Exposure Assessment of Airborne Acrylamide for Occupationally Exposed Workers by Using an Isotope-Dilution Gas Chromatography Coupled with Mass Spectrometry

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Objectives: To develop a highly sensitive analytical method for very low acrylamide (AA) exposure and to conduct an occupational exposure assessment by the developed method.

Methods: Seventy-five air samples from four plants were collected and analyzed using an isotope-dilution gas chromatography coupled with mass spectrometry (GC/MS).

Results: This isotope-dilution GC–MS method is sufficiently sensitive for assessing very low AA level as 4.37 ng m⁻³, which is 10- to 7500-fold lower than the current analytical method. Field study showed that most airborne AA was gaseous rather than particulate. The personal exposure levels in workers ranged from 4.37 × 10⁻³ to 94.90 μg m⁻³ with a mean of 12.08 μg m⁻³. Fifty percent of personal 8-h time-weighted average (TWA) concentrations in the AA production plant exceeded the threshold limit value of 30 μg m⁻³ set by American Conference of Governmental Industrial Hygienists.

Conclusions: The field study indicated that 8-h TWA concentrations in workers varied by two orders of magnitude. The highly sensitive method can be used in future health risk assessment of AA exposure, such as those in fast-food restaurants.

Keywords: acrylamide; exposure assessment; gas chromatography/mass spectrometry (GC–MS); isotope dilution; occupational exposure

INTRODUCTION

Acrylamide (AA) is a high-production chemical with several common industrial applications. Due to its existence in tobacco smoke (Smith et al., 2000) and food (Tareke et al., 2002), it may also represent a ubiquitous environmental pollutant of high importance to environmental health.

The AA (CAS No.79-06-1) is odorless, white, crystalline (molecular weight: 71.08), highly soluble in polar solvents, and stable in solution. It is produced by hydration of acrylonitrile and is used to produce polyacrylamides (Smith and Oehme,
which are used for manufacturing numerous products, including adhesives, mining chemicals, fibers, pharmaceuticals, animal feed, paper sizing, molded parts, textiles, and coagulant aids (NSC, 2006) as well as in biological laboratories for preparing polyacrylamide gels for electrophoresis (IARC, 1994). The estimated annual global production of AA is $2 \times 10^8$ kg (Twaddle et al., 2004). The US National Institute for Occupational Safety and Health estimated that 20 000 workers may have been exposed to AA in 1976 (IARC, 1986). The estimated number of laboratory workers exposed to AA in the preparation of electrophoresis gels is 100 000–200 000 (EPA, 1988). The AA is also produced by Maillard reaction from the amino acid asparagine with fructose or glucose upon heating at temperatures $>120^\circ$C (Mottram et al., 2002; Stadler et al., 2002). One study reported that 0.15–7.2% of AA evaporates from food products during heating (Eriksson et al., 2007). Therefore, housewives and chefs were potentially exposed to AA through inhalation. The AA is neurotoxic in animals and humans (Smith and Oehme, 1991) and causes carcinogenic, genotoxic, and reproductive toxicity effects in experimental animals. It has been classified as a probable human carcinogen by International Agency for Research on Cancer (IARC) (IARC, 1994). Numerous toxicology studies have reported neurotoxic effects in humans due to occupational exposure to AA (Calleman et al., 1994; Hagmar et al., 2001; Kjuus et al., 2004). In order to protect workers from adverse health effects due to AA exposures, the American Conference of Governmental Industrial Hygienists (ACGIH) set its threshold limit value (TLV) at 30 g m$^{-3}$ in workplaces (ACGIH, 2009).

The US Occupational Safety and Health Administration (OSHA), however, has set the permissible exposure limit at 300 g m$^{-3}$ (OSHA, 2003). Exposure to AA has been a concern in the workplaces. Studies have assessed AA exposure in workers involved in production, handling, maintenance, and polymerization of AA (Calleman et al., 1994; Bull et al., 2005; Jones et al., 2006) and laboratory use of AA (Pantusa et al., 2002). One study reported that laboratory workers who weigh and prepare AA solution to synthesize polyacrylamide gels for electrophoresis receive AA exposures of 13 ± 24 g m$^{-3}$ and 4 ± 7 g m$^{-3}$, respectively (Pantusa et al., 2002). The other three showed that production factory workers were exposed to AA ranged from 4 to 282 g m$^{-3}$ (mean: 28 g m$^{-3}$) and 10 to 282 g m$^{-3}$ (mean: 30 g m$^{-3}$) in UK and 1070 ± 880 g m$^{-3}$ in China (Calleman et al., 1994; Bull et al., 2005; Jones et al., 2006). One study showed that 0.15–7.2% of the AA evaporated from food products during heating ranged from $2 \times 10^{-5}$ to 4.4 $\mu$g m$^{-3}$ (Eriksson et al., 2007). Due to the fact that even low levels of AA may cause health effects and constitute a cancer risk of concern (Granath et al., 2001), a highly sensitive analytical method is needed to improve the assessment of very low AA exposures.

Occupational exposure to airborne AA can be analyzed by high performance liquid chromatography-ultraviolet (HPLC-UV), gas chromatography-electron capture detection (GC-ECD), and gas chromatography-nitrogen phosphorus detection (GC-NPD). The limit of detections (LODs) of airborne AA are between 4 and 5 $\mu$g m$^{-3}$ by HPLC-UV method (Bull et al., 2005; Jones et al., 2006), 30 $\mu$g m$^{-3}$ by GC-ECD method (Calleman et al., 1994), and $4 \times 10^{-2}$ $\mu$g m$^{-3}$ by GC-NPD method (Pantusa et al., 2002). The LOD of these methods is relatively high. The poor LOD for airborne AA hinders their quantitation in air monitoring. To our knowledge, a highly sensitive and specific analytical method for airborne AA has not yet been described in the literature.

There are two purposes of the study. Firstly, to develop a highly sensitive isotope-dilution gas chromatography coupled with mass spectrometry (GC–MS) method for very low AA exposure. Secondly, to conduct an occupational exposure assessment in AA production and application plants using the developed method.

METHODS

Chemicals

AA and $^{13}$C$_3$-labeled AA were purchased from Sigma (St Louis, MO, USA) and Cambridge Isotopes (Cambridge, MA, USA), respectively. Methanol (HPLC grade) was obtained from Sigma-Aldrich (Mallinckrodt, Milwaukee, WI, USA). The helium for the GC–MS, which was purchased from Sanfu Co. (Hsin Chu, Taiwan), was 99.999% purity. The sampling train consisted of a Swinnex cassette (SKC, Inc., Eighty Four, PA, USA), a 13-mm glass fiber filter (SKC 225-16), gasket (SKC 225-3201), a standard silica gel tube (75/150) (SKC 226-10), and a sampling pump (SKC, Inc., AirChek 2000).

Analytical methods

Instrumentation. Samples were analyzed using an Agilent 6890 gas chromatograph connected with an Agilent 7683 autosampler and a split/splitless injector operated in splitless mode. For mass spectrometric detection of AA, an Agilent 5973 Series of mass spectrometer was fitted with a quadrupole mass filter and operated under electron impact mode.
Chromatographic separation was performed using a WAX™-10-fused silica capillary column (30 m × 0.25 mm, 0.25 μm film thickness, Supelco). Helium was used as a carrier gas, and the flow rate was set at 1.0 ml min⁻¹. Injector temperature was set at 225°C. Oven temperature was set at 100°C for 0.5 min, ramped from 100 to 190°C at 15°C min⁻¹, held for 9.5 min, and then increased from 190 to 240°C at 20°C min⁻¹. Mass spectrometer temperature was 240°C. The mass spectrometer was operated in selected ion monitoring (SIM) mode by monitoring m/z 71 for AA and m/z 74 for the internal standard (IS).

**Calibration curve, LOD, and limit of quantification.** The stock standard solution was prepared by dissolving 1 mg of AA in 1 ml methanol, and calibration standards of 0.095–95.0 μg ml⁻¹ were prepared from the stock solution. Another stock solution of IS was prepared by dissolving 1 mg of 13C₃-labeled AA in 1 ml methanol (1 mg ml⁻¹). The stock solution containing IS was further diluted to prepare calibration standards and then analyzed by GC–MS in SIM mode by monitoring m/z 71 and 74 for AA and 13C₃-labeled AA, respectively. The LOD and limit of quantification (LOQ) were determined using signal-to-noise (S:N) ratios of 3 and 10, respectively.

After analysis of the standard solutions, a calibration curve was constructed by plotting the peak area ratios (AA peak area: 13C₃-labeled AA peak area) (Y) versus AA concentration (X). An excellent linear relationship was obtained with Y = 1.71X - 0.13 (r = 0.9998). The LOD was calculated as 2.1 ng ml⁻¹, which corresponded to 4.37 × 10⁻³ μg m⁻³, and LOQ was 6.9 ng ml⁻¹ corresponding to 1.43 × 10⁻² μg m⁻³.

**Field study**

**Subject recruitment and plants description.** Four plants associated with AA production (A) and application (B, C, and D) in Taiwan were selected for analysis. The plants were located in the northern and southern areas of the island. Forty-five male workers directly exposed to AA in four plants voluntarily participated and gave informed consent. In plant A, AA was produced from acrylonitrile in aqueous solution by using a batch process in an outdoor facility; it was the only one AA production plant that manufactured 30–48% AA solution. Workers might have been exposed to high AA levels at the sampling/testing site and at the final product packing site when sampling/testing AA or when packing 30–48% AA product solution into barrels. The three application plants conducted the AA application operations using batch processes in closed buildings. Plant B manufactured the highest volume (120 tonne month⁻¹) of AA application products and the others produced between 7.9 and 10.0 tonne month⁻¹. Plant B produced strengthened resins from powder AA, and plants C and D produced synthetic resins and styrene–butadiene rubber but used materials derived from the 30–48% AA solution. The prime sources of potential AA exposures in these three plants were during sampling of AA residue in the intermediate and final products. Workers in plants B and C were also potentially exposed to AA when pouring powder AA (plant B) or liquid AA solution (plant C) into reaction tanks and when packing final products into barrels. These sites were selected for area sampling. Thirty sampling sites were analyzed. Table 1 presents the descriptions of the four plants.

A self-administered questionnaire was used to collect data of the study subjects, such as age, weight, height, gender, work history, use of personal protective equipment (PPE) such as disposable latex gloves and dust masks, alcohol consumption, smoking status, and medical history. The subjects were also asked about skin symptoms and peripheral nervous system, such as numbness or tingling in hands or legs. Personal samples were collected from the workers from the start of a shift until the end of the shift.

**Area and personal sampling.** The AA sampling was performed using the OSHA Analytical Method 21 (OSHA, 1985). The sampling train consisted of a 13-mm glass fiber filter placed in a Swinnex cassette followed by a standard (75/150) silica gel tube and a personal sampling pump. Gas phase AA was collected using silica gel tubes, and particulate phase AA was collected using 13-mm glass fiber filters. The airflow sampling rate was 1 l min⁻¹, and the maximum sampling volume was 480 l. Before sampling, the flow rate was calibrated with a DryCal-Lite primary flow meter (SKC, Inc.), and the actual flow rate was recorded. Sampling duration varied and depended on the duration of the tasks performed by the subjects. Both area and personal samples were collected. For area sampling, the sampling head was placed at the breathing level of a typical adult (1.3–1.5 m above the ground). Area samples were collected for 1 or 3 consecutive days among these four plants. For personal sampling, workers wore a personal sample collection system in their breathing zone while they performed their duties throughout the shift (~8 h) for 1 or 3 consecutive days. The sampling pump was identical to that used for the area samples and was strapped to the left side of the waist. Workers wore the systems concurrently with area sample and were allowed to move freely throughout
the working area during their normal job duties. After sampling, the ends of the silica gel tube were sealed with plastic caps, and the glass fiber filters were placed in vials. The samples were then chilled and transported to the laboratory for analysis.

**Sample analysis**

For AA analysis in real samples, the front (150 mg) and back (75 mg) sections of the silica gel tubes were placed in two separate teflon-capped vials. Each vial containing the gasket/glass fiber filter or the silica gel was then spiked with 50 μl of 13C3-labeled AA solution (10 μg ml⁻¹), which served as the IS. All vials were then immediately extracted with 1 ml methanol by agitation in a water bath at 30°C for 2 h. The supernatant was used for analysis. One microliter of the extractant was injected into the GC–MS for analysis.

**Quality assurance and quality control**

The reproducibility of this method was assessed by repeated analysis of five different concentrations of AA standard solutions five times within 1 day; this experiment was repeated on 7 different days. The following amounts, 0.45, 1, 10, 50, and 80 μg of AA and 0.5 μg of 13C3-labeled AA, were spiked onto the silica gel tubes and onto the filters. All experiments were performed in triplicate. The tubes were allowed to stand overnight at 4°C and then the filters were immediately extracted. The silica gel tubes and filters were placed in separate extraction vials with Teflon-lined caps and AA was extracted using 1 ml of methanol by agitation in a water bath at 30°C for 2 h. Recovery efficiency was measured by comparing the peak area observed by direct analysis of the AA standard solutions by GC–MS with those in recovered AA after methanol extraction of the same standards spiked into the sampling tube and filter.

**Statistical methods**

One-way analysis of variation (ANOVA) was used to test factory-to-factory variation in age, body mass index [BMI, mass (kg) height (m)⁻²], working duration, lifestyle information, and PPE use. The Spjot-voll/Stoline test [Tukey honestly significant differences (HSD) for unequal N-test] was used for post hoc comparisons. The Mann–Whitney and Student’s t-tests were used to compare 8-h time-weighted average (TWA) concentrations between personal and area samples for each plant and the total samples. Statistical analyses utilized the Statistical Package for the Social Sciences (SPSS) version 11.0, (SPSS Inc., Chicago, IL, USA).

**RESULTS AND DISCUSSIONS**

**Method performance**

The LOD of our GC–MS method was 2.1 ng ml⁻¹, which corresponds to 4.37 × 10⁻³ μg m⁻³ based on an air volume of 480 l. Compared to the LODs of the HPLC-UV, GC-ECD, or GC-NPD methods [between 4 and 5 μg m⁻³ (Bull et al., 2005; Jones et al., 2006), 30 μg m⁻³ (Calleman et al., 1994), and 4 × 10⁻² μg m⁻³ (Pantusa et al., 2002), respectively], the proposed isotope-dilution GC–MS method provides superior sensitivity. The reproducibility of this method was expressed by intra-day and inter-day relative standard deviations (RSD). The intra-day RSD was 2.0–5.9% and the inter-day

<table>
<thead>
<tr>
<th>Plant</th>
<th>Process</th>
<th>Process review</th>
<th>Prime source of potential exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>AA production</td>
<td>Batch processes to produce AA in aqueous solution, which is piped to storage</td>
<td>In-process sampling/testing of AA. In-process packing of AA product solution into barrels.</td>
</tr>
<tr>
<td>B</td>
<td>AA products—strengthened resins</td>
<td>The highest volume batch processes using powder AA to form liquid products transferred to storage and tanks</td>
<td>In-process sampling of residual AA liquid products. In-process pouring of powder AA.</td>
</tr>
<tr>
<td>D</td>
<td>AA products—styrene–butadiene rubbers</td>
<td>Batch processes using 30–48% AA solution to form liquid products transferred to storage and tanks</td>
<td>In-process sampling of residual AA liquid products.</td>
</tr>
</tbody>
</table>
RSD was 1.6–8.0% (Table 2). The average recovery for AA ranged from 78.6 to 99.1% and from 87.6 to 98.6% in the glass fiber filter and the silica gel tube, respectively (Table 3). A major advantage of this method is that loss of analyte during sample preparation can be compensated by adding stable isotopic\(^{13} \text{C}_3\)-labeled AA to serve as an IS, thus making this the best form of internal standardization (Webb and Carter, 1997). This isotope-dilution mass spectrometry can improve accuracy of quantification.

**Field study of airborne AA concentrations**

Figure 1 shows the typical GC–MS chromatograms generated for an air sample in a silica tube and a filter.

In the forty-five male workers recruited for this study, average age was 40.4 years old, average BMI was 23.6 kg m\(^{-2}\), and average working period was 13.6 years (Table 4). Half (50%) of them smoked, 29.6% drank alcohol, and 82.5% of them wore PPEs, such as disposable latex gloves and dust masks. The factory-to-factory variation in age and working duration were statistically significant (\(P < 0.05\) by one-way ANOVA). The post hoc comparisons by Tukey HSD indicated that the workers in plant A were significantly older than those in plants B and D and had more years of working experience than those in plant B. Area and personal sampling were performed in the four plants. Forty-five personal samples and 30 area samples were successfully collected and analyzed.

For each sample, the AA was separately analyzed in a silica tube and filter using isotope-dilution GC–MS method. The AA concentrations in area and personal samples were equal to the summation of AA content in the silica gel and the filter. Sample analysis showed that 100% AA was detected in the silica gel tubes from plants A, B, and C but not in those from plant D (60.7%); however, 100% AA was detected in filters from plant B. A possible explanation is that the plants used different forms of AA raw materials. That is, powder was used in plant B and liquid AA solution was used in the other plants. In total, AA was detected in 48.9% (22 of 45) of the silica gel tubes and in 20% of the filter samples for personal samples; it was detected in 100% of silica gel tubes and in 30% of filter samples for area samples (data not shown). These data show that airborne AA existed in gaseous form rather than particulate form. Overall, the 8-h TWA of AA concentration ranged from 4.37 × 10\(^{-3}\) (LOD) to 94.90 μg m\(^{-3}\) with a mean (standard deviation, SD) of 12.08 (20.78) μg m\(^{-3}\) for personal samples and 0.23 to 17.40 μg m\(^{-3}\) with a mean (SD) of 24.31 (42.69) μg m\(^{-3}\) for area samples (Table 5). There was significant difference between the mean 8-h TWA concentration for total personal and area samples (\(P < 0.05\)).

It is convenient to compare the results with the ACGIH TLV, but this comparison must be rough, because the TLV is defined in terms of the inhalable fraction, and the Swinnex sampler recommended in the OSHA method that we used probably does not collect the inhalable fraction. In plant A, the mean (SD) 8-h TWA concentrations for the workers were 33.82 (28.50) μg m\(^{-3}\) in the range of 0.98–94.90 μg m\(^{-3}\) and were 55.62 (55.79) μg m\(^{-3}\) in the range of 9.06–217.40 μg m\(^{-3}\) for area samples, which exceeded the TLV of 30 μg m\(^{-3}\) set by ACGIH. There was no significant difference between the mean 8-h TWA concentration for personal and area samples. Fifty percent (5 of 10) of the personal 8-h TWA levels exceeded the TLV, and these individuals had been engaged in sampling/testing AA solution at the reaction tank, the crude product tank, the refined product tank as well as packing 30–48% AA product solution into barrels. Notably, one worker who had packed 30–48% AA product solution into barrels had a maximum exposure concentration of 94.40 μg m\(^{-3}\). The high exposure in this case was likely caused by working close to the emitted source when packing AA product solution. Although 80% of the workers had used PPEs, two workers had not routinely worn

### Table 2. Intra- and inter-day precision obtained by repeated measurements of AA standard

<table>
<thead>
<tr>
<th>AA concentration (μg ml(^{-1}))</th>
<th>RSD (%)</th>
<th>Intra-day (n = 5)</th>
<th>Inter-day (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.095</td>
<td>4.51</td>
<td>2.63</td>
<td></td>
</tr>
<tr>
<td>0.190</td>
<td>4.42</td>
<td>2.58</td>
<td></td>
</tr>
<tr>
<td>0.450</td>
<td>2.47</td>
<td>1.47</td>
<td></td>
</tr>
<tr>
<td>0.950</td>
<td>2.03</td>
<td>1.60</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3. Recovery of AA in glass fiber filters and in silica gel tubes

<table>
<thead>
<tr>
<th>AA in glass fiber filter (μg ml(^{-1}))</th>
<th>Recovery (%)</th>
<th>AA in silica gel tube (μg ml(^{-1}))</th>
<th>Recovery (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.45</td>
<td>99.1</td>
<td>0.45</td>
<td>98.2</td>
</tr>
<tr>
<td>1</td>
<td>78.6</td>
<td>1</td>
<td>87.6</td>
</tr>
<tr>
<td>10</td>
<td>91.2</td>
<td>10</td>
<td>97.9</td>
</tr>
<tr>
<td>50</td>
<td>94.3</td>
<td>50</td>
<td>94.6</td>
</tr>
<tr>
<td>80</td>
<td>93.4</td>
<td>80</td>
<td>98.6</td>
</tr>
</tbody>
</table>

Sample size = 3.
masks or latex gloves while packing AA product solution. However, as the fact that the neurotoxic effects of AA are cumulative, and since it is a probable human carcinogen, exposures should be as low as reasonably achievable. The exposure controls such as reducing exposure frequency/duration

Fig. 1. Typical GC–MS chromatograms generated from a real sample after methanol extraction. The upper chromatogram (A) was obtained from an analysis of the AA in a silica gel tube and the lower chromatogram (B) obtained from an analysis of the AA in a glass fiber filter after an 8-h sampling.
during sampling/testing AA solution and packing AA product solution as well as setting up local exhaust ventilation during packing AA product solution can significantly decrease exposures. The use of respirators or disposable latex gloves will also reduce personal exposures during operation. Additionally, 72.7% (8 of 11) area samples exceeded the 8-h TWA TLV; these locations were at the reaction tank, the crude product tank, the refined product tank as well as the site of AA product solution packing. The maximum exposure concentration (217.40 μg m⁻³) was monitored at the reaction tank. The likely explanation is that maximum AA production was at the work site, and the vapor phase of AA was emitted predominantly from the reaction tanks. The airborne AA in plant A was greater than that in the other three plants.

The average 8-h TWA concentrations in workers in plants B, C, and D were 6.35 μg m⁻³ (range: 4.11–8.81 μg m⁻³), 5.14 μg m⁻³ (range: 2.13–8.12 μg m⁻³), and 0.11 μg m⁻³ (range: 4.37 × 10⁻³ μg m⁻³ (LOD)–0.28 μg m⁻³), respectively, and those in area samples from plants B, C, and D were 6.49 μg m⁻³ (range: 4.03–9.69 μg m⁻³), 6.67 μg m⁻³ (range: 2.54–14.17 μg m⁻³), and 0.32 μg m⁻³ (range: 0.23–0.46 μg m⁻³), respectively. Significant difference in the mean 8-h TWA concentration for personal and area samples in plant D was found (P < 0.05). Both plants B and C had the same levels of airborne AA concentrations, and plant D presented the lowest AA concentrations, probably because plants B and C had enclosure of operation and both had automatic production. Furthermore,

during sampling/testing AA solution and packing AA product solution as well as setting up local exhaust ventilation during packing AA product solution can significantly decrease exposures. The use of respirators or disposable latex gloves will also reduce personal exposures during operation.

Table 5. Comparisons on 8-h TWA concentrations of AA among four plants (μg m⁻³)

<table>
<thead>
<tr>
<th>Plant</th>
<th>Sample type</th>
<th>n</th>
<th>Mean±SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Personal</td>
<td>10</td>
<td>33.82±28.50</td>
<td>0.98–94.90</td>
</tr>
<tr>
<td></td>
<td>Area</td>
<td>11</td>
<td>55.62±55.79</td>
<td>9.06–217.40</td>
</tr>
<tr>
<td>B</td>
<td>Personal</td>
<td>8</td>
<td>6.35±1.64</td>
<td>4.11–8.81</td>
</tr>
<tr>
<td></td>
<td>Area</td>
<td>8</td>
<td>6.49±2.39</td>
<td>4.03–9.69</td>
</tr>
<tr>
<td>C</td>
<td>Personal</td>
<td>4</td>
<td>5.14±2.69</td>
<td>2.13–8.12</td>
</tr>
<tr>
<td></td>
<td>Area</td>
<td>6</td>
<td>6.67±4.34</td>
<td>2.54–14.17</td>
</tr>
<tr>
<td>D</td>
<td>Personal</td>
<td>23</td>
<td>0.11±0.06</td>
<td>ND–0.28</td>
</tr>
<tr>
<td></td>
<td>Area</td>
<td>5</td>
<td>0.32±0.10</td>
<td>0.23–0.46</td>
</tr>
<tr>
<td>Total</td>
<td>Personal</td>
<td>45</td>
<td>12.08±20.78</td>
<td>ND–94.90</td>
</tr>
<tr>
<td></td>
<td>Area</td>
<td>30</td>
<td>24.31±42.69</td>
<td>0.23–17.40</td>
</tr>
</tbody>
</table>

*TLV–TWA set by ACGIH and permissible exposure limit in Taiwan: 30 μg m⁻³.

ND: Not detected (below 4.37 μg m⁻³).

*P < 0.05 comparing personal samples to area samples.

Table 4. Demographic data of study subjects among four plants

<table>
<thead>
<tr>
<th>Plant</th>
<th>n</th>
<th>Age±SD (year), mean–SD, (range)</th>
<th>BMI±SD (kg m⁻²), mean–SD, (range)</th>
<th>Working years±SD, (range)</th>
<th>Cigarette smoking (%), mean–SD, (range)</th>
<th>Alcohol drinking (%), mean–SD, (range)</th>
<th>Personal protective equipment (%), mean–SD, (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>10</td>
<td>46.67±8.22 (30–57)</td>
<td>24.69±3.66 (18.81–32.18)</td>
<td>17.93±9.07 (1–34)</td>
<td>20.0</td>
<td>13.3</td>
<td>80.0</td>
</tr>
<tr>
<td>B</td>
<td>8</td>
<td>35.83±7.99 (24–51)</td>
<td>23.08±3.48 (17.65–28.13)</td>
<td>8.33±6.75 (2–21)</td>
<td>75.0</td>
<td>25.0</td>
<td>100.0</td>
</tr>
<tr>
<td>C</td>
<td>4</td>
<td>39.33±5.20 (32–46)</td>
<td>23.97±1.32 (22.79–25.86)</td>
<td>9.67±2.66 (6–13)</td>
<td>90.0</td>
<td>66.7</td>
<td>100.0</td>
</tr>
<tr>
<td>D</td>
<td>23</td>
<td>39.04±5.33 (28–55)</td>
<td>23.28±2.31 (18.59–28.73)</td>
<td>14.75±8.75 (1–65)</td>
<td>86.5</td>
<td>33.3</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>40.43±7.44 (24–57)</td>
<td>23.62±2.80 (17.65–32.18)</td>
<td>13.62±8.63 (1–65)</td>
<td>80.0</td>
<td>29.6</td>
<td>82.5</td>
</tr>
</tbody>
</table>

Plant A: AA production; plants B–D: AA-containing commercial products. The factory-to-factory variation in age and working duration was statistically significant (P < 0.05 by one-wayANOVA). In post hoc comparisons by Tukey HSD, we found that the workers in plant A were significantly different from B and D in age and were significantly different from B in working years.

The factory-in-factory variation in age and working duration was statistically significant (P < 0.05 by one-wayANOVA). In post hoc comparisons by Tukey HSD, we found that the workers in plant A were significantly different from B and D in age and were significantly different from B in working years.
most of workers in plant D were stationed 100 m away from the production area.

The health hazard of occupational exposure to AA included skin irritation, neurotoxic effects, and increased cancer risk (Calleman et al., 1994; Granath et al., 2001; Hagmar et al., 2001; Kjuus et al., 2004). Although 11% of the workers had skin irritations, none had peripheral nervous symptoms, such as numbness or tingling in hands or legs. Since even low AA levels may cause health effects and to protect workers from adverse health effects, the airborne AA concentrations in plant A should be decreased to TLV 30 μg m⁻³.

Several studies have assessed AA exposure in workers involved in production, handling, maintenance, and polymerization of AA (Calleman et al., 1994; Bull et al., 2005; Jones et al., 2006) as well as laboratory use of AA (Pantusa et al., 2005). Compared to studies performed elsewhere, the AA exposures observed in this study were relatively low, probably because of strict government regulations. The occupational exposure limits are 300 μg m⁻³ in the UK and China but only 30 μg m⁻³ in Taiwan. The low concentrations of AA in the workplace demonstrate the need of analytical methods with high sensitivity and specificity, and our isotope-dilution GC–MS method successfully meets the requirement.

CONCLUSIONS

Although AA is an important industrial chemical, it is also present in tobacco smoke and food and is classified by the IARC as a probable human carcinogen. Thus, AA-exposed workers, smokers, housewives, chefs, and consumers of certain foods are at risk of AA exposure. According to the analysis of personal samples collected in the workplace, the 8-h TWA concentrations in workers ranged from 4.37 × 10⁻³ (LOD) to 94.90 μg m⁻³ with a mean of 12.08 μg m⁻³. The field study indicate that the requirement of measuring airborne AA below the magnitude of nanograms per cubic meter level cannot be achieved by current analytical methods, such as HPLC-UV, GC-ECD, GC-NPD, or even GC-MS. This study demonstrated that the isotope-dilution GC–MS method offers several advantages, including simple preparation, excellent accuracy, and specificity. Therefore, accurately measured AA exposures for workers was as low as 0.11 μg m⁻³, which is particularly important when assessing very low AA levels in general workplaces and fast-food restaurants. These data are critical for future occupational epidemiology studies of the potential health effects of AA exposure.

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