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- Comparison of urinary hippuric acid, toluene and *o*-cresol as biological exposure indices for workers exposed to toluene -

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- Comparison of urinary hippuric acid, toluene and *o*-cresol as biological exposure indices for workers exposed to toluene -

2001 6

가

가

	
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1.	4
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3.	5
4.	14
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1.	15
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3.	18
4.	20
5.	23
.	27
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	34
	41
ABSTRACT	43

1.	6
2.	8
3.	10
4.	12
5.	13
6.	15
7.	16
8.	18
9.	20
10.	22
11.	24

1.		6
2.		7
3.		8
4.		9
5.		10
6.		11
7.	-	12
8.	-	13
9.		20
10.		21
11.	-	21
12.		28

가 , ,
- 가
.($p < 0.05$). 1ppm

가

(, BMI,
, , , ,)

가

가 가 가 .
가
- 1ppm

가 .



: , , , ,
- ,

•

, 92.13, 110.6

(Budavari, 1996),

가

가

(Anger, 1985 ; , 1993 ; , 2000).

(American Conference of Governmental Industrial

Hygienist, ACGIH) 8 가

(Threshold Limit Value - Time Weighted Average, TLV-TWA) 50ppm

(2000 TLV and BEIs, ACGIH, 2000),

TLV-TWA 100ppm,

(Threshold Limit Value - Short Term Exposure

Limit, TLV-STEL) 150ppm (,

, 2000).

가

(Ikeda Hara, 1980 ; Brugnone, 1986 ;

, 1993).

가

가 . ACGIH(TLV and BEIs, 2000) (, 1999)

가 (end of shift)

(ACGIH, TLVs and BEIs, 2000)

(, 1999).

가 (Ogata, 1985 ; , 1996).

가 (Nise, 1992),

가 (Catillina Chamoux, 1980; Villanueva , 1994).

가 (Dossing, 1982; De Rosa , 1987; , 1996).

Tardif (1999) -

가 (, 1993; ,
 1996) . Fustinomi (2000)
 .
 (1987);
 (1988); (1989); (1991); (1993);
 (1993); (1996); (1997); (2000)
 가 - (1988);
 (1993); (2000)
 . 가

•

1.

10

56

. 10

3

가

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2.

가.

(, ,)

(2001-20)

(PAS-500,

MSA, USA)

0.1 - 0.2 l/ min

70mm

(Coconut shell charcoal no. 226-01, SKC, USA)

6

()

.

10M~~2~~

, BMI(Body Mass Index),

가

3.

가.

(National Institute for Occupational Safety and Health, NIOSH)

가 /

(Gas Chromatograph / Flame Ionization Detector, HP 5890 series ,
USA, GC/FID)

(reagent grade) toluene(Sigma, St Louis,
MO, USA)

Carbone Disulfide (Junsei, Tokyo, Japan) 1Mℓ

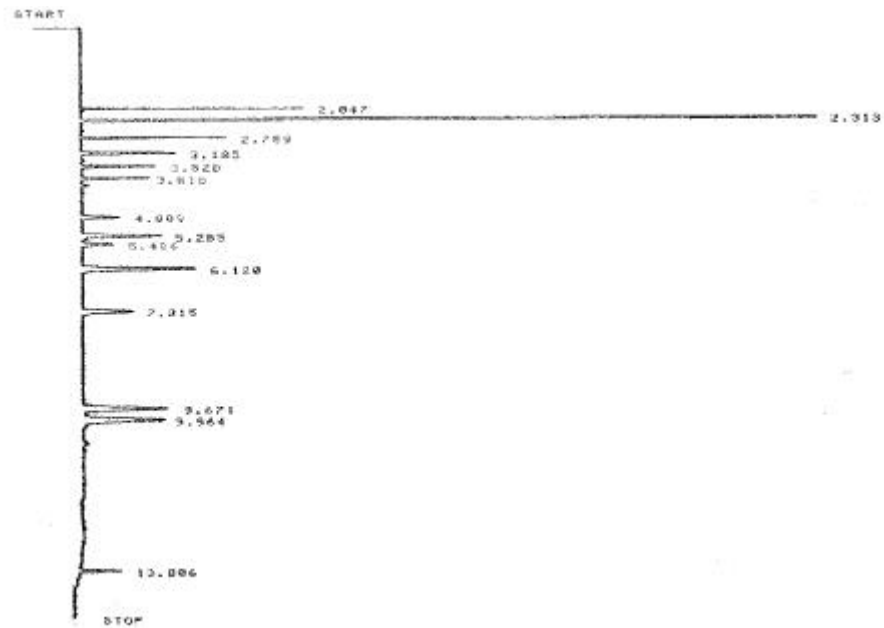
30 1μℓ .

1 .

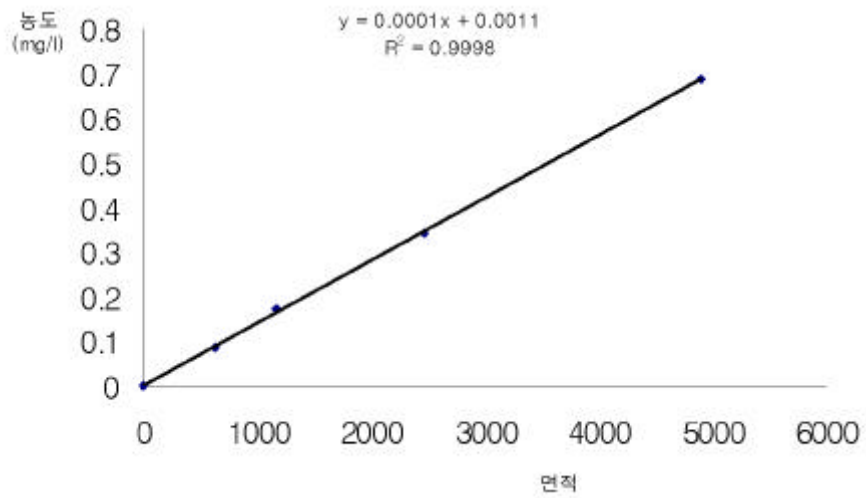
1.

Descriptions	Conditions
Instrument	HP 5890 series
Detector	Flame ionization detector
Column	hp-ffap capillary column (25m x 0.32mm ID x 0.52 μ m film thickness)
Temperature	Injection port : 210 Detector : 250 Column oven : 60
Carrier gas	N ₂ , 1 <i>ML</i> / min
Flow rate	100 <i>ML</i> / min
Injection volume	1.0 μ l
Split ratio	100 : 1

(retention time) 1 6.1
2



1.



2.

/ (High Performance Liquid Chromatograph/ Ultra Violet Detector, Varian 9050, USA, HPLC/ UVD)

hippuric acid(Sigma, St Louis, MO, USA)

0.2 Mℓ [pH 3.3

20mM KH₂PO₄(Sigma, St Louis, MO, USA) : Acetonitrile (Sigma, St

Louis, MO, USA) = 85 :15 (V:V)] 1.8Mℓ 10 syringe filter

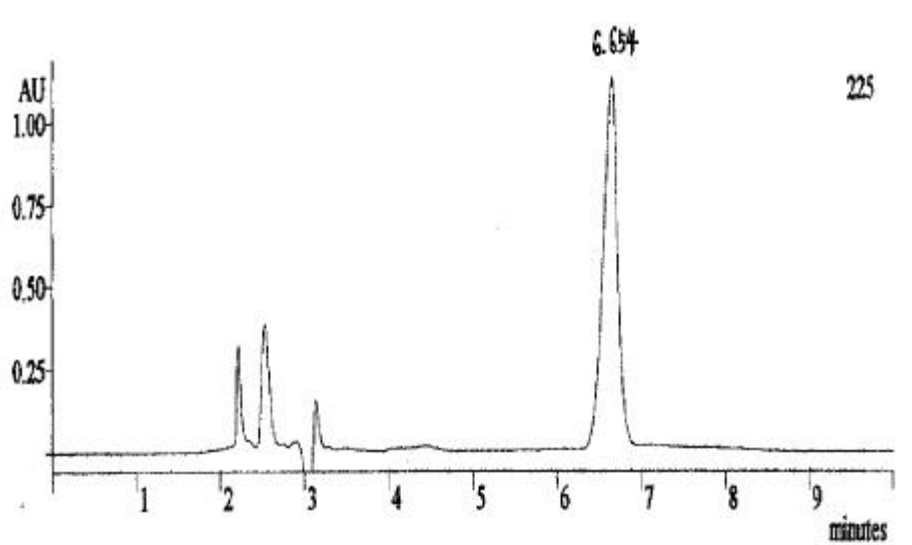
2

2.

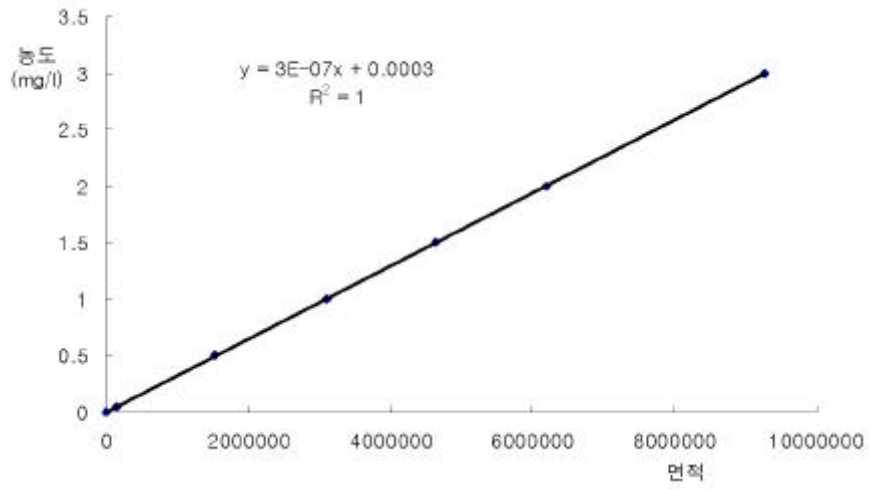
Descriptions	Conditions
	Varian HPLC 9012 Solvent delivery system
Instrument	9050 UV-Vis Detector 9300 Autosampler
Column	C ₁₈ (250mm * 4.6 mm, 5, phenomenex, USA)
Temperature	Column oven : 25 ()
Mobile phase	20 mM KH ₂ PO ₄ (ph3.3) : Acetonitile = 85 : 15 (V:V)
Flow rate	1.0 Mℓ/ min
Injection volume	20 μℓ
Wave length	UV 225nm

3 6.6

4 .



3.



4.

Inoue (1998)

/

toluene

acetonitril 1Mℓ

1Mℓ

4

100μℓ methanol(Merck, Darmstadt, Germany) 가 10

syringe filter

450Mℓ acetonitril 60% perchloric acid(GFS chemical, Columbus, OH,

USA) 1Mℓ phosphoric acid(Merck, Darmstadt, Germany) 50μℓ가

550Mℓ

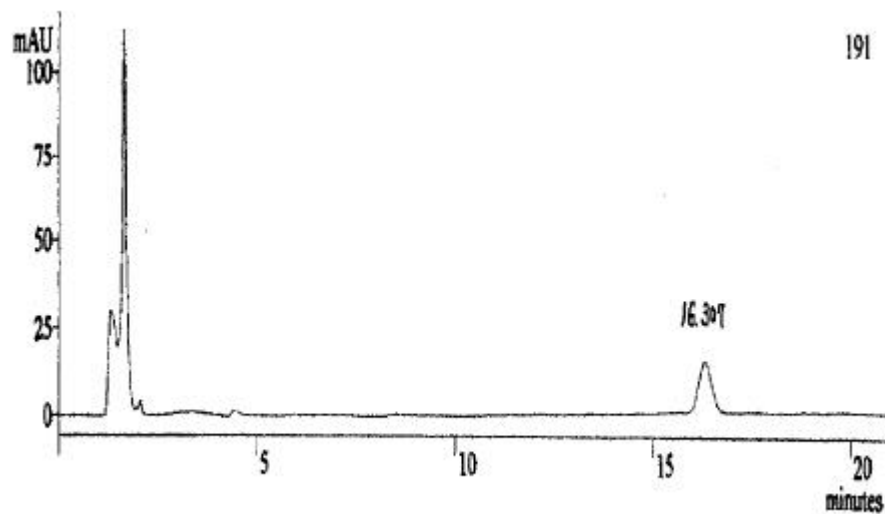
3

3.

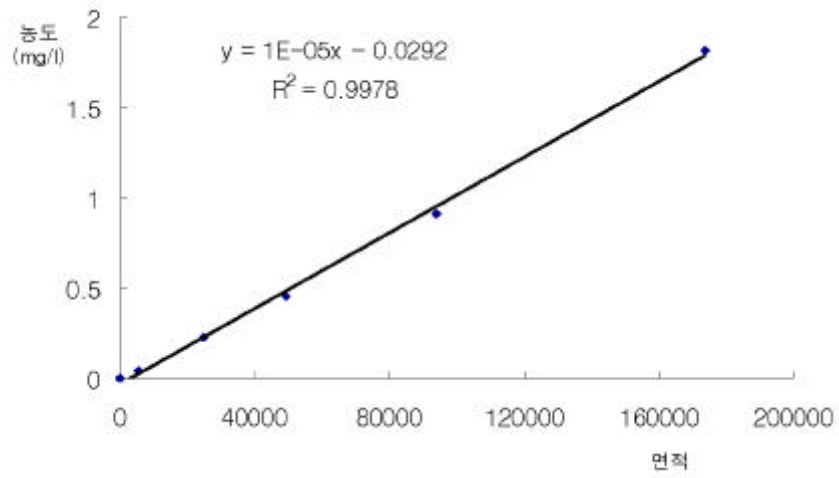
Descriptions	Conditions
	Varian HPLC 9012 Solvent delivery system
Instrument	9050 UV-Vis Detector 9300 Autosampler
Column	C ₁₈ (250mm * 4.6 mm, 5, phenomenex, USA)
Temperature	Column oven : 25 ()
Mobile phase	450 ml Acetonitril + 550 ml (60% Perchloric acid 1ml + phosporic acid 50 ul + Water 548.5 ml)
Flow rate	1.5 <i>ml</i> / min
Injection volume	20 <i>μl</i>
Wave length	UV 191nm

5 16.3

6 .



5.



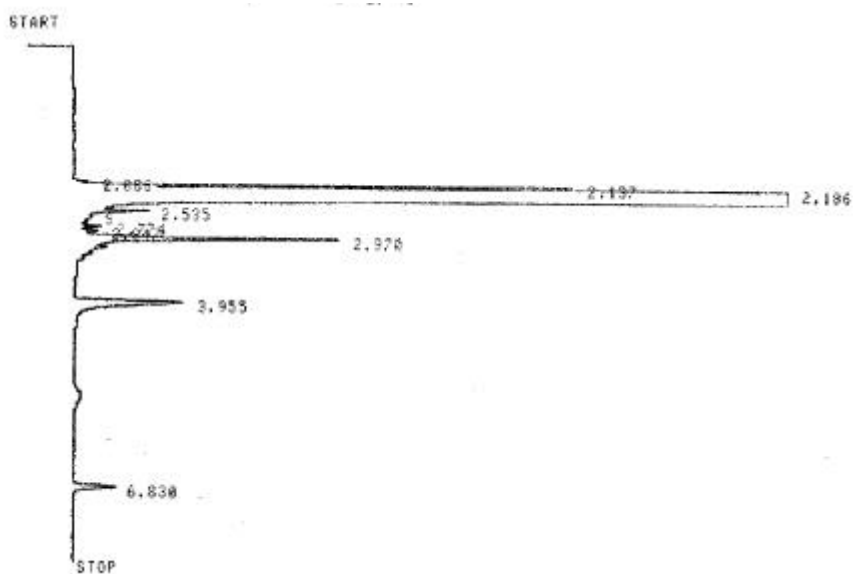
6.

, isopropyl ether(Junsei, Tokyo, Japan)
 가 /
 o-cresol(Sigma, St Louis, MO, USA)
 1Mℓ
 4Mℓ Hydroclolic acid(Junsei, Tokyo, Japan) 1Mℓ 가
 100 (Water bath) 30 가 .
 Isopropyl ether 1Mℓ 가 5
 3000rpm 8 Isopropyl
 ether .
 4 .

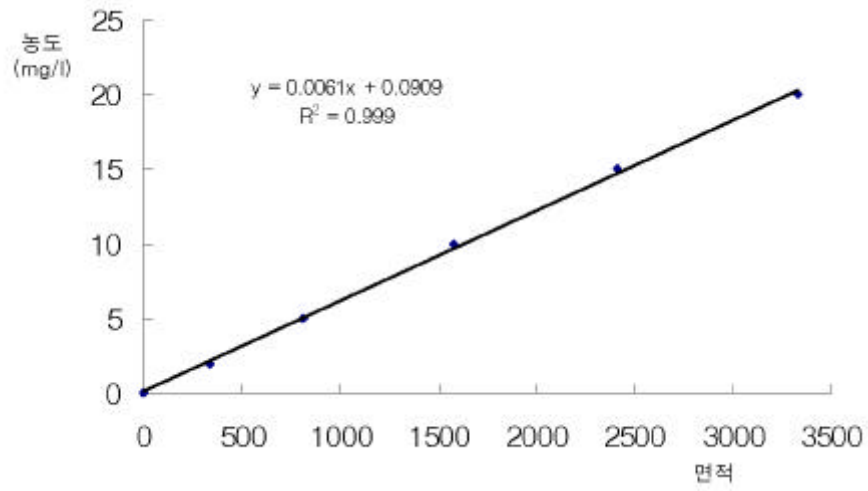
4.

Descriptions	Conditions
Instrument	HP 5890 series
Detector	Flame ionization dector
Column	Ultra-2 capillary column (25m x 0.32mm ID x 0.17 μ m film thickness)
Temperature	Injection port : 250 Ditector : 250 Column oven : 80
Carrier gas	N ₂ , 1 <i>Me</i> / min
Flow rate	100 <i>Me</i> / min
Injection volume	1.0 μ l
Split ratio	10 : 1

- 7 6.8
8 .



7. -



8. -

Creatinine Automatic analyzer

5 .

5.

Descriptions	Conditions
Instrument	Hitach 747 Automatic Analyzer(Hitachi, Japan. 1995)
Wave length	Main length : 505 nm Sub length : 600 nm
Sample volume	14 μ l

1.06 ± 0.43g/ ,

0.84 ± 0.35 g/ .

(Limit of detection, LOD) NIOSH(1995)

0.086 mg/ , 0.05 mg/ ,
0.05 mg/ , - 1.68 mg/ .

4.

, BMI, , , , ,

, *t*- ,

, , -

t- .

SPSS 10.0 for Windows

•

1.

56 가
 13.268 ± 18.994 ppm 1ppm , 1 - 10
 ppm , 10 - 50 ppm , 50 ppm 4
 6 .

6. ()

	(ppm)	(ppm)*		(ppm)
	56	13.268 ± 18.994	0.000	85.180
- 1	13	0.505 ± 0.283	0.000	0.820
1 - 10	20	5.209 ± 2.876	1.100	9.410
10 - 50	19	18.364 ± 9.665	10.120	44.240
50 -	4	70.840 ± 16.696	52.980	85.180

* \pm , (n=56)

2.

, , BMI, ,
 , ,

7 .

7.	()	(n=56)
		(%)
		56 (100%)
		0 (0%)
	- 29	9 (16.1%)
()	30 - 39	32 (57.1%)
	40 -	15 (26.8%)
	- 20	14 (25.0%)
BMI (kg/ m ²)	21 - 25	34 (60.7%)
	26 -	8 (14.3%)
		16 (28.6%)
()	1 - 9	27 (48.2%)
	10 -	13 (23.2%)
		27 (48.2%)
		29 (51.8%)
		35 (62.5%)
		21 (37.5%)
		55 (98.2%)
		1 (1.8%)
		18 (32.2%)
()	1 - 2	27 (48.2%)
	3 -	11 (19.6%)

56 .

29 , 30 - 39 , 40 9

(16.1%), 32 (57.1%), 15 (26.8%) BMI(/ ²) 20

, 21 - 25 , 26 14 (25.0%), 34 (60.7%), 8 (14.3%)

. 56 16 (28.6%) 27

(48.2%) (10) , 13 (23.2%) .

35 (62.5%)

21 (37.5%) .

1 (1.8%) 55 (98.2%)

. 56 18 (32.2%) 1

, 27 (48.2%) 1 -2 , 11 (19.6%) 3

.

3.

가

8

8.

			*	*	-	*
			(g/ g creatinine)	(mg/ g creatinine)	(mg/ g creatinine)	
		56	1.324 ± 1.118	0.141 ± 0.191	1.820 ± 2.550	
	- 29	9	1.583 ± 1.784	0.166 ± 0.132	3.077 ± 4.999	
	30 - 39	32	1.297 ± 0.900	0.130 ± 0.223	1.341 ± 0.737	
()	40 -	15	1.226 ± 1.114	0.151 ± 0.147	2.083 ± 2.907	
BMI	- 20	14	1.795 ± 1.532	0.181 ± 0.143	3.036 ± 4.824	
(kg/ m ²)	21 - 25	34	1.071 ± 0.862	0.134 ± 0.221	1.414 ± 0.837	
	26 -	8	1.575 ± 1.060	0.101 ± 0.110	1.411 ± 0.795	
		16	1.777 ± 1.372	0.149 ± 0.166	1.702 ± 0.919	
	1 - 9	27	1.083 ± 0.650	0.153 ± 0.235	1.700 ± 2.260	
()	10 -	13	1.267 ± 1.432	0.106 ± 0.104	2.211 ± 4.179	
		27	1.184 ± 0.992	0.192 ± 0.247	1.710 ± 2.270	
		29	1.454 ± 1.226	0.094 ± 0.099	1.920 ± 2.823	
		35	1.312 ± 1.003	0.124 ± 0.211	1.356 ± 0.756	
		21	1.344 ± 1.313	0.170 ± 0.150	2.591 ± 3.989	
		55	1.330 ± 1.127	0.139 ± 0.192	1.815 ± 2.573	
		1	0.963 ± 0.000	0.260 ± 0.000	2.028 ± 0.000	
		18	1.029 ± 0.538	0.215 ± 0.279	1.767 ± 2.693	
	1 - 2	27	1.274 ± 1.128	0.120 ± 0.134	1.449 ± 0.878	
()	3 -	11	1.929 ± 1.586	0.072 ± 0.068	2.812 ± 4.469	

* ± , BMI ; Body Mass Index = / ²

29 , BMI 20 BMI 26 ,
 , , ,
 , 3 ,
 29 , BMI 20 , ,
 , , ,
 . - 29 , BMI
 20 , 10 , ,
 , ,
 가 (p>0.05).

4.

9

9.

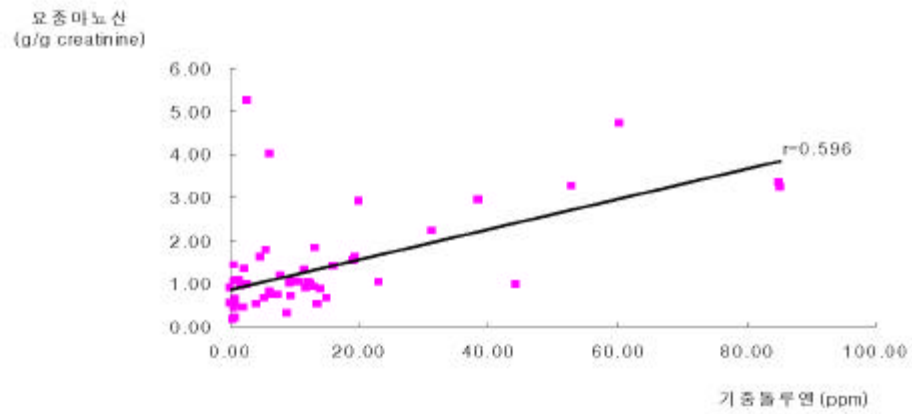
(ppm)	(g/ g creatinine)	(mg/ g creatinine)	(mg/ g creatinine)
1.000			
0.596**	1.000		
- 0.051	0.079	1.000	
0.037	0.523**	0.232	1.000

**P<0.01

R=0.596

95%

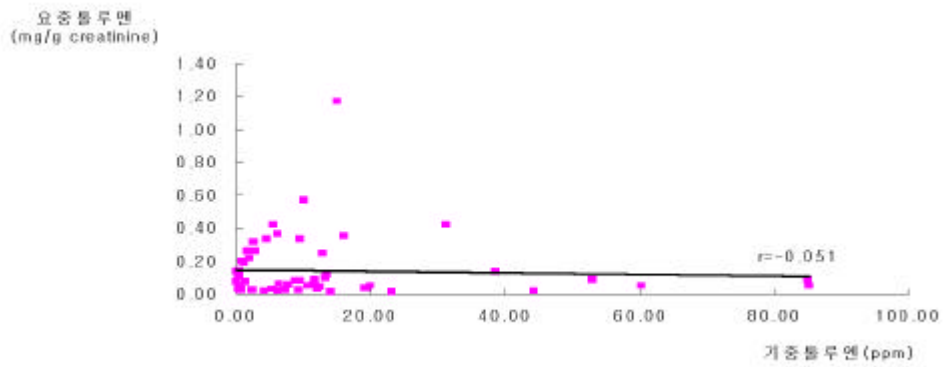
(p<0.05).



9.

R = -0.051 95%

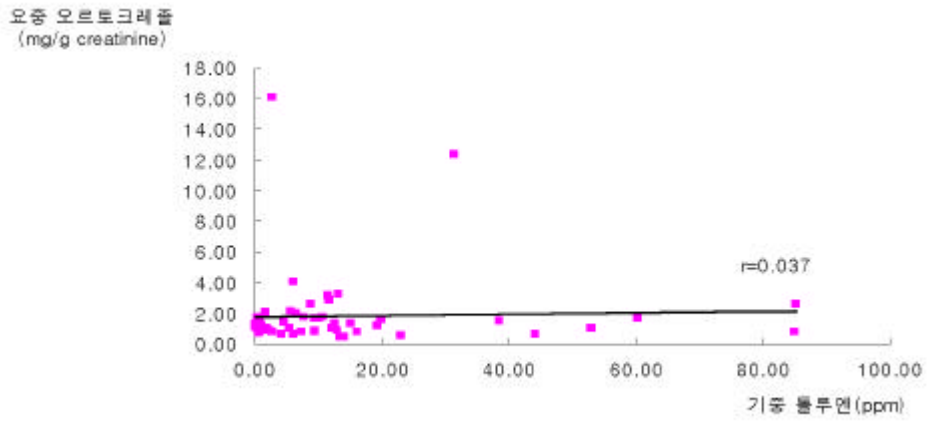
(p > 0.05).



10.

R = 0.037 95%

(p < 0.05).



11.

가 10ppm (10%)

, - 10 .

10. 10ppm

(ppm)	(g/ g creatinine)	(mg/ g creatinine)	(mg/ g creatinine)
1.000			
0.158	1.000		
0.130	0.491**	1.000	
0.037	0.815**	0.339*	1.000

**P<0.01 , *P<0.05

가 10 ppm

, , - R=0.158, R=0.130,
R=0.037 (p>0.05).

5.

11

11.

(ppm)	*			*			- *			
	(g/ g creatinine)		p-	(mg/ g creatinine)		p-	(mg/ g creatinine)		p-	
56	0.588 ± 0.398	1.324 ± 1.118	0.000	0.029 ± 0.019	0.141 ± 0.190	0.000	1.149 ± 1.037	1.819 ± 2.550	0.047	
- 1	13	0.461 ± 0.378	0.561 ± 0.381	0.287	0.024 ± 0.012	0.070 ± 0.057	0.011	0.797 ± 0.399	1.114 ± 0.292	0.037
1 - 10	20	0.572 ± 0.338	1.317 ± 1.209	0.000	0.029 ± 0.011	0.159 ± 0.140	0.000	1.171 ± 1.006	2.157 ± 3.389	0.245
10 - 50	19	0.587 ± 0.419	1.364 ± 0.685	0.000	0.027 ± 0.015	0.186 ± 0.284	0.000	1.181 ± 1.185	2.005 ± 2.653	0.048
50 -	4	1.090 ± 0.391	3.647 ± 0.721	0.004	0.060 ± 0.048	0.069 ± 0.023	0.717	2.029 ± 1.628	1.536 ± 0.806	0.669

* ±

가 (p<0.05).

(Occupational Safety and Health Administration, OSHA) 8 가 (TLV-TWA) 100ppm

1% , 1% -10% , 10% -50% , 50% 4
 (1ppm , 1ppm -10ppm , 10ppm -50ppm , 50ppm)

, , -

.

가 1ppm

0.461 ± 0.378 g/ g creatinine, 0.561 ± 0.381 g/ g creatinine
 가 가 (p=0.287),
 - 0.024 ± 0.012 mg/ g
 creatinine, 0.797 ± 0.399 mg/ g creatinine, 0.070 ± 0.057 mg/ g
 creatinine, 1.114 ± 0.292 mg/ g creatinine 가

가 (p<0.05).

1ppm 10ppm ,
 가 (p<0.05) -
 가 (p=0.245).

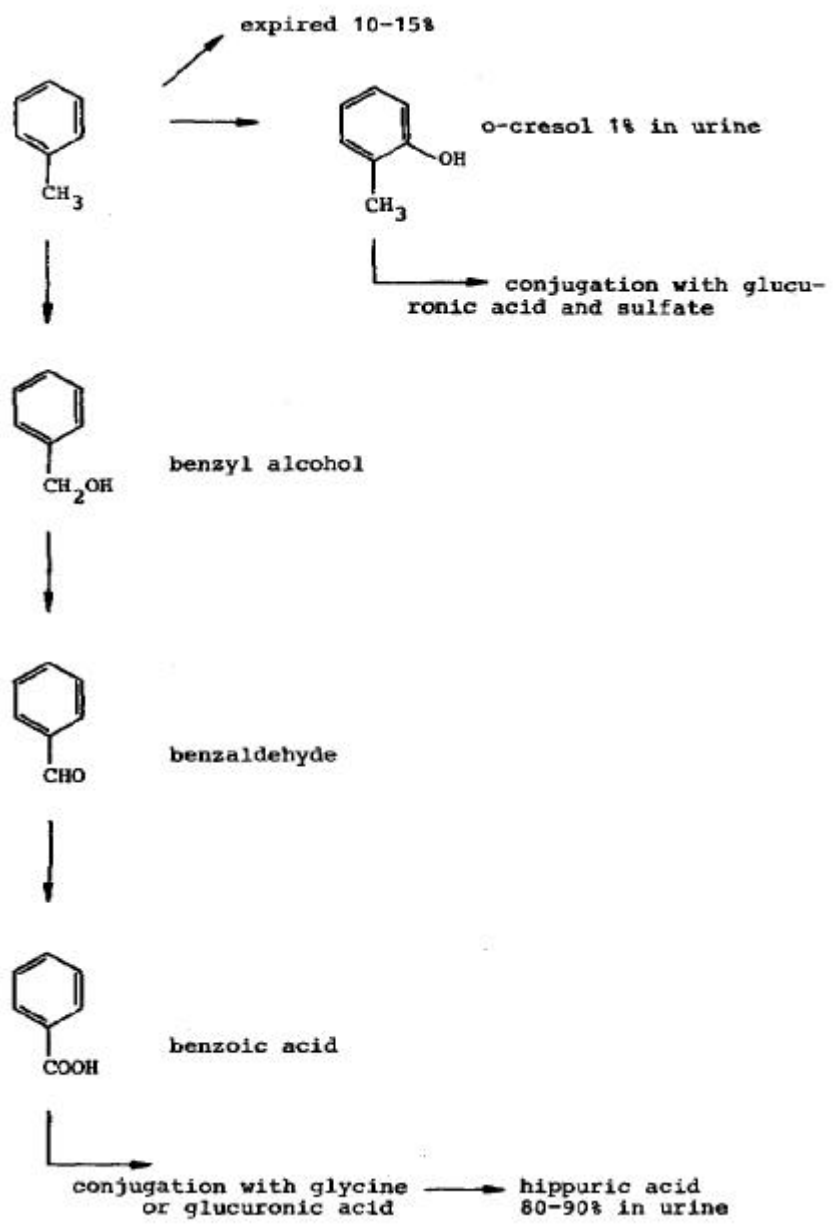
10ppm 50ppm , ,
 - 가 (p<0.05).

50ppm 1.090 ± 0.391 g/ g
 creatinine, 3.647 ± 0.721 g/ g creatinine

가 (p<0.05) -
0.060 ± 0.048 mg/ g creatinine, 2.029 ± 1.628 mg/ g creatinine,
0.069 ± 0.023 mg/ g creatinine, 1.536 ± 0.806 mg/ g creatinine
가 (p>0.05).

•
 ,
 10 -
 15% (mixed function
 oxidation system) benzylalcohol, benzaldehyde, benzoic acid
 benzoic acid glycine
 (hippuric acid) , 1% o-cresol, m-cresol,
 p-cresol benzoyl glucuronide (Ogata , 1970; Koga,
 1978; Hasegawa, 1983; Wallen, 1986; ,1988; Baelum, 1990;
 2000). - -
 (Cohr , 1979), -
 -
 (Dossing, 1982; De Rosa , 1987;
 , 1988; Tardif , 1998).

12 .



12.

(cited Peter Arlien-Sborg, Solvent neurotoxicity, 1992)

18.994 ppm (1993) 72ppm, 99.2 ppm

(1988) 77.7ppm, (1993) 34.4 ppm, (1996) 35.0 ppm, (2000) 13.269 ±

creatinine (1988) 9.51 g/ g creatinine, (1993) 1.78 g/ g creatinine, (1996) 1.50 g/ g creatinine, (1993) 1.60 g/ g creatinine, (2000) 2.95g/ g creatinine

1.324 ± 1.118 g/ g

(1988) 0.776 mg/ g creatinine, (1993) 0.283 mg/ g creatinine

1.820 ± 2.550 mg/ g creatinine

0.141 ± 0.191 mg/ g creatinine

BMI,

(1996)

(2000)

가

(1996)

(2000)

,

가

,

.

$r=0.596$

(1988),

(1993),

(1996),

(2000)

$r=0.481$

$r=0.684$

.

$r=-0.051$

-

$r=0.037$

50%

가 10ppm

,

-

10ppm

-

.

.

NIOSH

1ppm

, 50ppm

-

가 (p>0.05), 가

(p<0.05),

가

가

가

가 가

1ppm

가

가

1ppm

가

가

가

가

가

가

•

, , -

, ,

.

(, BMI,

, , , ,)

가

가 가

가

- 1ppm

가

가

가

가

가

o-cresol

, 1993

ALDH2 genetic polymorphism

1997; 9(2): 332-340

-glucosaminidase activity

3(2): 166-176

N-acetyl-

1993;

19(2): 177-183

1986;

. 1987; 20(2): 228-235

, , . 가
1996; 3(2):
165-176

, , , , , .
1993; 3(2):
188-193

. 가 1996; 4: 122-139

, , , .
1989; 22(4): 480-485

, , , .
o-cresol 1988; 27(2): 4-11

, , , , , , , .
1988; 21(2):
374-379

가
2000; 12(3): 405-420

1991; 1(2): 192-199

, 2000.

. 1995.

2000; 33(1): 45-50

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indices of toluene exposure by liquid chromatography on dynamically modified silica. *Journal of Chromatography* 1982; 229: 141-148

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<

>

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,

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2000 10

—
No. _____

:	
:	
:	
:	-
:	cm
:	kg

1. 0
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 , , , , , () ()

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2. ? 0 .
 가. ()
 . ()
 . ()

3. ?
 () ()

4. (,
) ?
 () ()

5. ?
 가. ()
 . 1 - 2 ()
 . 3 ()

ABSTRACT

Comparison of urinary hippuric acid, toluene and *o*-cresol as biological exposure indices for workers exposed to toluene

Jung Ho Hwang
Department of Occupational Health
Graduate School of
Health Science and Management
Yonsei University

(Directed by Professor Jaehoon Roh, M.D., Ph.D.)

Organic solvents, which are very necessary in many industrial fields, have various uses and are now increasingly consumed. Especially, as toluene is widely used as a substitute material for benzene, the chances of workers' occupational exposure to toluene are becoming higher than ever before.

This study was performed to compare the urinary hippuric acid, toluene and *o*-cresol as indices for biological exposure for workers exposed to toluene in air the statistical differences of various individual characteristics, the correlations between each biological exposure index and the concentration of individual exposure to toluene in air, and the statistical differences of the indices depending on sampling time points.

The results of the study are as follows;

1. Factors such as age, BMI, benzoic acid containing foods, alcohol,

smoking, drug, coffee did not affect the excretion of urinary hippuric acid, urinary toluene and urinary o-cresol.

2. For urinary hippuric acid, the correlation with the individual exposure concentration to toluene in air was statistically significant ($r=0.596$, $p<0.05$) and the correlations for urinary toluene and o-cresol were $r=-0.051$ and $r=0.037$, respectively, thus the correlations were not statistically significant and low. Besides in cases lower than 10ppm, the correlation between the concentration of individual exposure to air-toluene and three biological monitoring indices was not statistically significant.

3. Difference of biological exposure indices in the beginning of work and end of shift to individual exposure to toluene in air were statistically significant that the urinary hippuric acid, toluene, and o-cresol in end of shift were higher than beginning of work. However, in cases lower than 1ppm, difference of the urinary toluene and o-cresol were statistically significant in the beginning of work and end of shift, but urinary hippuric acid was not.

We concluded that, while the individual characteristics (e.g., age, body mass index, benzoic acid containing foods, alcohol, smoking, drug, coffee) did not affect the excretion of urinary hippuric acid, toluene and o-cresol. But excretions changes through the beginning of work and the end of shift have the statistical significance, so sampling time at the end of shift was very important.

Although the excretion of urinary hippuric acid showed significant correlation with the exposure to toluene in air, urinary toluene and o-cresol was recommended to be used as a subsidiary index in very low concentration of toluene in air.

Key words : biological exposure index, toluene in air, urinary hippuric acid, urinary toluene, urinary o-cresol, end of shift