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Inhalation and dermal exposure to toluene among printing workers in a plastic bag factory

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Abstract

Purpose – The purpose of this paper is to explore inhalation levels and dermal exposure to toluene among printing workers who wore no personal protective equipment; it is conducted in a plastic bag factory. Using a charcoal cloth pad (CCP) as a dermal sampler to assess skin permeation of liquid toluene is also investigated.

Design/methodology/approach – In total, 27 stationary air samples as well as urine and dermal samples were collected over 9 days from 11 printing workers. Six pieces of CCP were wrapped on each of the workers' fingers for the dermal sample collection. Air samples were collected and analyzed according to NIOSH No. 1501, and 65 post-shift urine samples were collected and analyzed using gas chromatography equipped with headspace sampler (GC-HS/FID). Multiple linear regression was employed to analyze the association between the studied variables.

Findings – The mean (SD) urinary toluene (UTol) level was 13.42 (9.72) ug/L. Toluene on the CCP (TolCCP) was a meaningful predictor for UTol (p-value = 0.027) with r and r^2 values of 0.441 and 0.195, respectively. The r and r^2 of the model using the toluene time-weighted average concentrations in air were 0.739 and 0.546, respectively. The absorbed dose of toluene determined from the TolCCP ranged from 1.05 to 91.94 mg, accounting for 12.3 percent of the threshold limit value (TLV).

Originality/value – Dermal exposure was insignificant when workers wore respirators, but when not, dermal absorption could contribute to the overall uptake and exposure above the TLV. Appropriate gloves should be assigned to the workers to reduce dermal exposure to toluene.

Keywords Dermal, Toluene, Printing, Charcoal cloth pad, Urinary toluene

Paper type Research paper

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Introduction

Toluene is an aromatic hydrocarbon compound widely used as a solvent in paint, lacquer and thinner, and as a cleaning and dying agent in many industries including printing. A serious health concern of toluene is its effect on the central nervous system which can be temporary, such as headaches, dizziness or unconsciousness. However, effects such as poor coordination, cognitive impairment and vision and hearing loss may become permanent with repeated exposure[1]. The major chemical routes of entry in occupational settings are inhalation and dermal exposure. "Skin notation" (S or Sk or H) indicates that these substances are capable of penetrating the skin in a significant quantity to cause health effects. However, the "S" assigned to some certain chemicals differs among countries and organizations[2]. The permeability coefficient (Kp) was proposed as a criterion for skin notation in occupational settings[3]. However, most Kp values obtained from prediction use physicochemical data of the chemicals and some from *in vivo* and/or *in vitro* experiments; thus, they varied from source to source, e.g. Kp of toluene = 0.5375 cm/h[4]; 0.031 cm/h[5] and 0.000079 cm/h[6] An experiment and field study was conducted to assess skin absorption ability of toluene among printing workers[7]. For the field study, no association was found between dermal contact and biomarkers, i.e. hippuric acid and urinary toluene (UTol). However, the experiment involving volunteers who washed their hands with toluene could detect toluene in exhaled air after approximately 30 min of washing. This demonstrated the skin absorption ability of toluene.

The use of a charcoal cloth pad (CCP) was developed and has been used to assess volatile chemicals on the skin in a laboratory setting by Cohen since 1989[8]. A number of field studies have been conducted to assess the use of CCP for dermal exposure to toluene and benzene[9, 10]. The correlation between biomarkers and dermal exposure was not found due to low dermal exposure. However, other research[10] suggested that CCP could be a useful tool to quantify the probability of dermal exposure to organic solvents and provide estimates of the potential contribution of the dermal pathway to systemic exposure.

Recently, chemical concentrations in the workplace have been reduced due to better control technology and OELs have been reduced dramatically; thus, new biomarkers that are more sensitive and accurate need to be developed. Unchanged chemicals such as toluene and benzene in tissues were studied and have been suggested to be used as biomarkers[11–14]. The Headspace/GC technique used for very light volatiles in samples was employed. As a consequence, in 2010, the ACGIH established 0.03 mg/L toluene in urine and 0.02 mg/L toluene in blood as the BEI for toluene[15]. This reflected the inhalation exposure limit and threshold limit value-time-weighted Average (TLV-TWA on the basis of an 8 h/day or 40 h/week work schedule, is normally referred to as TLV) of 20 ppm reduced from 50 ppm in 2007[16]. Toluene is widely used in industry as a solvent substitute for benzene and has the potential for dermal absorption. Thus, small amounts of toluene permeating the skin may affect its internal dose. The improper label of "skin notation" and lack of tools to assess dermal absorption may impact the protection of the workers' health. This study was conducted in a plastic bag factory where the workers wore neither respirator nor gloves. The study aimed to investigate toluene exposure of the printing workers and the potential of CCP as a dermal sampler to assess the skin permeation of liquid toluene through the association of toluene exposure and UTol.

Methods and materials

Factory and subject

The printing department in a plastic bag factory had 11 workers and 7 rotogravure printing machines, 2 large and 5 small. The factory design included a high roofed building with good general ventilation, but no local exhaust at the machines. The two large machines were set 5 meters apart and separated from the small ones which were set 1.5 meters apart from each other by a concrete wall. The samples and data were collected for nine days during the day

shift to obtain the target sample size (see SAMPLING STRATEGY). During the nine days of data collection, only two to four machines, including one large machine, ran on any one day. Most of the time, the employees worked around the machine; positioning a roll of plastic bags in place, setting up a paint tray to the right position, pouring the paint and solvent in the tray and mixing them with a wooden stick until achieving the right color and viscosity, inspecting the products and checking the level of paint in the trays. Three to four workers operated the machine and all performed the same job, but varying in work duration. They sat on chairs near the machines to monitor them and repeated the work mentioned above as needed (Plate 1). None of the workers wore personal protective equipment (PPE) such as a respirator, gloves or chemical protective clothing. While working, the employees cleaned off paint splashed on the machines and wiped their dirty hands with a cloth wetted with solvent several times daily. When the printing pattern and color changed, the workers cleaned the rollers of the printing machine with a cloth wetted with solvent after a piece of hard paper was used to take most of the paint off. Moreover, at the end of the work shift when the workers had to clean the machines, equipment and work areas, a cloth wetted with solvent was used again. Therefore, all workers received toluene both by inhalation and dermal exposure. The solvent was composed of 60 percent toluene, 30 percent IPA and 10 percent ethyl acetate. Approximately 200 to 350 liters of the solvent was used each day depending on the quantity of products and size of patterns.

An interview was conducted to recruit only the workers who did not present urinary tract and kidney disease, visible skin disease and/or skin damage and did not have potential exposure to solvents outside the workplace. Thereafter, all 11 workers in the printing department were recruited to participate in the study. Their demographics are presented in Table I. The workers wore company a T-shirt, trousers or jeans and sneakers to work. Data were collected and started after the study protocol was approved by the Ethics Review Committee for Human Research, Faculty of Public Health, Mahidol University. The protocol number was 219/2556, COA. No. MUPH 2014-074.

Plate 1.
Printing workers and workplace

Sampling strategy

All workers refused to carry the air sampling pump. Nevertheless, according to their work pattern, i.e. working around and sitting near the machine at all times, the stationary samples could adequately reflect the workers' exposure. In total, 27 samples, with 2–4 samples daily based on the number of machines run on that day, were collected by hanging personal pumps to the running machines closest to workers and the samplers were set at the workers' breathing zone (Figure 1). During the full shift, two consecutive samples, one in the morning (8:30 a.m. to 12:00 p.m.) and another one in the afternoon (1:00 to 4:30 p.m.), were collected to prevent a breakthrough. The TWA concentration was calculated from the two samples as $(C_1 \times T_1 + C_2 \times T_2)/(T_1 + T_2)$, where C is the concentration and T is the sampling time.

Regarding air sampling, the personal air sampling pumps were calibrated in line with the charcoal tubes according to good industrial hygiene practices both before and after air sampling. The average of the before and after flow rates were used to calculate the total air volume. Sample tubes differing in before and after flow rates greater than 5 percent were discarded. All samples and field blanks were kept in separated zip lock bags and carried back to the lab in an ice box. During air sampling, the researchers observed and recorded the characteristics of the job and time the participants spent at each location in order to calculate TWA toluene concentration.

For dermal sampling, the selected activated charcoal cloths (ACC – 100 percent activated woven carbon cloth, thickness 0.1 cm, surface density 240 gm/m^2) were tested for their

	n (%)		*n* (%)
Sex		*Age (years)*	
All males	11 (100)	< 30	6 (54.5)
		> 30	5 (45.5)
Smoking		*Years of work experience*	
None	0 (0)	< 1 year	7 (63.6)
		> 1 year	4 (36.4)
Alcohol consumption		*Education*	
None	0 (0)	Elementary	9 (81.8)
		Junior high school	2 (18.1)

Table I. Characteristics of the subjects

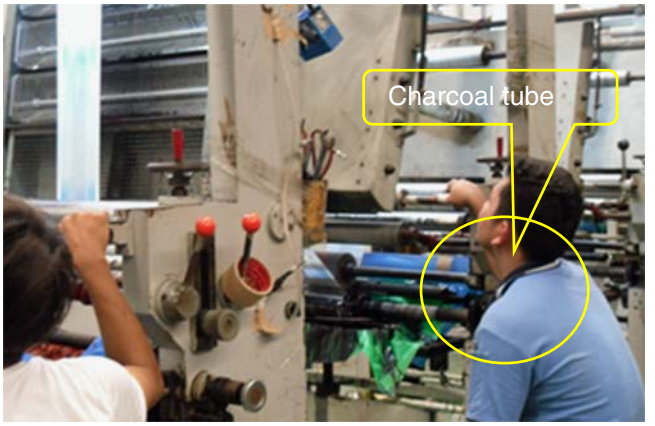

Figure 1. Air sampling equipment and sampler

absorption capacity in the lab. In total, 12 pieces of the 2 × 2 cm ACC pads were hung in a beaker placed in a tightly closed jar containing 99.99 percent of toluene at room temperature. Three pads were drawn from the jar at 24, 48, 72 and 96 h and analyzed for toluene. The amount of toluene in the samples taken at all intervals was approximately 34.29 ± 0.30 mg; thus, this was claimed as the maximum absorption capacity of the pad. The pads were tested in the field by wrapping them around the worker's fingers under normal working conditions for 4 h, revealing that toluene in the samples was well below the maximum capacity. However, to prevent exceeding the capacity of the pad, which may result in loss of toluene, the sampling time was limited to 4 h.

The sample stability was also determined by spiking 17,382.6 mg of toluene on 30 ACC pads and placing each one in a 1.8 ml glass vial sealed with an aluminum crimp cap and PTFE septum. They were stored at −20°C for 0, 7, 14, 20, 30 and 50 days. Five samples and blanks were extracted and analyzed for each period. After 14 days (the set of the 20th day), toluene loss of more than 10 percent was found, i.e. the stability of the sample at −20°C was at least 14 days.

The dermal sampler, CCP, was prepared from the ACC; 2 × 2 cm^2 of ACC was placed between aluminum foil and a gauze patch then stitched together on medical tape using a stapler (Figure 2). The samplers were preheated in an oven at 120°C for 2 h purging the contaminants and then stored in a desiccator overnight before storage in a sealed bottle until use.

The workers' hands were inspected and the surface area was measured. Six samplers were wrapped around the most likely part to be in contact with the solvent on both hands, i.e. the thumb, index and middle fingers (Plate 2) The samplers were changed every break

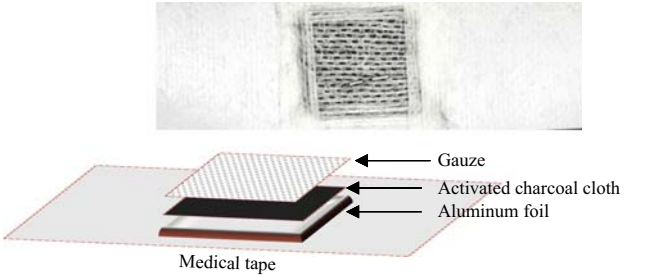

Figure 2.
Dermal sampler (size 2 × 2 cm^2)

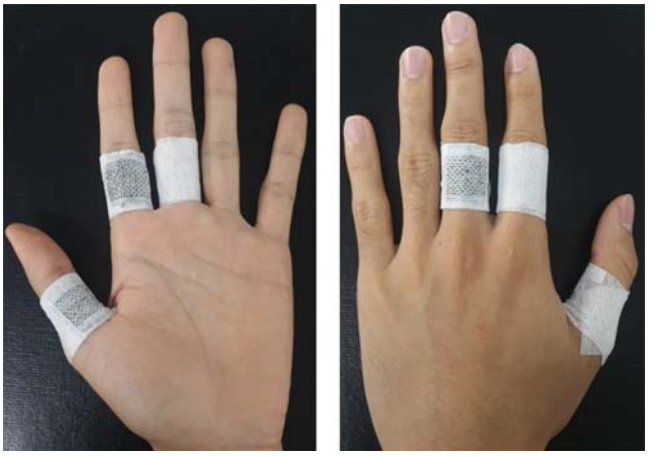

Plate 2.
Dermal samplers on the worker's hands

including before going to the lavatory. All removed samplers were kept in sealed containers separately for each worker and stored in an ice box during transport to the lab. In the lab, the samples were stored at −20°C until analyzed by GC/FID using the same method and conditions as the air samples within two weeks.

Concerning urine sampling, 65 urine samples were collected from the workers at the end of work shifts within the same day of dermal and air collection. The sample and data were collected for nine days to obtain at least 62 urine samples according to sample size calculation to determine the relationship between dermal exposure and urinary toluene based on the correlation coefficient of the two variables in the previous study, $r = 0.35$[11] using the equation as follows[17]:

$$n = \frac{\left(Z_{\alpha/2} + Z_{\beta}\right)^2}{C^2} + 3,$$

where n is the number of samples; $\alpha = 0.05$; $Z_{\alpha/2} = 1.96$; $\beta = 0.2$; $Z_{\beta} = 0.84$; and:

$$C = \frac{1}{2}\ln\left(\frac{1+r}{1-r}\right) = 0.365.$$

Then:

$$n = \frac{(1.96 + 0.84)^2}{0.365^2} + 3 = 61.85 \approx 62 \text{ samples.}$$

Whole urine samples were collected in 240 ml polypropylene bottles by the workers and consigned to the researcher. The volume and collection time were recorded. Only some amount of the urine was put in 15 ml cleaned and labeled polystyrene tubes. The sample tubes were placed in an ice box to transport to the laboratory and stored at −20°C until analyzed simultaneously with the laboratory blanks within two weeks.

Analysis

Three replicates were analyzed per air and dermal sample by gas chromatography equipped with a flame ionization detector (GC/FID) (Model GC-450, serial no. BR 1102M 044 Bruker, USA); and capillary column HP-Wax bonded polyethylene glycol length 60.0 m, diameter 320 μm, film thickness 0.25 μm (Agilent Technology, USA). The LOD (3 × SD) and LOQ (10 × SD) were 0.022 and 0.075 μg/l, respectively. The calibration curve was prepared at 15 different concentrations to cover the expected toluene concentration. The percentage of toluene recovery within 1 day and between days varied from 100.22 to 103.31 and 100.48 to 104.12, respectively. The coefficient of variance within 1 day and between days varied from 0.05 to 1.17 percent and 0.05 to 1.04 percent, respectively. The operating conditions of the GC/FID are presented in Table II.

The GC-HS/FID was used to analyze urine, i.e. the automated headspace sampler (Model 7697AG 4557-64000, serial no. 13500014 Agilent Technology, USA). The GC used an FID (Model 7890B G 3440B, serial no. 13513119, Agilent Technology, USA) and capillary column HP-Wax bonded polyethylene glycol length 60.0 m, diameter 320 μm, film thickness 0.25 μm (Agilent Technology, USA).

The calibration curve was prepared to cover the expected concentration. The LOD and LOQ were 0.361 and 1.202 μg/l, respectively. The percentage of toluene recovery within 1 day and between days varied from 100.22 to 103.31 and 100.48 to 104.12, respectively. The coefficient of variance within 1 day and between days varied from 1.39 to 2.24 percent and 1.46 to 1.81 percent, respectively. The above values were obtained and the GC-HS/FID conditions are shown in Table III.

Statistical analysis

The data were statistically analyzed using the software package SPSS for Windows, release 11.5 (SPSS Inc., Chicago, IL, USA). The p-value < 0.05 was considered to be statistically significant. Descriptive statistics were used to describe the characteristics of the samples, i.e. toluene in urine, toluene in air and toluene in CCP. Multiple linear regression was employed to evaluate the association between urinary toluene and its expected influencing factors, e.g. inhalation exposure and quantity of toluene in CCP.

Results

Inhalation exposure (Table IV) the TWA concentration for all workers over nine days range between 4.34 to 509.36 mg/m3 and the mean (SD) was 164.21(±118.13) mg/m^3, which exceeded the TLV of 75 mg/m^3. Among these, 46 of 65 TWAs exceeded the TLV. Whereas, the urinary toluene (UTol), an indicator of toluene uptake, of the workers varied by person and by workload on each day, the mean (SD) of the UTol was 13.42 (9.72) μg/L and the range was 2.12–48.5 ug/L. Among these, only three urine samples contained toluene exceeding the BEI of 30 μg/L, and 26 samples exceeded the 50 percent BEI.

Table II.
The operating conditions of GC/FID

GC-FID conditions	
Column	Capillary Column HP-Wax Bonded Polyethylene Glycol length 30.0 m, diameter 250 μm, film thickness 0.25 μm
Carrier gas	He
Pressure program	9.8 psi (3 min) to 11.0 psi (1 psi/min, hold 3 min)
Injector	Volume 1 μl
Injection technique	Split mode (10:1)
Injector temperature	200°C
Oven temperature	45°C (3 min) to 60°C (5°C/min, held 1 min) and to 100°C (10°C/min, held 2 min)
Detector temperature	250°C
Retention time	7.26 in

Table III.
The operating conditions of GC-HS/FID

Headspace condition	
Transfer temperature	120°C
Thermostat time	10 min
Needle temperature	120°C
GC cycle time	20 min
Sample temperature	80°C
Pressurized	0.15 min
Inject	1 min
GC-FID condition	
Column	Capillary Column HP-Wan Bonded Polyethylene Glycol length 60.0 m, diameter 320 μm, film thickness 0.25 μm
Carrier gas	He
The flow rate of the carrier gas	Constant at 0.8 ml/min
Injector	Volume 1 μl
Injection technique	Splitless mode
Injector temperature	200°C
Column temperature	45°C (1 min) to 100°C (10°C/min, held 2 min) and to 150 °C (15°C/min, held 2 min)
Detector temperature	250°C
Retention time	7.88 min

Worker no.	Hand surface area (cm^2)	N	Exposed duration (h)	Mean (SD) 8 h TWA (mg/m^3)	Mean (SD) UTol (ug/L)	Mean (SD) TolCCP (mg/cm^3)	Mean (SD) Skin absorbed dose (mg)
A	599.82	2	5.10 (0.57)	6.78 (3.09)	5.48 (2.13)	18.15 (2.05)	4.41 (0.98)
B	577.28	7	5.11 (1.33)	104.37 (91.86)	9.9 (7.03)	78.84 (44.72)	16.64 (12.27)
C	648.26	8	6.08 (1.04)	184.87 (141.60)	12.16 (8.98)	92.54 (48.41)	28.48 (18.09)
D	529.83	9	5.99 (1.94)	218.78 (142.99)	15.52 (14.34)	65.09 (39.10)	17.69 (13.69)
E	547.82	7	5.71 (1.51	176.14 (101.73)	12.8 (5.98)	95.59 (43.80)	22.51 (15.06)
F	610.75	7	6.94 (1.46)	255.93 (113.14)	24.77 (10.77)	164.13 (39.09)	55.05 (18.57)
G	539.48	6	6.35 (0.61)	164.88 (132.80)	12.75 (7.38)	86.47 (41.74)	22.82 (13.97)
H	570.22	8	6.76 (1.00)	131.28 (77.70)	15.31 (9.20)	160.43 (93.56)	49.40 (26.97)
I	608.68	6	4.93 (1.57)	85.67 (65.53)	7.35 (4.49)	113.17 (51.49)	24.04 (19.03)
J	536.45	2	5.50 (0.71)	105.27 (1.62)	14.52 (8.87)	94.95 (54.52)	21.32 (9.86)
K	466.1	3	5.83 (0.29)	231.09 (91.93)	6.64 (3.53)	50.83 (28.75)	11.06 (6.50)
Total mean (SD)			5.96 (1.39)	164.21 (118.13)	13.42 (9.72)	100.86 (61.66)	29.13 (21.12)

Notes: Kp = 0.000079 cm/h (5); N = number of samples and sampling days

Table IV. TWA (8 h), post-shift urinary toluene, toluene in CCP and level of potential dermal exposure of the employees by machine and date of collection

For skin exposure, the absorbed dose of toluene through the skin of the workers' two hands was determined from toluene on the CCP (TolCCP), to determine whether the TolCCP is a meaningful predictor for UTol. The quantity of toluene in all the CCP samples was below the maximum absorption capacity of the pad, but above the LOQ for toluene analysis. The average quantity of toluene on CCP and its SD was 100.86 and 61.66 mg/cm^3, respectively, ranging from 7.50 to 319.20 mg/cm^3. The scatterplot of the UTol and the independent variables (TWA and TolCCP) (Figure 3) showed a good linear relationship, i.e. TWA and TolCCP were promised predictors of the UTol. The relationship between UTol and the two variables was analyzed using multiple linear regression (Equation (1)). The correlation coefficient, r, and the coefficient of the determinant, r^2 of the model were 0.734 and 0.539, respectively:

$$\text{UTol}\ (\text{mg/L}) = 0.002 + 0.00005\ \text{TWA}\ (\text{mg/m}^3)) + 0.00003\ \text{TolCCP}\ (\text{mg}). \quad (1)$$

The β coefficient (Equation (2)) of TWA was 0.631 and that of TolCCP was 0.210; thus, the inhalation exposure (TWA) had a greater impact on the urinary toluene (UTol) level than that of the skin absorption (TolCCP):

$$Z_{\text{UTol}} = 0.631\, Z_{\text{TWA}} + 0.210\, Z_{\text{TolCCP}}. \quad (2)$$

Nevertheless, this was unsurprising because toluene is known to be readily absorbed from the lungs and much better than from the skin[18]. Furthermore, the surface area of the two hands, approximately 600 cm^2[19], was very small compared with 18,000 cm^2 of the lungs[19].

Because TolCCP is a significant predictor contributing to urinary toluene, the dermally absorbed dose (SkDose) was calculated using TolCCP. The SkDose varied between 0.75 and 31.92 mg when Kp was 0.000079 cm/h, as suggested by Tsuruta[6]. The toluene mixture was used and the exposure time constituted the workers' work period for each day (Table IV). The dermally absorbed dose accounted for approximately 12.3 percent of the TLV.

Discussion and conclusion

Because the BEI of toluene is based on a direct correlation with the TLV, the concentration of urinary toluene of 0.03 mg/L could be expected when the TWA concentration was at TLV.

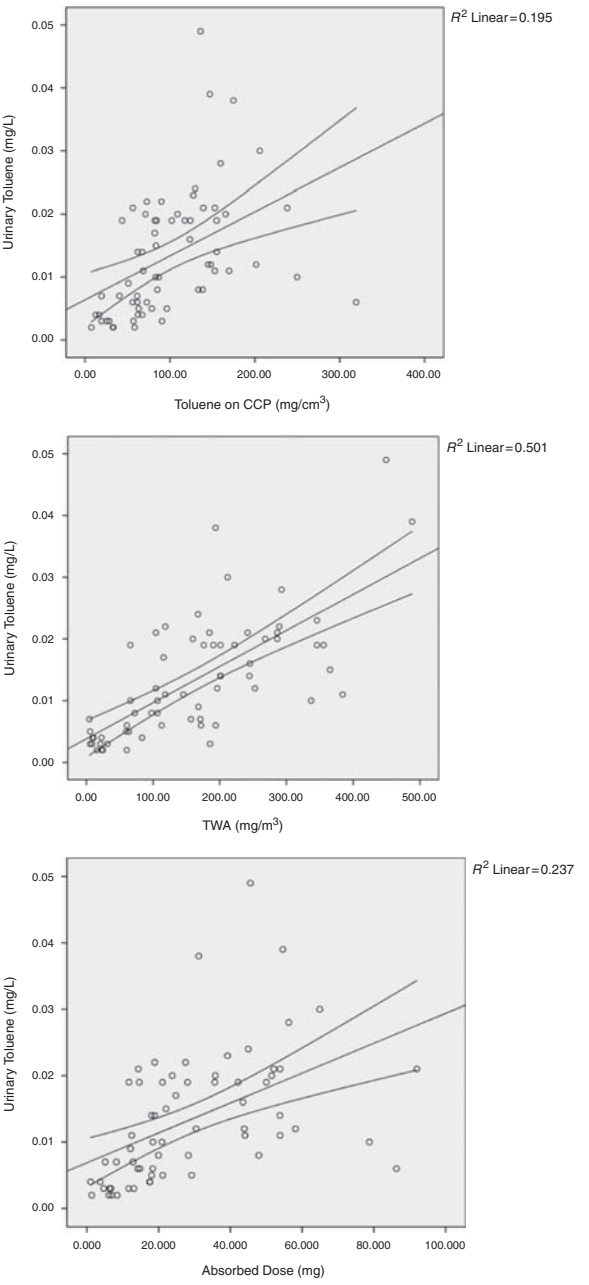

Figure 3.
The scatterplot of the UTol and TWA, TolCCP and absorbed dose

However, the TWA concentration of toluene in this study was higher compared with urinary toluene, i.e. the average of TWA was higher than TLV while that of urinary toluene was well below the BEI. The TWA concentration obtained from the area samples was likely overestimated. When the workers refused to carry air sampling equipment, stationary sampling

was selected confidently because the workers spent most of their working time around the machine. Thus, according to our observation, the equipment was attached to the machine at the workers' seated breathing zone to best represent the workers' inhalation, though located close to the paint tray. Based on the results, the size of the room and good general ventilation in the workplace could have more impact on the exposure concentration of the workers than the location of the workers[20] (see Plate 1 and Figure 1). One foot away from the breathing zone at the sitting level, the toluene concentration at the workers' standing breathing zone could be significantly lower. Nevertheless, due to the urinary toluene, 3 and 26 of 65 urine samples contained toluene above the BEI and 50 percent BEI, respectively. At this level of exposure, workers should wear respirators as a minimum safety precaution.

The dermally absorbed dose accounted for approximately 12.3 percent of TLV, which seemed insignificant regarding the general situation where the workers wore respirators. However, in this case, the dermal absorption could contribute to the total uptake and cause the exposure above the occupational exposure limit. Three workers were identified with urinary toluene levels exceeding the TLV. If they wore respirators, it is certain that their exposure would not reach even 50 percent TLV, and if they wore only suitable gloves, their exposure may or may not have reached TLV.

The CCP could possibly be a good dermal sampler for dermal absorption among printing workers or others who clean their hands with solvent wetted cloth instead of washing with the solvent. When wiping hands with the solvent wetted cloth, the solvent would contact the activated carbon at only the surface of the CCP and this would simulate the method of the printing worker's skin exposure to the solvent. The amount of toluene on CCP, well below the maximum absorption capacity of the pad, could serve as evidence to support this concept. Furthermore, when substituting the SkDose for TolCCP in the linear regression model (Equation (1)), the correlation and the power of determinants, r and r^2, were improved to 0.739 and 0.546, respectively:

$$\mathrm{UTol(mg/L)} = 0.002 + 0.00005\ \ \mathrm{TWA(mg/m^3)} + 0.00011\ \ \mathrm{SkDose(mg)}. \qquad (3)$$

The r and r^2 of the SkDose itself in the model to predict urinary toluene was 0.487 and 0.237, respectively, i.e. the SkDose, which takes both the skin surface area of the two hands and exposure time into account produces a better prediction of toluene uptake of the workers. Therefore, it may be concluded that the CCP could be a good dermal sampler when the solvent wetted cloth was used for wiping skin.

Based on the findings from this study, toluene could permeate through the skin at significant levels and contribute to those from the inhalation exposure causing health effects. Therefore, appropriate PPE for dermal protection should be assigned to all toluene workers with potential skin exposure.

Limitations of the study

There are two limitations to this study. First, as the study protocol approved by the Ethics Review Committee had to be followed strictly, the study relied on the cooperation of the participants. The workers normally do not wear respirators and did not cooperate with the request to do so during the study. Therefore, the urinary toluene from inhalation was estimated from the best previous study[11] to obtain the urinary toluene from the dermal absorption. Thus, the results may have deviated from the true values.

Second, the skin permeation coefficient (Kp) of toluene on human skin is new, and currently, no studies have been conducted among humans. Therefore, the Kp value obtained from the octanol/water partition coefficient and molecular weight were used to estimate the dermal absorption dose. This may have affected the results and led to erroneous estimations of dermal absorption doses.

Despite such limitations, the results remain useful to some extent. However, for further study on dermal permeation of any chemicals, these two limitations should be eliminated or reduced to increase the benefit of the study.

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