THE RECOVERY AND DETECTION OF TRACE METHAMPHETAMINE RESIDUES DEPOSITED ON LABORATORY COAT MATERIALS

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THE RECOVERY AND DETECTION OF TRACE METHAMPHETAMINE RESIDUES DEPOSITED ON LABORATORY COAT MATERIALS

by

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LIST OF UNITS

%	percent
g	gram
µg	microgram
ng	nanogram
mg	milligram
cm	centimetre
cm^2	square centimetre
mol	mole
fpm	feet per minute
ppb	parts per billion
min	minute
mL	Millilitre
µL	microlitre
mΩ	milliohm
m	meter
mm	millimetre
µm	micrometer
°C	degree Celcius
s	seconds
rpm	revolutions per minute

LIST OF ABBREVIATIONS

% recovery	Percentage of recovery
% RSD	Precent relative standard deviation
ACN	Acetonitrile
AIHA	American industrial hygiene association
ANOVA	Analysis of variance
ANSI	American national standards institute
ATR-FTIR	Attenuated total reflectance-Fourier transform infrared spectroscopy
ATS	Amphetamine
C14	N-Tetradecane
CE-PDA	Capillary electrophoresis and photodiode array detection
CF	Chloroform
CNS	Central nervous system
COVID-19's	Coronavirus disease 2019
DCM	Dichloromethane
DESI	Desorption electrospray ionization
DESI-MS	Desorption electrospray ionization-mass spectrometry
df	Degree of freedom
DLLME	Dispersive liquid-liquid microextraction
DOE	Design of experiment
EF	Enrichment factor
EI-MS	Electrospray ionization-mass spectrometry
EPA	Environmental protection agency
FDAA	(S)-(−)-1-fluoro-2,4-dinitrophenyl-5-alanine amide
FID	Flame ionisation detector
FTIR	Fourier transform infrared spectroscopy
GC	Gas chromatography
GC-FID	Gas chromatography- flame ionisation detector
GC-FTIR	Gas chromatography- Fourier transform infrared spectroscopy
GC-MS	Gas chromatography-mass spectrometry
HFBA	Heptafluorobutyric acid
IPA	2-propanol

IR	Infrared
LLE	Liquid-liquid extraction
LOD	Limit of detection
LOQ	Limit of quantitation
m/v	Mass to volume ratio
m/z	Mass to charge ratio
MDA	3,4methylenedioxyamphetamine
MDEA	3,4-methylenedioxy-N-ethylamphetamine
MDMA	3,4-methylenedioxy-methamphetamine
MeOH	Methanol
MS	Mass spectrometry
NADA	National anti-drug agency
NaOH	Sodium hydroxide
NIOSH	National Institute for Occupational Safety and Health
PBD	Plackett-burman design
PFC	Prefrontal cortex
PPE	Personal protective equipment
p-value	Probability value
QC	Quality control
RSM	Response surface methodology
SN1	Substitution of intramolecular nucleophilic
SPME	Solid phase microextraction
TFA	Trifluoroacetyl
TFAA	Trifluoroacetic anhydride anhydrous
THS	Thirdhand smoke
UNODC	United Nations Office on Drugs and Crime
α-cleavage	Alpha-cleavage

LIST OF APPENDICES

PEMULIHAN DAN PENGESANAN SISA METAMFETAMIN SURIH YANG DIDEPOSITKAN PADA BAHAN KOT MAKMAL

ABSTRAK

Pengendalian dan pemprosesan dadah terlarang berkemungkinan mencemarkan permukaan kelengkapan pelindung diri yang digunakan oleh juruanalisis di dalam makmal pengujian dadah. Pencemaran dadah sedemikian, jika ada, mungkin membawa kepada pendedahan jangka panjang yang berbahaya. Justeru, pemantauan pencemaran yang mungkin berlaku adalah penting untuk mengurangkan kemudaratan yang terhasil daripada pendedahan tersebut. Dengan menggunakan metamfetamin sebagai petunjuk pencemaran, kajian ini bertujuan untuk memulih semula dan mengesan sisa metamfetamin surih yang didepositkan pada bahan kot makmal. Dalam kajian ini, metamfetamin dipilih sebagai bahan sasaran kerana kelaziman rampasan yang tinggi di Malaysia dan sentiasa dihantar ke makmal forensik untuk analisis. Suatu prosedur pengekstrakan cecair-cecair penyebaran (DLLME) pada mulanya dioptimumkan, diikuti oleh terbitan metamfetamin menggunakan asid trifluoroasetik dan akhirnya pengesanan melalui kaedah kromatografi gas-spektrometri jisim (GC-MS). Metamfetamin dengan kepekatan yang diketahui telah diletakkan ke atas tujuh jenis kot makmal dan peratusan pemulihan mereka kemudiannya ditentukan dan dibandingkan. Berdasarkan pengoptimuman kaedah gerak balas permukaan, prosedur DLLME menggunakan kombinasi 685 µL diklorometana sebagai pelarut pengekstrakan dan 1000 µL 2-propanol sebagai pelarut serakan dengan vorteks selama 90 saat dan pengemparan pada 500 rpm selama 5 minit telah digunakan untuk pemulihan semula metamfetamin daripada substrat kain.

Metamfetamin terbitan didapati memberi keputusan yang lebih baik bagi pengesanan metamfetamin surih dengan kaedah GC yang disahkan (lineariti: y= 0.0017 x - 0.4698, R^2= 0.9993; had pengesanan: 7.80 ng/mL; had pengkuantitian: 23.40 ng/mL; kepersisan intra-hari: 3.35 - 3.76 %; kepersisan antara hari: 4.65 - 6.50 %; kejituan: 94.92% - 106.01%). Pengesanan metamfetamin juga disahkan melalui perbandingan dan padanan dengan pengkalan data spektrum jisim. Peratusan pemulihan semula metamfetamin daripada tujuh jenis bahan kot makmal telah ditentukan dengan peratusan melebihi 45% pada tiga tahap kepekatan yang berbeza, termasuk 0.5, 1.5, and 3 µg/100 cm^2. Kesimpulannya, kajian ini telah berjaya memulihkan semula dan mengesan sisa metamfetamin surih yang didepositkan pada bahan kot makmal berdasarkan prosedur DLLME-GC-MS yang dicadangkan.

THE RECOVERY AND DETECTION OF TRACE METHAMPHETAMINE RESIDUES DEPOSITED ON LABORATORY COAT MATERIALS

ABSTRACT

Illicit drugs handling and processing could potentially contaminate the surfaces and personal protection equipment used by the analysts in drug testing laboratories. Such drug contamination, if any, might lead to long-term harmful exposure. Therefore, the monitoring of possible contamination is crucial to reduce the harmfulness resulted from the exposures. Using methamphetamine as a contamination indicator, this study aimed to recover and detect trace methamphetamine residues deposited on the laboratory coat material. In this study, methamphetamine was chosen as the target substance due to its high prevalence of seizures in Malaysia which is often ended up in the forensic laboratory for analysis. A dispersive liquid-liquid microextraction (DLLME) procedure was firstly optimised, followed by the derivatisation of methamphetamine using trifluoroacetic acid anhydride and finally the detection by gas chromatography-mass spectrometry (GC-MS) method. Known concentrations of methamphetamine were deposited on seven types of laboratory coat materials, and their recovery percentages were then determined and compared. Based on the response surface methodology optimisation, DLLME procedure utilising 685 µL dichloromethane as extraction solvent and 1000 µL 2-propanol as disperser solvent in combination with vortexing for 90 seconds and centrifugation at 500 rpm for 5 minutes was used for the recovery of methamphetamine from fabric substrate. Derivatised methamphetamine was found to provide enhanced responses for the detection of trace

methamphetamine through the application of validated GC method (linearity: y= 0.0017 x - 0.4698, R^2= 0.9993; limit of detection: 7.80 ng/mL; limit of quantification: 23.40 ng/mL; intra-day precision: 3.35 - 3.76%; inter-day precision: 4.65 - 6.50%; accuracy: 94.92% - 106.01%). The presence of methamphetamine was also confirmed through the comparison and matching with mass spectral database. Percentage recoveries of methamphetamine from seven types of laboratory coat materials were determined to be more than 45% at three different concentration levels covering 0.5, 1.5, and 3 µg/100 cm^2. To conclude, this study had successfully recovered and detected the trace methamphetamine residues deposited on laboratory coat materials based on the proposed DLLME-GC-MS procedure.

CHAPTER 1

INTRODUCTION

1.1 Background of study

Methamphetamine, a type of amphetamine-type stimulants, causes stimulatory effects on the central nervous system, including enhanced alertness and agitation (National Center for Biotechnology Information, 2022). Additionally, it might also result in adverse health effect such as behavioural changes, skin-related reactions, and respiratory problems (Kuhn et al., 2019). Dizziness, eyes and skin irritation, as well as breathing difficulties are among the methamphetamine-related signs and symptoms (Zamanian et al., 2017; National Center for Biotechnology Information, 2022). From the perspective of forensic science, the analysis of methamphetamine allows the detection of drug related activities, focusing on the determination of its presence in the seized or biological samples, and followed by its quantification. However, there is a frequently overlooked aspect, involving the contamination by such drug substance during the handling and processing of methamphetamine, particularly in drug testing laboratories.

Methamphetamine could be exposed to the laboratory employees through both dermal absorption and inhaled exposure routes. An estimated 67% of methamphetamine could be breathed, leaving 33% to be ingested, according to a study where the drug substance was deposited on the surface of surrounding environments such as walls, countertops, and floors (Kuhn et al., 2019). Bentur *et al*. (2013) also reported that the workers from the analytical laboratory had suffered dizziness, eyes and skin irritation, breathing problems, and sporadic migraines due to prolonged occupational exposure to illicit drugs. Previous studies emphasised on the significant exposure to methamphetamine among the laboratory personnel, and in one way the drug substance

might have contaminated their personal protective equipment (PPE) especially laboratory coat due to the sorption effect of methamphetamine on cloth materials (Morrison et al., 2015). Therefore, the detection of methamphetamine residues from laboratory coat is important to protect their safety and well-beings.

All laboratory workers must wear laboratory coats in most routine drug testing operations to protect and minimise exposure from incidental contact to the worker's skin and personal cloth. It is specified in the policy guideline and emphasised during laboratory-specific safety training (NIH-OSHC, 2016; NIOSH, 2020). However, the procedure for cleaning and decontamination of laboratory coat was less concern in drug testing laboratories. To the author's knowledge, it was unclear how the cleaning and decontamination of laboratory coat was carried out in these laboratories.

A level of methamphetamine present that poses no health hazards is referred to as a "safe level" (Wright et al., 2019). A "reference value" is used to establish a safe level and it is represented by a quantity of a substance in each surface area tested. In term of drug, it is the volumetric amount of a substance that can be present without harming human health. In the case of the United States, variations in the acceptable amount were found, ranging from 0.05 µg/100 cm^2 to 1.5 µg/100 cm^2, even among states (Kuhn et al., 2019). Furthermore, the federal government of the United States or consensus organisations have not established any occupational exposure limits and scientific information for the outcomes of drug testing (NIOSH, 2020). Note that there is no permissible surface methamphetamine level available in Malaysia. In fact, there was a very limited availability of guidelines, standards, and regulations for methamphetamine remediation. The only guidelines for such methamphetamine control were the Dangerous Drugs Act 1952 (Revised 1980). Therefore, the continuous occupational exposure to methamphetamine especially for those who worked in

controlled substance laboratories might have suffered unintended exposure by inhalation and skin contact, which might result in adverse health outcomes and needing immediate actions.

1.2 Problem statement

The importance in detecting illicit methamphetamine contamination has long been recognised especially in clandestine drug laboratories due to the significant demand of the illicit drug by the users, increasing the domestic manufacturing and international trafficking activities. It was undoubtable that the exposures to the methamphetamine residue may result in acute and long-term adverse health impacts, where several studies were carried out testing the drug residues within the clandestine laboratories, both in active and inactive stages. From another perspective, such contamination was also seldom reported in those drug testing laboratories. Note that these laboratories are always exposed to the risk of drug substance originated from the seized narcotic and toxicological samples which contained drugs. During the handling and processing of these samples, the analysts are frequently subjected to threat, potentially affect their health and safety, even they were protected by the PPE such as laboratory coats. Furthermore, airborne methamphetamine could be produced while handling or processing, and they might also contaminate the bench and any surfaces within the drug testing laboratories. In view of this, the analysts are probably exposed to the unintentional occupational exposure of methamphetamine with their routine daily works dealing with drug substances.

While earlier studies had predominantly focused on the procedure and guidelines on the recovery of methamphetamine from non-porous surfaces, including granite, limestone, marble, glass plate and drywall (Madireddy *et al*., 2013; Abdullah

& Miskelly, 2010; Patrick *et al*., 2009), testing of such drug substances from porous surfaces are seldom reported. However, porous materials, such as the laboratory coats, are the substrate which carry the highest chance of methamphetamine contamination, as they are the must-wear protection by every analyst during sample processing and analysis in the drug testing laboratory. In other words, these people are always in risk where the contaminated laboratory coats are the sources of exposure.

The procedure and guidelines for methamphetamine testing, as well as the guidance and protocol in the management of contaminated residue on porous materials are less available, particularly in term of direction and regulation as pointed out by EPA (2016). It was agreed that the recovery of methamphetamine from the non-porous surface had been approached by previous research using wipe technique and proven to be effective. However, it was less effective when the procedure was applied to recover the methamphetamine from porous surfaces. Conventionally, liquid-liquid extraction (LLE) method used to recover methamphetamine from any surface required large volume of organic solvent, and therefore a dispersive liquid-liquid microextraction (DLLME) technique was to be explored in a combination with gas chromatography-mass spectrometry (GC-MS) detection. Therefore, this research contributes to the existing literature on the studies of an analytical procedure to recover the methamphetamine from porous surface, specifically the fabric materials, for its determination through the application of gas chromatographic technique.

1.3 Scope of study

Methamphetamine-related problem is a global issue, East and South-East Asia are predicted to have the second greatest number of users (corresponding to 10 million users) (UNODC, 2022b). In Malaysia, methamphetamine is the most abused drugs

according to the National Anti-Drug Agency since 2017, replacing opiates (NADA, 2021). Furthermore, it continues to be the most manufactured ATS worldwide (UNODC, 2019), probably due to its simplicity in the manufacturing procedure using simple chemical ingredients. With that, significant demand for illicit methamphetamine was reported every year with huge number of the narcotic samples submitted to the forensic drug laboratories for testing.

Accordingly, this research explored the detection of methamphetamine residues from porous materials, but only the fabric materials that made up laboratory coat were investigated. It was noted that laboratory coat is a compulsory PPE, and the fabric materials are in contact to the skin of an analyst. All laboratory workers are required to worn laboratory coats in most routine drug testing operation to protect and minimise the risk exposure based on the policy guideline. Therefore, long term exposure could be arisen due to the inhalation of vapour methamphetamine and direct contact of the drug with the skin. The study focused on laboratory coat materials was an initiation to establish a method to detect the contamination which can further explore to other surfaces within a laboratory.

In the present study for the detection of methamphetamine, a DLLME technique in a combination with GC-MS detection was used. DLLME technique firstly developed by Assadi and colleagues was found to provide a good solution to various pre-treatment of sample prior to gas chromatography analysis. Furthermore, a design of experiment (DOE) has been applied in various functional areas, one being research to determine the inter-relationship between variables and to determine the significant ones. In the current study, the optimisation of DLLME technique was carried out involving Plackett-Burman Design.

1.4 Aim and objectives

The aim of this research is to study the detection of trace methamphetamine residues based on the response surface methodology optimised protocol from different types of laboratory coat materials. To achieve the aim, the objectives were set as follows:

i. To validate a gas chromatography method for the detection of methamphetamine.
ii. To establish the optimised conditions of DLLME procedure for the recovery of methamphetamine through a Plackett-Burman Design.
iii. To investigate the recovery of methamphetamine from laboratory coat materials using the established extraction procedure and detection method.

1.5 Significance of study

The novelty of this study would be the establishment of response surface methodology optimised extraction and detection protocol for the detection of low-level methamphetamine, specifically from porous materials. The protocol would also allow for good recoveries of methamphetamine, in addition to its detection to monitor the contamination level of laboratory coats. Since the laboratory coat is an important PPE worn by the analyst, the readily available of an extraction and analytical method would allow for the screening and monitoring of contamination within a drug testing laboratory. In a long-term observation, the periodical testing based on the proposed method would help in detecting such contamination in early stage to prevent consecutive health risks and allow for proper decontamination and planning strategies.

In addition, the protocol introduced in this study was to minimise the usage of solvent and to improve extraction sensitivity. Conventionally, LLE method which consumes a large amount of organic solvent has been used for the preparation and

extraction of target substance. However, it was undoubtable that exposure to organic solvents might lead to another form of health risk. Utilisation of DLLME would aid in minimising the use of solvents and to be completed in a shorter time.

This study would determine the efficiency of extraction of the solvent extraction in recovering the methamphetamine from various laboratory coat materials. The method could then be applied on the actual laboratory coats collected from the drug testing laboratories to determine if there is any contamination. Compilation of background data on contamination could aid in providing insight on the cleanliness of a drug testing laboratories and making decisions on requirement of decontamination and remediation approaches. The determination on the sources of illicit drugs contamination allows for improvement and enhancement of policies related to handling and processing of forensic evidence.

CHAPTER 2

LITERATURE REVIEW

2.1 Illicit Drugs

Illicit drugs are substances which national or international regulations forbid for non-medical use (Degenhardt & Hall, 2012 ; UNODC, 2021a). In the context of international drug control, illicit drugs can be referred as “narcotic drug”, indicating any substance, either natural or synthetic, which is listed in the Schedules I and II of the Single Convention on Narcotic Drugs (1961) and that Convention as amended by the 1972 Protocol Amending the Single Convention on Narcotic Drugs (1961). Single Convention on Narcotic Drugs of 1961 is the international drug control schedule to classify certain substances for the medical and scientific purposes and prevent their diversion into illicit channels. Figure 2.1 illustrates the classification of drug substances in Single Convention on Narcotic Drugs of 1961 (UNODC, 2016).

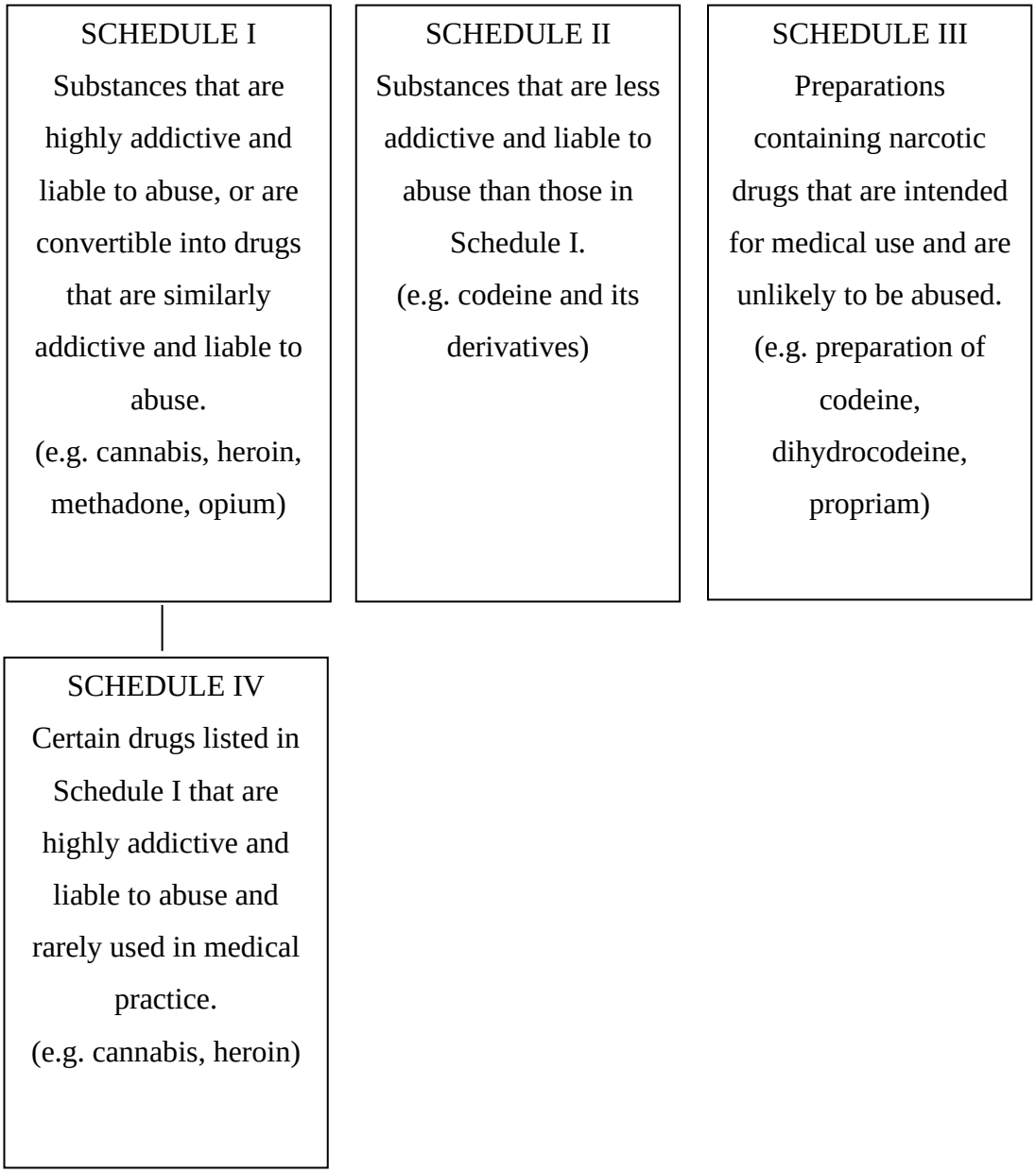

Figure 2.1: Single Convention on Narcotic Drugs of 1961.

Generally, oral intake, intranasal “snorting” the powder, inhaling the smoke or needle injection are the common ways to consume illegal drugs. Misuse of illicit drugs was reported have contributed to the increase in the crime rates, health issues and job issues (Netherland & Hansen, 2016). It has long been assumed that illegal drugs, in addition to the alleged active ingredient, could have significant negative health effects to the user or even cause premature death (Frances, 2013). In fact, majority of the illicit drugs that muddles all aspects of their manufacture, delivery, and preparation for use

are incompatible with the quality assurance, sterile production, and precise dosage administration associated with Good Manufacturing Practice (Gouveia et al., 2015). Furthermore, illicit drugs, both plant-based and synthetic drugs, could escape into the environment and even when present in low amounts in the ambient air, such illicit drugs are suspected of causing long-term negative health effects (Degenhardt & Hall, 2012). They had been reported as the most recent group of emerging pollutants to be identified in the aquatic environment (Frances, 2013). Moreover, some illicit drugs are more polar than contaminants of historical concern and are not readily absorbed by subsoils or other low-organic-matter products which could enter the surface or groundwater (Pal et al., 2013).

2.2 Methamphetamine

Methamphetamine (Figure 2.2) is a principal member of a larger class of substances known as "amphetamine-type stimulants (ATS)," which also includes "ecstasy-type drugs" such as 3,4-methylenedioxy-methamphetamine (MDMA), popularly referred to as "ecstasy," 3,4-methylenedioxyamphetamine (MDA), and MDEA (3,4-methylenedioxy-N-ethylamphetamine) (Morais, 2015). Methamphetamine base, also known as (2S)-N-methyl-1-phenylpropan-2-amine, has a molecular formula $C_{10}H_{15}N$ and molecular weight of 149.23 g/mol. The salt form that is found most frequently is methamphetamine hydrochloride with a molecular mass of 185.69 g/mol and melting point at 170°C. It is considered as less volatile due to the molecule's strong intermolecular hydrogen bonding. The solvent including methanol, dichloromethane and chloroform could dissolve the methamphetamine (UNODC, 2006). Consequently, for sample extraction and analytical analysis of methamphetamine, methanol, dichloromethane, and chloroform are frequently utilised as solvents.

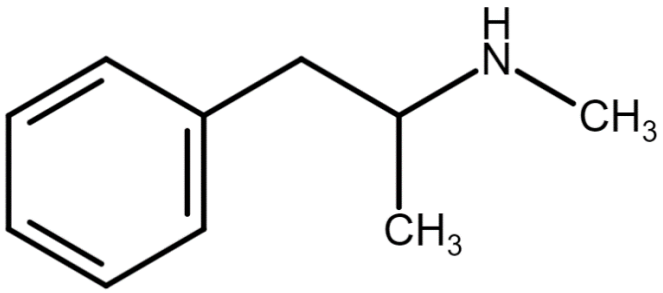

Figure 2.2: Methamphetamine structure.

Methamphetamine produced illegally comes in a variety of forms. Powder, crystals (often referred to as "Crystal," "Ice," or "Shabu"), and tablets (usually referred to as "Yaba") are some of these forms (UNODC, 2006; Petit et al., 2012). Generally, there are two isomeric forms of methamphetamine, namely the d-methamphetamine (dextrorotatory methamphetamine) and l-methamphetamine (laevorotatory methamphetamine) (Lee et al., 2006). The d-methamphetamine, also known as the s-methamphetamine, has the most physiologic and behavioural effects and the greatest capacity to stimulate the central nervous system (CNS) which is more effective dopamine releaser compared to l-methamphetamine (Morais, 2015). The substance known as "ice" or "crystal meth" is the chemical name for s-methamphetamine hydrochloride, which usually appears as white or transparent crystals (Cruickshank & Dyer, 2009). Crystalline methamphetamine, specifically, is considerably more potent as a highly harmful substance with a high level of dependence on liability (O'Neill, 2014).

2.3 Health effects of methamphetamine

When methamphetamine is injected or smoked, the symptoms are immediate; and it can last about 20 minutes after oral ingestion or five minutes after snorting. The

abuse of methamphetamine by injection and smoking has higher bioavailability, faster onset of action, and stronger peak effects than snorting or swallowing, and are also more prone to cause dependence (O'Neill, 2014). The half-life of methamphetamine could be longer (ranging from 8-12 hours) as compared to other stimulants such as nicotine and cocaine (Romanelli & Smith, 2006).

Methamphetamine is known as a psychomotor stimulant drug with powerful physiological effects on both peripheral and central nervous systems, causing physical and psychological changes of upon consumption (Panenka *et al*., 2013). It is a CNS stimulant that causes intoxication or irreversible changes of neuronal by stimulating dopamine and norepinephrine receptors (Anglin et al., 2000; Winslow et al., 2007), altering and impairing the dopaminergic circuits in the brain (Ares-Santos et al., 2013). It could damage the prefrontal cortex (PFC), a component of the dopaminergic mesocortical system essential for regulating cognitive behaviour, affective function, consciousness, and language processing (Tehrani et al., 2019). Acute toxic use of methamphetamine might also produce life-threatening effects on the central nervous and cardiovascular systems, such as the high body temperature, heart arrhythmia, stroke, stomach cramps, and trembling, especially with high dosage consumption. Additionally, it might also induce elevated anxiety, insomnia, violent impulses, paranoia, and hallucinations (Anglin et al., 2000). On the other hand, long-term use of methamphetamine might lead to irritable and paranoid state along with little or no sleep (Romanelli & Smith, 2006).

During the intake of methamphetamine by the drug users, residual smoke pollutant could be present on surfaces and in dust are known as thirdhand smoke (THS). These substances can be released again into the gas phase interact with other contaminants and oxidants to form secondary pollutant (Yeh et al., 2022). On the other

hand, THS could be passively taken by non-users through a variety of exposure routes due to its presence in the air, dust, and on surfaces. The residue exposure in humans could be occurred by skin absorption, inhalation of gaseous substances or aerosol particles, or both. The gas-phase of methamphetamine will enter rapidly to bloodstream and brain have an immediate effect to human body (Yeh et al., 2022). Inhalation was also reported to be the main route of exposure by Ares-Santos et al. (2013).

People who were not directly involved in drug intake was found not to experience any acute health effects (Bitter, 2017). Chronic exposure of methamphetamine might result in serious neurological damage as well as harm to the heart, lungs, and other organ systems. It could also lead to personality changes, psychotic symptoms, and lips and tongue ulcers (Ares-Santos et al., 2013). In certain instances, chronic and repeated methamphetamine inhalational exposure was resemblant with significant pulmonary injury (Zamanian et al., 2017).

2.4 Global statistics of methamphetamine

Methamphetamine is a rapidly evolving global issue (UNODC, 2016; UNODC, 2022). According to the UNODC (2022a), methamphetamine continues to dominate global ATS trafficking, according to data released on seizures of the drug. A record amount of approximately 525 tonnes of ATS was confiscated in 2020, representing a 15% year-over-year rise and a growing trend was seen from 2010 to 2020. Methamphetamine is comprised for 72% of the ATS confiscated globally between 2016 and 2020. The number of nations reporting with methamphetamine seizures had increased five-fold from 84 between 2006 and 2010 to 117 between 2016 and 2020 (UNODC, 2022b).

A significant area for the strategy's implementation for methamphetamine manufacture and trafficking by UNODC is the East and Southeast Asia as these two regions had hosted the biggest methamphetamine markets in the world (UNODC, 2021a). Seizures of methamphetamine have been rising in the two biggest markets; they increased by 7% in North America and by 30% in South-East Asia compared to 2021, respectively. Moreover, methamphetamine seizures from the South-West Asia also reached a high record level, rising by 50% in 2020 compared to 2019 (UNODC, 2022b). Methamphetamine availability seems to have increased concurrently with demand in the Southeast Asia. Despite COVID-19's limits on commerce and transportation movement, countries in the region have verified seizures in 2020 totalling at least 169 tonnes, increased by 20% from the 141 tonnes seized in 2019. It was estimated that 0.7% of the world's population, or 34 million people aged 15 to 64, used amphetamines in the previous year. Note that the estimation was based primarily on self-reported responses to general population surveys (UNODC 2022a; UNODC 2022b).

2.5 Production of methamphetamine

Methamphetamine is a class of synthetic drugs that can be synthesised and manufactured in a clandestine drug laboratory (Hamdan *et al*., 2015). In 1893, Nagai Nagayoshi, a Japanese scientist first synthesised the methamphetamine from ephedrine after six years of the discovery of amphetamine (Maxwell & Brecht, 2011). Methamphetamine can be quickly synthesised from simple chemical components unlike cocaine which is a plant-derived drug and final products comprises trace amounts of precursor compounds (pseudoephedrine, ephedrine and 1-phenyl-2-propanone), chemicals (such as hydrochloric acid, toluene and mercuric acid) and synthetic methods (Kunalan et al., 2009; Onoka et al., 2020). The Leukart reaction (see in Figure 2.3)

involves the chemical reaction where phenylacetone (also known as 1-phenyl-2-propanone and benzyl methyl ketone) is condensed with N-formylmethylamine in the presence of formic acid, was first used to produce methamphetamine in clandestine drug laboratories. The finished product is a racemic containing an equal mixture of d-methamphetamine and l-methamphetamine, but it might also be contaminated with phenylacetone. In addition, the "P-2-P method" also known as reductive amination (Figure 2.3) produces methamphetamine utilising phenylacetone (1-phenyl-2-propanone) as the precursor in combination with aluminium, methylamine and mercuric acid (Onoka et al., 2020).

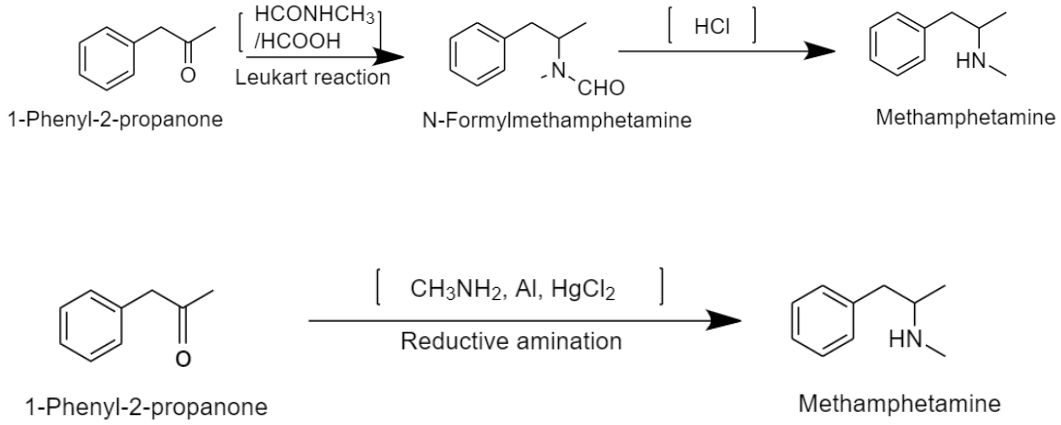

Figure 2.3: Leukart reaction and Reduction amination method.

Nagai method utilising the natural substance, namely the ephedrine or pseudoephedrine compounds, replaced the "P-2-P method" to produce the "ice" form of methamphetamine and the product is potent. The preparation method of "ice" reduced the β-hydroxyl group on the ephedrine or pseudoephedrine using a combination of iodine and red phosphorous as demonstrated in Figure 2.4. Ephedrine or pseudoephedrine, red phosphorous and hydriodic acid is first heated, filtered, made the solution basic, and then extracted. Then, the extracted product is crystallised as the

hydrochloride salt from hydrogen chloride gas or from acetone/ether with hydrochloric acid or from trichloromonofluoromethane and hydrogen chloride gas. The hydrochloride salt of methamphetamine stays volatile and does not decompose when heated thus it will allow the abuser to inhale the methamphetamine fumes (Lee et al., 2008). In Moscow method, iodine and water are combined instead of hydriodic acid (Figure 2.4) (Man et al., 2009). The Birch Reduction technique which is also known as Nazi method used ephedrine or pseudoephedrine in combination with lithium and anhydrous ammonia to produce the methamphetamine (Onoka et al., 2020).

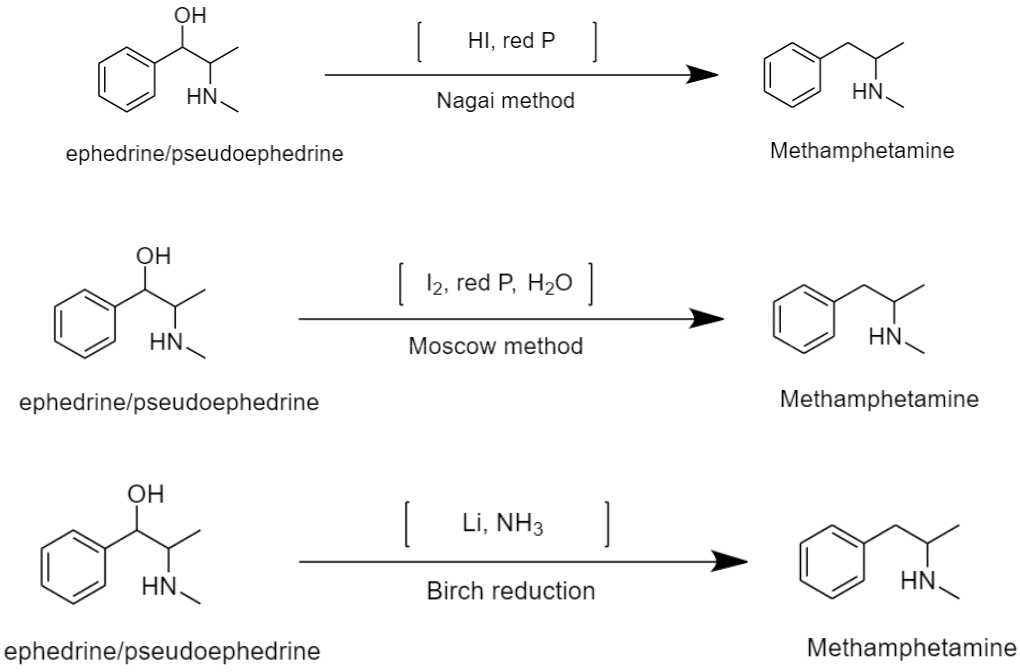

Figure 2.4: Reduction of ephedrine or pseudoephedrine (Nagai, Moscow, and Birch Reduction).

Additionally, Emde method (Figure 2.5) established the configurations of ephedrine by reducing chloroephedrine by chloride reducing agent, contrast to the phosphorous-based reducing agent such as hypophosphorous acid or red phosphorous approach (Lee et al., 2008). This scheme underwent the substitution of intramolecular

nucleophilic (SN1) or substitution of intermolecular on the -OH of the ephedrine or pseudoephedrine with chloride (Onoka et al., 2020).

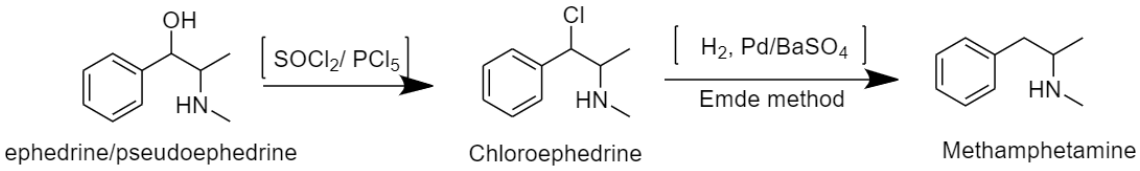

Figure 2.5: Emde method.

The rising popularity of methamphetamine manufacture might be attributed to its relatively easier manufacturing method, detailed instructions widely available in books and on the internet, and the availability of ingredients that could be found in daily life (Morais, 2015 ; UNODC, 2021b). In Malaysia, the number of methamphetamine manufacturing facilities demolished had declined from 16 in 2015 to 4 in 2020 (UNODC, 2021a). However, it might have certain clandestine laboratories which had successfully escaped the monitoring of law enforcement teams. Furthermore, a decrease on the dismantling of clandestine laboratories was not reflected on the seizure, where greater amount of illicit methamphetamine was seized at the same period. Such statistics might also suggest that certain portion of these dug substances could have been trafficked into Malaysia through illegal routes and enter the market.

2.6 Contamination of methamphetamine in drug testing laboratory

Drug residues could be present in almost all areas within forensic laboratories. With that, people might be exposed to low levels of these drug during their handling and analyses (Sisco & Najarro, 2019). The unintended occupational exposure to illicit substances among personnel working in controlled substance laboratories are

concerned. In fact, the forensic drug laboratory analysts could be highly exposed to methamphetamine in the air, hands or on the laboratory surfaces and workplace through contact, direct transmission, and/or airborne particle suspension (Sisco et al., 2019). Methamphetamine was one of the most prevalent drug substances with average amounts of 1.3 ng/cm^2 on the surfaces of the workspace (Sisco & Najarro, 2019). When handling and opening large amounts of drugs, this substance may be released in aerosolised form throughout the laboratory, appearing as particulates (Sisco et al., 2018). Drug residues could be deposited easily to surfaces by contact or through depositing airborne drug particulates (Sisco & Najarro, 2019).

NIOSH (2020) reported that chemists (9 of 13) who had handled cases contained detectable methamphetamine levels with the range of 1.1–33 ng/swab using handwipe sampling method. Other than the chemists, the detectable stages of illicit drugs withinside the air samples of a few personnel (5 of 9) who had not to contact with the drugs were also measured. The unintentional exposure of illicit substances to the laboratory staff was mainly due to their work procedures and surroundings. For instance, methamphetamine detected in the surface samples taken from the computer keyboards were ranged from 0.0079 to 0.046 µg/100 cm^2. Besides, twelve out of thirteen laboratory benches samples had methamphetamine levels, ranging from 0.0017 to 0.45 µg/100 cm^2. Furthermore, the average face velocities of the six out of the eight fume hoods in the laboratory bench areas recorded above 150 feet per minute (fpm) velocity that did not meet the standards set by the American National Standards Institute (ANSI) and the American Industrial Hygiene Association (AIHA). It was noted that turbulent flow may occur at speeds greater than 150 fpm. Therefore, a lower velocity (60-80 fpm) was required for an ideal laboratory conditions and hoods with superior containment properties. The potential exposure control gaps were also occurred due to

the lack of specificity or personnel awareness of respiratory protection programmes to the laboratory workers (NIOSH, 2020).

Moreover, it was possible for trace amounts of drugs to be deposited on surfaces during the processing and handling of drug seizures in forensic laboratories (Sisco et al., 2018). Certain surfaces in the testing laboratory surpassed the standard stated limit for methamphetamine contamination (NIOSH, 2020). For examples, methamphetamine (0.11 µg/100 cm^2) was found in a surface sample taken from a dusty shelf in the laboratory which exceeded the standard state or local threshold of 0.1 µg of methamphetamine per 100 cm^2 area. Surfaces were regularly touched such as electrical balances, benches, instruments, doorknobs, storage cabinets and microscopes had been observed with detectable methamphetamine residues (Sisco & Najarro, 2019; Sisco et al., 2018).

Special attention should be given to cleaning or using mitigation techniques in drug testing laboratories. Workspaces and laboratories should be constructed and kept in such a way as to minimise the number of surfaces on which drug residues could contaminate. The surfaces of workspaces and laboratories was suggested to be cleaned regularly and the exhaust ventilation system's particulate filters in the fume hood shall be renewed periodically in accordance with the guidelines set by the American National Standards Institute (ANSI) and the American Industrial Hygiene Association (AIHA) (Armenta et al., 2014). It is necessary to perform an appropriate risk assessment and/or put measures in place to eliminate or reduce any danger to the individual, the laboratory staff (Sisco et al., 2020).

NIOSH (2020) advised that chemist should wear PPE, especially laboratory coat during analysis, and it was suggested to change weekly for cleaning purpose. However, the workers may be less knowledgeable about the risks posed by drugs and

the awareness on the utilisation of PPE requirements may be lower. Therefore, the continuous exposure to methamphetamine which might contaminate laboratory coat due to the sorption effect of methamphetamine to cloth materials (Morrison et al., 2015; Sisco et al., 2020). With time elapsed, a high danger risk could be arisen to people during the seizure, handling, and storage of illicit drugs, causing their unintended entry into the human body through skin absorption, or inhalation of dust or vapour (Doran et al., 2017). NIOSH (2020) highlighted that workers in drug testing laboratories have less attention on the cleaning of the laboratory coat. Furthermore, there was lack of method for the testing of surface contamination on porous materials such as laboratory coat. Therefore, this study was carried out to detect the methamphetamine residues on laboratory coat so that with the proposal of suitable testing procedure, a worker can work under a safe situation in the drug testing laboratory.

2.7 Methamphetamine studies on porous materials

The current techniques to extract methamphetamine from various porous fabric fabrics are shown in Table 2.1.

Table 2.1: Methamphetamine studies on different porous materials

Samples	Sampling method	Instrumentation	References
Clothes (natural and synthetic fibre)	Not applicable	Desorption electrospray ionization (DESI)-mass spectrometer (MS)	Talaty et al. (2008)
Clothes, blankets, and upholstery	Solid phase microextraction (SPME)	Gas chromatography-mass spectrometry (GC-MS)	Morrison et al. (2015)
Artificial leather	Wipe sampling	Electrospray ionisation-mass spectrometry (EI-MS)	Bitter (2017)

Talaty et al. (2008) studied the methamphetamine detection from clothing samples using desorption electrospray ionization (DESI). In the study, 2.5 ng of the methamphetamine was spiked onto natural fibre (100% cotton) and synthetic fibre (100% polyester) samples. Subsequently, DESI was used to analyse the samples and the presence of methamphetamine was determined by identifying the protonated molecules through the mass spectra at m/z 150. The improved handheld instrumentation was found to provide a quick and accurate analysis of relevant chemical, but the recovery percentage was not mentioned in the study (Talaty et al., 2008).

A study was conducted through an experiment where fabric materials were exposed to 15–30 ppb (91–183 µg/m^3) gas-phase of methamphetamine up to 60 days and subsequently analysed by solid phase microextraction-gas chromatography-mass spectrometry (SPME-GC-MS). It examined the binding of gas-phase methamphetamine to porous materials, including clothes, blankets, and upholstery, and established the recovery efficiencies of SPME-GC-MS for methamphetamine. Methamphetamine ranging from 6.1-54 µg/100cm^2 was successfully detected from the fabric materials at a laboratory condition with 30% relative humidity. With a higher relative humidity at 60%, relatively greater amount of methamphetamine was detected, ranging between 9-94 µg/100cm^2. Consequently, methamphetamine absorbed to fabrics could attribute a serious risk to human at very low air concentrations (Morrison et al., 2015).

A wipe sampling on artificial leather using a glass fibre filter moistened with methanol, followed by extraction and analysis by electrospray ionisation-mass spectrometry (EI-MS) was conducted by Bitter (2017). In the study, the samples were firstly exposed to methamphetamine smoke with ambient conditions for 672 hours. Based on the analysis, the methamphetamine was detected at a very low amount with

low recoveries, indicating the extraction might not adequately efficient to recover the target substance from the surface (Bitter, 2017).

2.8 Sampling methods for methamphetamine

Before any sample analysis particularly for the chromatographic detection, the target substance must be sampled from any substrate and transferred into liquid form for subsequent extraction. To recover methamphetamine from the substrate, two procedures were reported in the literature, namely the wipe sampling and solid phase microextraction techniques.

2.8.1 Wipe sampling techniques

Wipe sampling can be done to evaluate possible methamphetamine contamination (Wright et al., 2019). Using a 4-inch by 4-inch (10.2 cm x 10.2 cm) cotton gauze wipe, methamphetamine wipe samples were obtained by wiping hard surfaces over a 100 cm^2 that were assumed to be contaminated. (Wright et al., 2019). In an earlier published sampling methodology, Lazarus developed a technique known as "surrogate procedure" that entailed taking bulk samples with wiping to detect the contamination of methamphetamine (Connor et al., 2016). Surface recoveries of methamphetamine could also be carried out using filter papers moistened with methanol and gauze dampened with methanol (Kuhn et al., 2019; Abdullah & Miskelly, 2010).

Based on the NIOSH 9106 method (2011), there were three types of wipe sampling techniques, namely the concentric squares wiping technique, blotting technique, and serial wiping. For concentric squares wiping technique, the procedure of wiping began in one corner of the square, moved in a clockwise concentric manner, and came to an end in the middle. The filter paper was folded so that the wiped portion was facing in, and the same wiping pattern was repeated in an opposite corner of the square.

For blotting technique, the pre-wetted gauze was firstly folded in half and half again. Using a firm pressure wipe or blot the template with at least five overlapping passes from top to bottom in a "Z" pattern and end it with a scooping motion. The procedure was repeated for at least five times on each horizontal pass, and the gauze was then folded with the exposed side faced inward. Using the fresh surface of the gauze, the same area was blotted again with at least five overlapping passes from left to right in an "N" pattern. Lastly, the gauze was rolled and inserted into a container. For the serial wiping technique, a series or repeated wiping steps on the same area using if a fresh gauze wipe moistened with suitable solvent. For all the three sampling methods, they are usually applied on non-porous surfaces, but not suitable to sample the target substance from porous substrates.

2.8.2 Solid Phase Microextraction (SPME)

Solid phase Microextraction (SPME) is a miniaturised and solvent-free sample preparation method for chromatographic-spectrometric analysis. The procedure allows the separation of analytes from a gaseous or liquid sample by absorption in, or adsorption on, a thin polymer coating applied to the solid surface of a filament, within an injection tube, or within a capillary (Pragst, 2007). Figure 2.6 shows the basic components of a SPME set up where it combines sampling, extraction, concentration, and sample introduction into a single step, addressing the need for a fast sample preparation procedure (Risticevic et al., 2009). The SPME procedure entails two main steps, namely the analyte partitioning between extraction phase and sample matrix, as well as the desorption of condensed extracts into an analytical instrument. Besides, SPME has been successfully extended to a wide range of compounds to be used in conjunction with gas chromatography (GC). Direct extraction, headspace extraction, and membrane safety extraction are the three basic extraction modes. During the

extraction, the coated fibre is inserted into the sample by direct extraction mode where the analytes are transferred directly from the sample matrix to the extracting process. In headspace extraction, the fibre is introduced into the headspace above the aqueous matrix in headspace sampling and there is the only extraction of volatile analytes. Such procedure is beneficial for the high-molecular weight interferences of samples. The uses of membrane-protected extraction method are more precise and reproducible when the samples contain high-molecular weight interfering compounds and non-volatile target analytes (Pawliszyn, 2012).

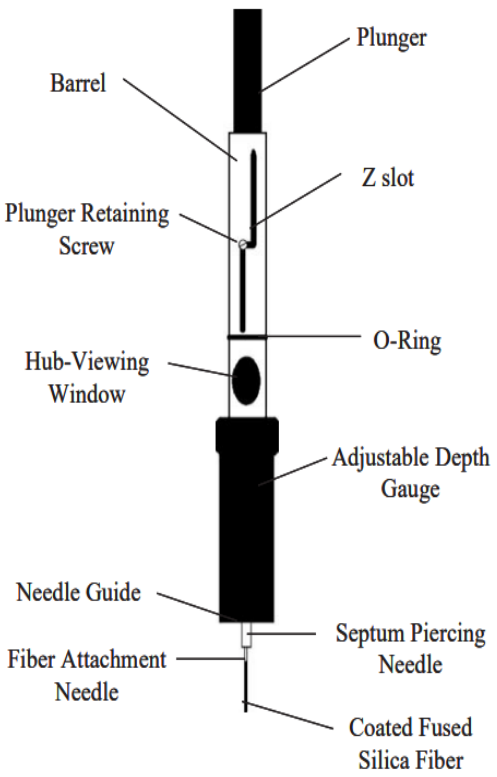

Figure 2.6: Commercial SPME device (Mester & Sturgeon, 2005).

As has been previously reported in the literature, SPME has been widely used in qualitative analysis of headspace SPME of hair, surface wipe, and methamphetamine indoor air measurement (Nishida et al., 2006; McKenzie et al., 2013; Shahvandi et al.,