, A. (2013). Methamphetamine-associated psychosis: A new health challenge in Iran. *Daru Journal of Pharmaceutical Sciences*, 21(1), 30.

Allen, A., & Cantrell, T. S. (1989). Synthetic reductions in clandestine amphetamine and methamphetamine laboratories: A review. *Forensic Science International*, 42(3), 183–199.

Andersson, K., Jalava, K., Lock, E., Finnon, Y., Huizer, H., Kaa, E., et al. (2007). Development of a harmonised method for the profiling of amphetamines: III. Development of the gas chromatographic method. *Forensic Science International*, 169(1), 50–63.

Brzeczko, A. W., Leech, R., & Stark, J. G. (2013). The advent of a new pseudoephedrine product to combat methamphetamine abuse. *American Journal of Drug and Alcohol Abuse*, 39(5), 284–290.

Choe, S., Heo, S., Choi, H., Kim, E., Chung, H., & Lee, J. (2013). Analysis of pharmaceutical impurities in the methamphetamine crystals seized for drug trafficking in Korea. *Forensic Science International*, 27(1–3), 48–51.

Cole, C., Jones, L., McVeigh, J., Kicman, A., Syed, Q., & Bellis, M. A. (2010). A Guide to Adulterants, Bulking Agents and Other Contaminants Found in Illicit Drugs (Review). Retrieved from the Liverpool: Centre for Public Health, Faculty of Health and Applied

Social Sciences, Liverpool John Moores University Website. Retrieved from www.cph.org.uk/showPublication.aspx?pubid=632.

Collins, M., Huttunen, J., Evans, I., & Robertson, J. (2007). Illicit drug profiling: The Australian experience. *Australian Journal of Forensic Sciences*, 39(1), 25–32.

Cooper, R. J. (2013). Over-the-counter medicine abuse—A review of the literature. *Journal of Substance Use*, 18(2), 82–107.

Dayrit, F. M., & Dumlao, M. C. (2004). Impurity profiling of methamphetamine hydrochloride drugs seized in the Philippines. *Forensic Science International*, 144(1), 29–36.

Hassanian-Moghaddam, H., Zamani, N., Rahimi, M., Shadnia, S., Pajoumand, A., & Sarjami, S. (2014). Acute adult and adolescent poisoning in Tehran, Iran; the epidemiologic trend between 2006 and 2011. *Archive of Iranian Medicine*, 17(8), 534–538.

Khajeamiri, A. R., Faizi, M., Sohani, F., Baheri, T., & Kobarfard, F. (2012). Determination of impurities in illicit methamphetamine samples seized in Iran. *Forensic Science International*, 217(1–3), 204–206.

Khalil, R., Khanfar, M., Abu Halaweh, M., Yacoub, M., & Bustami, M. (2011). Assessment of the preserving efficacy of the pharmaceutical syrups to identified air-borne microorganisms. *Trends in Applied Sciences Research*, 6, 198–203.

Ko, B. J., Suh, S., Suh, Y. J., In, M. K., & Kim, S. H. (2007). The impurity characteristics of methamphetamine synthesized by Emde and Nagai method. *Forensic Science International*, 170(2–3), 142–147.

Li, T. L., Giang, Y. S., Hsu, J. F., Cheng, S. G., Liu, R. H., & Wang, S. M. (2006). Artifacts in the GC–MS profiling of underivatized methamphetamine hydrochloride. *Forensic Science International*, 162(1–3), 113–120.

List of Narcotic Drugs under Control. Secretary for Food and Drug Affairs, Ministry of Health & Medical Education Iran [Persian language]. Retrieved from http://fdo.behdasht.gov.ir/uploads/114_1206_13.pdf. Accessed December 4, 2011.

Lock, E., Aalberg, L., Andersson, K., Dahlén, J., Cole, M. D., Finnon, Y., et al. (2007). Development of a harmonised method for the profiling of amphetamines V: Determination of the variability of the optimised method. *Forensic Science International*, 169(1), 77–85.

Lurie, I. S., Bailey, C. G., Anex, D. S., Bethea, M. J., McKibben, T. D., & Casale, J. F. (2000). Profiling of impurities in illicit methamphetamine by high-performance liquid chromatography and capillary electrochromatography. *Journal of Chromatography A*, 870 (1–2), 53–68.

Makino, Y., Urano, Y., & Nagano, T. (2005). Investigation of the origin of ephedrine and methamphetamine by stable isotope ratio mass spectrometry: A Japanese experience. *Bulletin on Narcotics*, 57(1–2), 63–78.

Mikuma, T., Iwata, Y. T., Miyaguchi, H., Kuwayama, K., Tsujikawa, K., Kanamori, T., et al. (2015). The use of a sulfonated capillary on chiral capillary electrophoresis/mass spectrometry of amphetamine-type stimulants for methamphetamine impurity profiling. *Forensic Science International*, 249C, 59–65.

Puthaviriyakorn, V., Siriviriyasomboon, N., Phorachata, J., Pan-ox, W., Sasaki, T., & Tanaka, K. (2002). Identification of impurities and statistical classification of methamphetamine tablets (Ya-Ba) seized in Thailand. *Forensic Science International*, 126(2), 105–113.

Sekine, H., & Nakahara, Y. (1990). Abuse of smoking methamphetamine mixed with tobacco: II. The formation mechanism of pyrolysis products. *Forensic Science International*, 35(3), 580–590.

Stojanovska, N., Fu, S., Tahtouh, M., Kelly, T., Beavis, A., & Kirkbride, K. P. (2013). A review of impurity profiling and synthetic route of manufacture of methylamphetamine, 3,4-methylenedioxymethylamphetamine, amphetamine, dimethylamphetamine and *p*-methoxyamphetamine. *Forensic Science International*, 224(1–3), 8–26.

United Nations Office on Drugs and Crime (UNODC). (2007). *2007 World Drug Report, United Nations Publication, Sales No. E.07.XI.5*. Retrieved from http://www.unodc.org/pdf/research/wdr07/WDR_2007.pdf.

United Nations Office on Drugs and Crime (UNODC). (2012). *Annual Report Questionnaire for the Islamic Republic of Iran for 2012*. Retrieved from http://www.unodc.org/documents/southeastasiaandpacific/2014/05/gsda/2014_Global_Synthetic_Drugs_Assessment_embargoed_Tokyo_web.pdf.

United Nations Office on Drugs and Crime (UNODC). (2014). *Vienna: 2014 Global Synthetic Drugs Assessment, Amphetamine-Type Stimulants and New Psychoactive Substances*. Retrieved from http://www.unodc.org/documents/scientific/2014_Global_Synthetic_Drugs_Assessment_web.pdf.

Wille, S. M., & Lambert, W. E. (2004). Phenmetrazine or ephedrine? Fooled by library search. *Journal of Chromatography A*, 1045(1–2), 259–262.