Determination of Formaldehyde Contamination in Wiping Media Used in Trace Pseudoephedrine Analysis

Ahmad Fahmi Lim Abdullah[a], Gordon M Miskelly[b]

[a]*Forensic Science Programme, School of Health Sciences,Universiti Sains Malaysia, Kelantan, Malaysia*
[b]*Forensic Science Programme, Department of Chemistry, The University of Auckland, Private Bag 92019, Auckland, New Zealand*

ABSTRACT: Pseudoephedrine can be used to measure the level of contamination and to evaluate the effectiveness of decontamination for surfaces at a clandestine laboratory which has been contaminated during its operations. Surface wiping using appropriate wiping media have been suggested by cleanup guidelines. Some wiping vehicle used for low levels of pseudoephedrine showed possible formaldehyde contamination that leads to the detection of a pseudoephedrine-formaldehyde adduct upon GC-MS analysis. A spectrofluorometric method based on the Hantzsch reaction was used to quantify extractable formaldehyde from cotton wool, Whatman 40 and Sartorious filter papers. Formaldehyde was initially present in all the wiping media at levels up to almost 1.0 g per filter, but a detergent wash greatly reduced the level of formaldehyde contamination. Formaldehyde levels slightly increased when washed and dried wiping media were exposed to laboratory air for a period of 18 h to 48 h, whereas a control in a clean sealed bottle showed no increase. Therefore, materials used as surface wiping media must be properly treated or protected against formaldehyde contamination if pseudoephedrine is to be recovered and analysed underivatised using GC-MS.

Keywords: formaldehyde, pseudoephedrine, wiping media, contamination, surface

Introduction

Pseudoephedrine [1] is one of the more common starting materials for clandestine methamphetamine synthesis, especially via the red phosphorus method [2, 3]. Although methamphetamine is the principal indicator for contamination assessment at a clandestine laboratory, pseudoephedrine can also be used for this role, especially when has been used as the sole precursor in a methamphetamine synthesis or in a situation when the synthesis process has not completely converted the precursor to methamphetamine. Since extraction of pseudoephedrine from pharmaceutical preparations may be performed in a separate precursor chemical extraction laboratory from that where the actual methamphetamine synthesis occurs, possibly as a means to avoid being detected by law enforcement personnel, the presence of only pseudoephedrine on surfaces of a suspected clandestine laboratory may indicate that it was an extraction laboratory.

Upon remediation of a former clandestine laboratory, pseudoephedrine can be used in addition to methamphetmine as a surrogate analyte to measure the effectiveness of decontamination, and therefore to aid in the determination of whether the property is considered adequately clean and safe for subsequent occupancy. Overseas clandestine laboratory cleanup guidelines recommend wipe samples to be taken from various surfaces of the structure before and after the cleanup when necessary [e.g. 4, 5, 6]. This implies that surface wiping is a vital step in the evaluation of the level of contaminants actually present [7]. A few criteria must be met when selecting a wiping vehicle – it must hold solvent, its matrix should not interfere with GC-MS identification, and it should not fall apart during the extraction process. Whatman 40 filter paper, Sartorius 1388 filter paper, cotton wool, and WEBCOL® skin cleansing alcohol swabs were potential candidates as wiping vehicles. However, when low levels of pseudoephedrine were recovered from such media and analysed underivatised by GC-MS in our laboratory, the results indicated there might be contamination from the wiping media since the chromatograms showed a peak with similar retention time and mass spectrum to that reported earlier for the pseudoephedrine-formaldehye derivative [8-10]. Several authors have reported that pseudoephedrine or ephedrine can react with aldehydes or ketones to form oxazolidines [8, 9, 11]. The formaldehyde-based oxazolidines have almost identical retention times to the parent drugs, but their mass spectra show a base ion at m⁄z 71 rather than the m⁄z 58 characteristic of the parent drugs when analysed underivatised by GC-MS [7, 10]. Formaldehyde is a ubiquitous contaminant, and so wiping media such as filter papers may contain or accumulate formaldehyde.

We conducted a study to qualify and quantify formaldehyde present in the wiping media based on the Hantzsch reaction of formaldehyde and acetylacetone (2, 4-pentanedione) in the presence of ammonia to give a di-acetyldihydropyridine (**Fig. 1)**. The di-acetyldihydropyridine fluoresces so that trace formaldehyde can be determined using a spectrofluorometer [12].

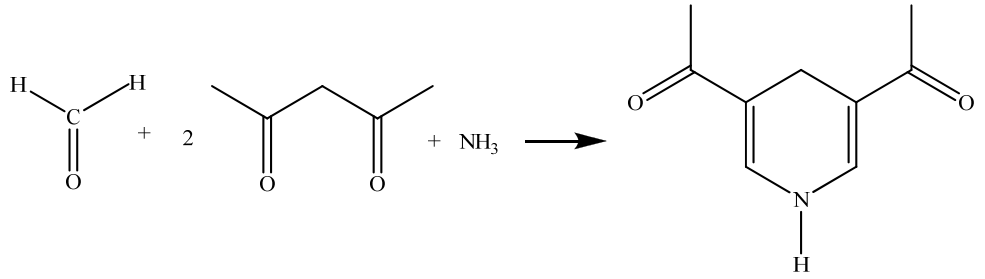

Fig. 1: Hantzsch reaction

Materials and Method

All chemicals were of analytical grade and were used as received. Water for solution preparation and rinsing of wiping media was from a Milli-Q purification system. Wiping materials selected were Whatman 40 filter paper, Sartorius 1388 filter paper, and cotton wool. WEBCOL® skin cleansing alcohol swabs were excluded from further investigation as it is wetted with iso-propanol.

The procedure used for the fluorometric analysis of formaldehyde was based on that reported by Belman [12].

(i) A working solution for the analysis was prepared by mixing equal volumes of 2.0 mol/L ammonium acetate solution (adjusted to pH 6) and 0.02 mol/L acetylacetone solution (adjusted to pH 6). Standards in the range 0 – 2.0 µg of formaldehyde were prepared by adding 5.0 mL of the working solution, the appropriate volume of 1.0 mg/mL formaldehyde solution, and making the volume to 10.0 mL with water. Each solution was then mixed, capped, and heated at 37-38°C for 1 h. All the tubes were then cooled to room temperature prior to analysis. A Hitachi F-2000 spectrofluorometer was used for the analysis with $_{ex}$ = 410 nm, $_{em}$ = 515 nm, and 10 nm bandwidth.

(ii) Sample preparation
Triplicates of cotton wool, Whatman 40 filter paper, and Sartorius 1388 were prepared (see sections *(a)*, *(b)* and *(c)*): 5.0 mL of the above working solution was then transferred into each of nine clean dry test tubes. Cotton wool (about 0.5 g) was put into each of three tubes, two pieces of Whatman 40 filter paper (5.5 cm in diameter) were put into each of three tubes, and two pieces of Sartorius 1388 (5.5 cm in diameter) were put into each of three tubes. All the tubes were made to 10.0 mL with water, capped and heated at 37-38°C for 1 h, they were then cooled to room temperature before measuring the fluorescence response.

a) Measurement of formaldehyde in untreated cotton wool and filter papers
Measurement of formaldehyde in untreated cotton wool (ca 0.5 g), Whatman 40 filter paper (5.5 cm in diameter) and Sartorius 1388 filter paper (5.5 cm in diameter) were performed as described above.

b) Washed cotton wool and filter paper
To remove any formaldehyde in the cotton wool, Whatman 40 and Sartorius 1388 filter papers, they were soaked in 5% Decon 90 for 30 min, sonicated for 10 min, then rinsed thoroughly with Milli-Q water, and dried at 50ºC in an oven. They were then reanalysed for formaldehyde as described in (ii).

c) Effect of exposure of Sartorius 1388 filter paper to laboratory air
Sartorious 1388 filter papers were cleaned and dried as described above, then they were exposed in two separate laboratories with a control in a sealed glass bottle over a period of 18 h to 48 h. The filter papers were then analysed for formaldehyde as described in (ii).

Results and Discussion

The calibration curve was linear over the range 0 to 0.2 µg formaldehyde in 10 mL solution. Formaldehyde was present in all the three sampling media in quantities up to almost 1.0 µg per filter, **Table 1**, with Sartorius 1388 filter paper having the most formaldehyde. The presence of formaldehyde in some paper products has been reported previously [13, 14]. The Decon 90 wash reduced

the amount of formaldehyde in all samples, particularly for the Sartorius 1388 filter paper, **Table 1**.

The effect of exposure to formaldehyde in the laboratory atmosphere was also examined. Sartorious 1388 filter paper was chosen for further investigation as it showed the least amount of formaldehyde after the washing process, plus it is durable to the washing and the base extraction process used for pseudoephedrine wipe analysis (with 4% NaOH solution and n-hexane). Exposure of cleaned Sartorius 1388 filters to a new (< 2 years) laboratory and an old laboratory led to slight increases in formaldehyde detected in the exposed samples from both laboratories, whereas the control showed no increase, **Table 2**. The sample labeled "re-used" in the table refers to Sartorius 1388 filter papers that had been previously used for pseudoephedrine extraction, which had then been cleaned and dried before performing the formaldehyde determination. Only a trace amount of formaldehyde was detected in this sample.

Table 1: Amount of formaldehyde in the tested wiping materials

Samples	Amount (μg)	
	Untreated	Washed
Cotton wool (0.5 g)	0.254	0.093
Whatman 40 (2 pcs of 55 mm diameter)	0.361	0.188
Sartorius 1388 (2 pcs of 55 mm diameter)	0.858	0.040

Table 2: Amount of formaldehyde in the tested wiping materials after exposure to ambient air

Sartorius 1388 Filter Paper	Amount (μg)
Untreated (control)	0.893
Clean and dried (control)	0.106
Clean and dried , exposed 18 h in old laboratory	**0.236**
Clean and dried , exposed 18 h in new laboratory	**0.203**
Clean and dried , kept 18 h in capped bottle (control)	0.089
Clean and dried , exposed 48 h in old laboratory	**0.258**
Clean and dried , exposed 48 h in new laboratory	**0.276**
Clean and dried , kept 48 h in capped bottle (control)	0.107
Re-used, clean and dried	0.058

We have reported earlier that when pseudoephedrine-containing samples that has been exposed to formaldehyde were analysed underivatised using GC-MS, a peak eluted at a retention time which was extremely close to that of pseudoephedrine but that had m/z 71 as its base peak [10], **Fig. 1**, rather than the m/z 58 which is expected for pseudoephedrine [15], **Fig. 2**.

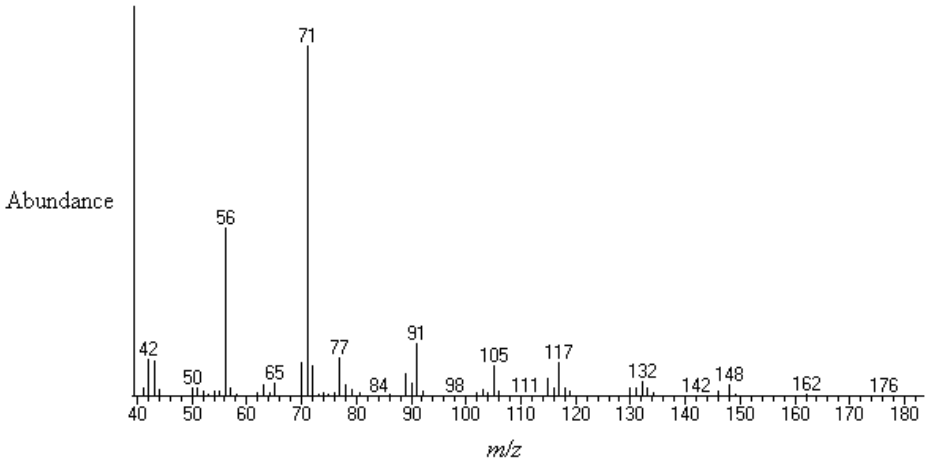

Fig. 1: GC-MS mass spectrum of pseudoephedrine-formaldehyde adduct

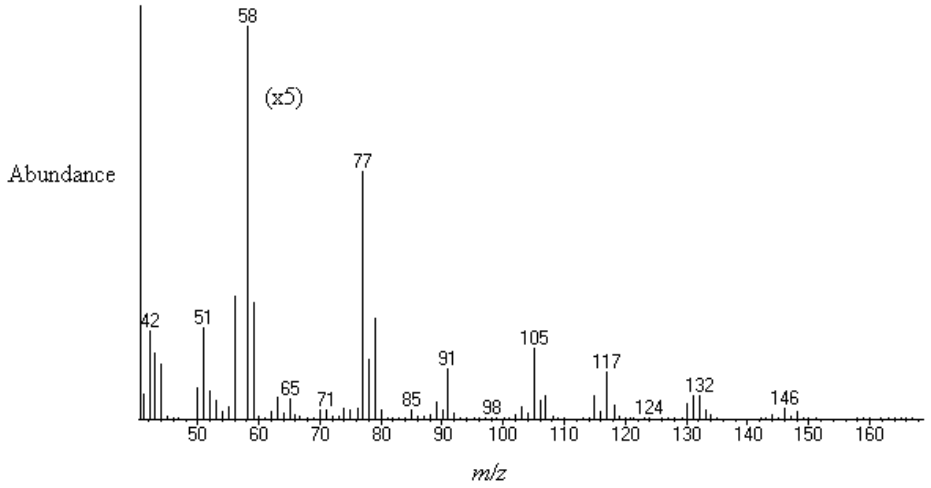

Fig. 2: GC-MS mass spectrum of pseudoephedrine

This altered GC-MS behavior of pseudoephedrine in the presence of a formaldehyde source has previously been reported to have led to the misidentification of pseudoephedrine as phenmetrazine [8]. Furthermore, Lewis et al. [9] have reported that the presence of formaldehyde in solvents or specimens during pseudoephedrine urinalysis leads to oxazolidine formation. Thus, formaldehyde-contaminated surfaces or wiping materials can lead to the observation of the formaldehyde adduct of pseudoephedrine when wipe samples are analysed [7, 10]. The formation of the pseudoephedrine-formaldehyde adduct could occur via the reaction pathway in **Fig. 3** as has been proposed earlier [9, 10].

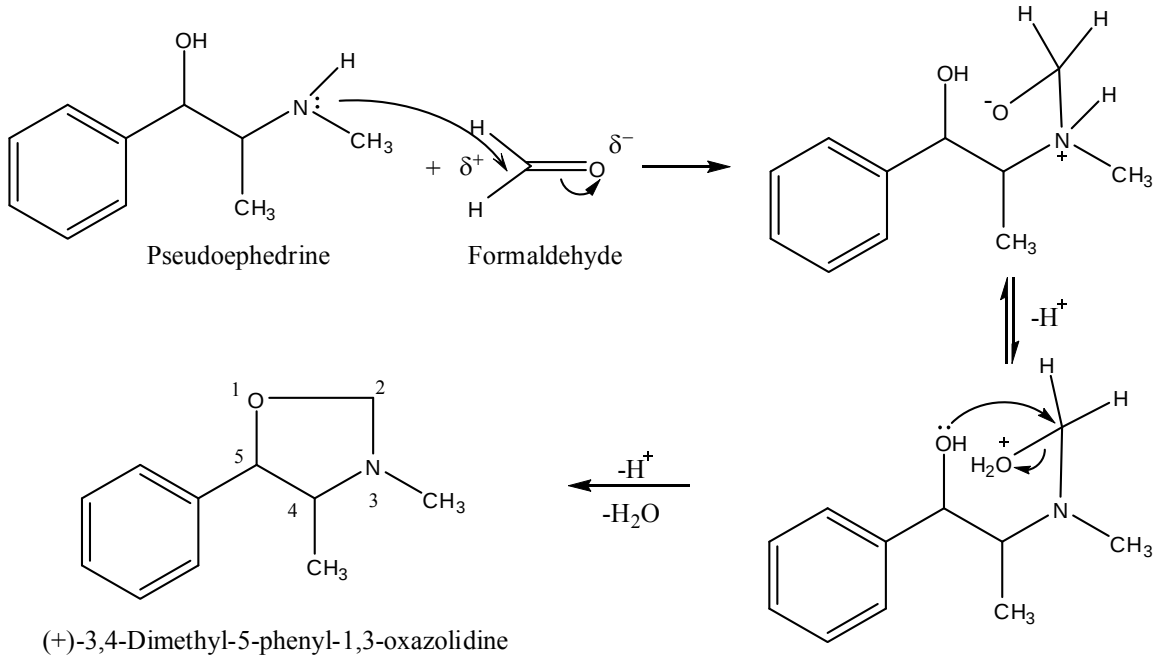

Fig. 3: Reaction of pseudoephedrine with formaldehyde

Conclusion

Since formaldehyde is potentially present in built environments, sample collecting vehicles, glassware and solvent used in pseudoephedrine extraction must be protected against formaldehyde contamination. Our results show that Sartorius 1388 filter paper was suitable as the wiping vehicle for pseudoephedrine surface recovery experiments, although similar filter papers should also be suitable following appropriate washing to remove formaldehyde. When used for collecting low level pseudoephedrine intended for GC-MS analysis, wipe materials should be pre-cleaned with Decon-90, dried and wrapped with aluminium foil prior to use.

Acknowledgements

Mr Glenn Boyes is thanked for the technical advice in fluorometric analysis, and scientists from ESR Ltd. for useful advice and material support.

References

1. Salocks, C. and K.B. Kaley. (2003). *Technical Support Document: Toxicology Clandestine Drug Labs/ Methamphetamine. Ephedrine and Pseudoephedrine.* 1(13): www.oehha.ca.gov/public_info/pdf/TSD%20Ephedrine%20Meth%20Labs%2010'8'03.pdf.
2. Skinner, H.F. (1990). Methamphetamine Synthesis via Hydriodic Acid/Red Phosphorus Reduction of Ephedrine. *Forensic Science International*. 48: 123-134.
3. Chan, K., et al. (2009). *Types of Clandestine Methamphetamine Laboratories Seized in Malaysia.* Department of Chemistry Malaysia.
4. *Guidance and Standards for Cleanup of Illegal Drug-Manufacturing Sites (FINAL)*. (2004). Alaska Department of Environmental Conservation: http://dec.alaska.gov/spar/perp/docs/druglab_guidance.pdf.
5. *Clandestine Drug Lab General Cleanup Guidance (July 1, 2006 Version)*. (2006) Minnesota Department of Health, Minnesota Pollution Control Agency: www.health.state.mn.us/divs/eh/meth/lab/guidance0606.pdf.
6. Clandestine Drug Lab Program, *Guidelines for Environmental Sampling at Illegal Drug Manufacturing Sites*. 2005, Washington State Department of Health: http://www.doh.wa.gov/ehp/cdl/guide-envirsamp.pdf.
7. Abdullah, A.F.L. and G.M. Miskelly. (2010). Recoveries of Trace Pseudoephedrine and Methamphetamine Residues from Impermeable Household Surfaces: Implications for Sampling Methods Used During Remediation of Clandestine Methamphetamine Laboratories. *Talanta*. 81: 455-461.
8. Lambert, E.E.W. (2004). Phenmetrazine or Ephedrine? Fooled by Library Search. *Journal of Chromatography A.* 1045: 259-262.
9. Lewis, R. (2000). Formation of an Interfering Substances, 3,4-Dimethyl-5-Phenyl-1,3-Oxazolidine, During a Pseudoephedrine Urinalysis. *J Forensic Science*. 45(4): 898-901.
10. Miskelly, G.M. and A.F.L. Abdullah. (2009). Formation of Trifluoroacetylated Ephedrine During the Analysis of a Pseudoephedrine - formaldehyde Adduct by TFAA Derivatization Followed by GC-MS. *Journal of Forensic Sciences*. 54(2): 365-367.
11. Neelakantan, L. (1971). Asymmetric synthesis II. Synthesis and Absolute Configuration of Oxazolidines Derived from (-)Ephedrine and Aromatic Aldehydes. *J Org Chem*. 36: 2256-60.
12. Belman, S. (1963). The Fluorimetric Determination of Formaldehyde. *Analytica Chimica Acta*. 29: 120-126.
13. Fisher, A.A., N.B. Kanof, and A.M. Biondi. (1962). Free Formaldehyde in Textiles and Paper -Clinical Significance. *Archieves of Dermatology*. 86: 753-756.
14. Möller, B. and A. Hensten-Pettersen, Biological Evaluation of Absorbent Paper Points. *International Endodontic Journal*. 18 (3): 183-186.
15. Smith, R.M. (2005). *Understanding Mass Spectra: A Basic Approach.* 2 ed. Hoboken, N.J: Wiley Interscience.

Additional information and reprint requests:
Ahmad Fahmi Lim bin Abdullah
(E-mail: fahmilim@kb.usm.my)
Forensic Science Programme
School of Health Sciences
Universiti Sains Malaysia
16150Kubang Kerian, Kelantan, Malaysia