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ORIGINAL ARTICLE

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Simplified procedures for estimation of biological occupational exposure limits

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Abstract

Objectives: To simplify the procedures to estimate biological occupational exposure limits (BOELs) by use of the ratio of geometric mean (GM) concentration of un-metabolized organic solvent in urine (U-GM) over GM organic solvent concentration in air (A-GM) (the [U-GM/A-GM] ratio).

Methods: Occupational Exposure Limits (OELs) and BOELs were cited from publications from the Japan Society of Occupational Health (JSOH) and the American Conference of Governmental Industrial Hygienists (ACGIH). Data on [U-GM/A-GM] and the SLOPE of exposure-excretion regression line were collected from published articles (men and women were treated separately). Correlation analysis and paired *t* test were employed as the method to examine statistical significances.

Results: Significant linear correlation was established between the SLOPE and the [U-GM/A-GM]. Thus, it was considered to be possible to calculate the SLOPE value from the [U-GM/A-GM]. Previously established equation of BOEL = SLOPE × OEL allowed to estimate BOEL values in 22 cases of data sets. The comparison of the estimated BOELs with the existing BOELs (JSOH's BOELs and ACGIH's BEIs) in terms of the ratio of [(estimated BOEL)/(existing BOEL)] showed that the ratios for the 22 cases probably distributed log-normally with a GM of 0.85, and the maximum was 5. Therefore, the estimated BOEL may be generally applicable in occupational health when BOEL remains yet to be established. In the worst case, the estimated BOEL may be five times greater than it should be. The recommended procedures for application of estimated BOEL values were described.

Conclusion: Simplified procedures for estimation of BOEL values are proposed.

KEYWORDS

biological occupational exposure limit, regression analysis, simplified procedures, solvent in air, solvent in urine

1 | INTRODUCTION

It has been well recognized that, in combination with occupational exposure limit (OEL), biological occupational exposure limit (BOEL) is an important guideline for prevention of excess exposure of workers to hazardous chemicals such as organic solvents (solvents in short),[1,2] and that the concentration of un-metabolized solvent in urine is a convenient marker for setting BOEL.[3] Nevertheless, it is also true that setting a BOEL needs a substantial database. The database for setting BOEL in addition to that for OEL setting for air-borne concentration is a double burden for industrial health scientists in charge. Cases of OELs and BOELs set by the Japan Society for Occupational Health (JSOH)[1] and the American Conference of Governmental Industrial Hygienists (ACGIH) (as TLV and BEI)[2] for selected solvents are shown in Table 1 as examples.

To solve this double burden problem, procedures were proposed in a previous article[4] to estimate the BOEL from a physico-chemical parameter, the partition coefficient of n-octanol and water (or P_{ow} in short), for a solvent for which the OEL is available. The procedures were further evaluated in a succeeding study[5] with affirmative results. The proposed procedures[4,5] are easy to practice. The calculation of the basic parameter, the SLOPE, however needs a bulk of exposure–excretion data of the solvent (for the definition and details of the SLOPE, see the Materials and Methods section below).

In this report, a further simplification of the procedures will be described, in which the ratio of a geometric mean (GM) for un-metabolized solvent in end-of-shift urine samples (U-GM in short) over the GM for air-borne level (A-GM in short) (and therefore [U-GM/A-GM] as the ratio) will be employed to estimate BOEL. By the present approach, the very limited efforts to measure a few pairs (eg about five or so) of un-metabolized solvent concentrations in end-of-shift urine and 8-hour average solvent exposure levels in air will help to estimate BOEL. There is no need of literature search for P_{ow}. It is quite expectable that this simplification will alleviate the burdens for setting BOEL and thus contribute to promote occupational health in solvent workplaces.

2 | MATERIALS AND METHODS

In this presentation, the word of SLOPE means the slope of the regression line taking the solvent exposure concentrations in air (in ppm) on the horizontal axis as an independent variable and the concentration of un-metabolized solvent in end-of-shift urine (in μg/L) on the vertical axis as a dependent variable.[4]

The data on U-GM (ie, the GM concentration of un-metabolized solvent in end-of-shift urine), the A-GM (ie, the GM of 8-hour time-weighted average exposure concentration of solvent in air) and the SLOPE were cited from previous publications[6-8] on a multiple solvent survey on acetone, ethylbenzene, methyl alcohol, methyl ethyl ketone, methyl isobutyl ketone, toluene, and xylenes. Exposure parameters not reported in the articles[6-8] were calculated from the original survey data. The data for dichloromethane,[9] 1,2 dichloropropane,[10] and tetrachloroethylene[11] were cited from other publications.[9-11]

Data employed in the present analysis are summarized in Table 2, in which the data for men and women were treated separately. The methods for determination of 8-hour time-weighted average intensity of the solvent exposure and the solvent concentration in the end-of-shift urine samples were also previously reported,[6,7,11] namely, for example, by diffusive sampling for air monitoring and by head-space gas chromatography for urinalysis. Regression analyses and paired *t* test were carried out after Ichihara.[12]

3 | RESULTS AND DISCUSSION

3.1 | Correlation of log [U-GM/A-GM] with log SLOPE

A significant close correlation ($r > 0.96$, $P < 0.01$) was observed when the correlation between log [U-GM/A-GM]

TABLE 1 Occupational Exposure Limits (OEL, TLV) and Biological Occupational Exposure Lilmits (BOEL, BEI), established by JSOH[1] and ACGIH[2]

Solvents	OEL (ppm)[a]	TLV (ppm)[b]	BOEL (mg/L)[a]	BEI (mg/L)[b]
Acetone	200	250	40	25
Dichloromethane	50	50	0.2	0.3
1,2-Dichloropropane	1	10	—	—
Ethylbenzene	50	20	—	—
Methyl alcohol	200	200	20	15
Methyl ethyl ketone	200	200	5	2
Methyl isobutyl ketone	50	20	1.7	1
Tetrachloroethylene	Pending	25	—	—
Toluene	50	20	0.06	0.03
Xylenes[c]	50	100	—	—

[a]Japan Society for Occupational Health.[1]
[b]American Conference of Governmental Industrial Hygienists.[2]
[c]All isomers.

TABLE 2 Database for organic solvents studied

Case no.	Solvent	M/W[a]	Reference no.	MW[b]	No. of cases	A-GM[c] (ppm)	U-GM[d] (μg/L)	SLOPE[e] (μg/L/ppm)
1	Acetone	M	6, 7	58.09	122	1.19	1029.1	187.60
2	Dichloromethane	M	9	84.93	30	8.40	41.1	3.22
3	1,2-Dichloropropane	M	10	112.99	35	6.76	76.7	7.95
4	Ethylbenzene	M	7	106.17	53	1.96	4.3	0.74
5	Methyl alcohol	M	6, 7	32.04	26	4.60	1976.5	112.50
6	Methyl ethyl ketone	M	6, 7	72.11	88	0.42	56.3	30.73
7	Methyl isobutyl ketone	M	6, 7	100.16	32	0.72	33.1	28.52
8	Tetrachloroethylene	M	11	165.81	50	16.59	249.8	2.65
9	Toluene	M	6, 7	92.14	109	3.53	7.8	0.90
10	Xylenes	M	6, 7	106.18	85	0.97	4.5	1.13
11	Acetone	W	6, 7	58.09	26	0.67	1018.2	296.50
12	Ethylbenzene	W	7	106.17	12	2.58	3.6	0.38
13	Methyl alcohol	W	6, 7	32.04	5	15.58	3677.3	97.19
14	Methyl ethyl ketone	W	6, 7	72.11	24	0.26	50.9	20.27
15	Methyl isobutyl ketone	W	6, 7	100.16	9	0.81	30.7	17.49
16	Tetrachloroethylene	W	11	165.81	12	10.48	197.7	3.12
17	Toluene	W	6, 7	92.14	19	5.59	12.1	1.36
18	Xylenes	W	6, 7	106.18	16	0.99	4.3	0.50

[a]M/W: Men or women.
[b]MW: Molecular weight.
[c]Geometric mean of solvent concentration in air.
[d]Geometric mean of solvent concentration in urine.
[e]For definition of the SLOPE, see the Materials and Methods section.

(in μg/L/ppm) (X) and log SLOPE (in μg/L/ppm) (Y) was examined (Figure 1). The equation was $Y = -0.423 + 0.923X$ ($r > 0.96$, $P < 0.01$). A close correlation ($r > 0.95$, $P < 0.01$) was also observed when anti-logarithms of the parameters [ie, [U-GM/A-GM](in μg/L/ppm) as X, and SLOPE (in μg/L/ppm) as Y] were subjected to the analysis. The observation suggested the feasibility that the SLOPE can be estimated from the [U-GM/A-GM] ratio. The proposed procedure based on this possibility to estimate BOELs is as follows.

3.2 | The proposed procedures to estimate a BOEL from [U-GM/A-GM]

The procedures previously described[4] is modified to use the [U-GM/A-GM]. The "SLOPE" is calculated from corresponding [U-GM/A-GM] ratio.

Step 1. Make a survey to obtain time-weighted average solvent exposure concentrations in air and solvent concentrations in end-of-shift urine samples in ≧5 pairs, and calculate A-GM, U-GM and then the [U-GM/A-GM].

Step 2. Covert the [U-GM/A-GM] (in μg/L/ppm) to the "SLOPE" by use of above-cited equation of $Y = -0.423 + 0.923X$ (X = log [U-GM1 in μg/L/ppm, and Y = log 'SLOPE' (in μg/L/ppm).

Step 3. C_{urine} = 'SLOPE' × C_{air} (see Step 2 in the proposed procedure in Reference [4] for the rationale of this equation). C_{urine} is the concentration of un-metabolized solvent in end-of-shift urine sample, and C_{air} is 8-hour time-weighted average solvent exposure concentration in air. "SLOPE" here should be estimated from U-GM/A-GM as described in Step 2. The unit of un-metabolized solvent in urine may be converted from μg/L to mg/L, as necessary.

Step 4. C_{urine} will be BOEL, when C_{air} is OEL.

3.3 | Estimation of BOEL by the present procedures

The results of BOEL estimation are summarized in Table 3 for six solvents. Results of calculation for 1,2-dichloropropane, tetrachloroethylene and xylenes were not given in the table because BOEL (or BEI) values are not available (ie, yet to be set and not existing) for these solvents. In addition, survey results were not available for women exposed to dichloromethane (Table 2). Two sets of existing OEL and BOEL

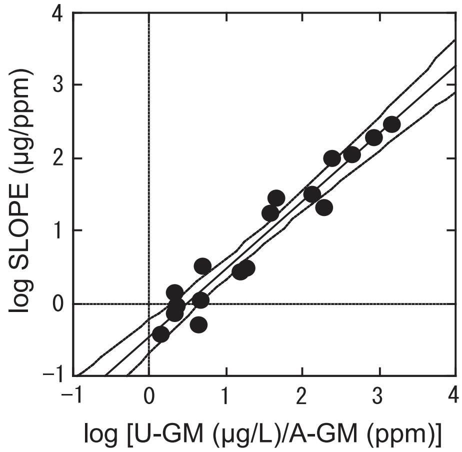

FIGURE 1 Significant correlation between log [U-GM/A-GM]. U-GM is the geometric mean (GM) of the un-metabolized solvent in end-of-shift urine samples, and A-GM is GM of 8-h time-weighted average of the exposure solvent level in air. SLOPE is the value shown in Table 2. The line in the middle is the calculated regression line, the equation of which is $Y = -0.423 + 0.923X$, where X = log [U-GM (μg/L)/A-GM (ppm), and Y = log SLOPE (μg/ppm) ($r > 0.96$, $P < 0.01$). Two dotted curves on both sides of the line show the upper and lower 95% confidence limits, respectively. Each dot (n = 18) represents one pair of [U-GM)/A-GM], and SLOPE

values (ie, OEL and BOEL values set by Japan Society for Occupational Health,[1] and TLV and BEI set by ACGIH[2]) (Table 1) were referred in Table 3.

3.4 | Evaluation of estimated BOELs through comparison with existing BOELs

For evaluation purpose, the [(estimated BOEL)/(existing BOEL)] was calculated in Table 3. When arithmetic means (AMs) and arithmetic standard deviations (ASDs) were calculated, ASDs were larger than corresponding AMs. Thus, log-normal distributions were considered. For all cases considered together (ie Section [C] in Table 3), the GMs were 0.85.

The maximum value was 4.94 for women exposed to methyl ethyl ketone, and the 2nd largest was 3.49 for men exposed to the same solvent. These large ratios were due to ACGIH's low BEI of 2 mg/L in contrast to JSOH's BOEL of 5 mg/L, whereas both ACGIH's TLV and JSOH's OEL are set at 200 ppm. Suppose BEI were 5 mg/L, the ratios would be 1.40 and 1.98, respectively, both of which are less than 2 (Table 3).

3.5 | Close correlation of the estimated BOELs with the existing BOELs

When the relationship of the estimated BOELs with the existing BOELs (ie, JSOH's BOELs and ACGIH's BELs) was examined, a very close and significant correlation was observed between the two sets (Table 3). The calculated regression equation was $Y = 0.268 + 1.487X$ where X was existing BOELs (ie, JSOH's BOELs and ACGIH's BEIs) and Y was estimated values. The slope (β) was close to 1 and the intercept (α) was next to zero suggesting that the regression line passes close to the origin. The observation suggested the validity of the estimated BOELs.

3.6 | Recommendation for practical application of estimated BOELs to prevent excess exposure of workers to solvents

The GM of 0.85 for JSOH and ACGIH cases in combination (the GM in Section [C] in Table 3) suggests that the application of estimated BOEL values is recommendable in general. In fact, the estimated BOELs correlate with the existing BOELs significantly (see the previous paragraph). The minimum value of 0.22 may indicate the presence of over-protection cases, which is however acceptable because the workers in concern will be on the safer side.

The maximum value is about 5. The choice of 5 as the safety factor (ie, division of the estimated BOEL by 5 in practical application) may depend on the severity of the expected health effects after excess exposure to the solvent such as irreversibility or ever progressiveness.

It should be noted that both OELs and BOELs are not the solid borderlines between safe and risky conditions. Both should be subjected to repeated re-considerations depending on the results of health survey. The ultimate target is the prevention of the health of workers from possible effects of potentially hazardous chemicals. In practice, a reference such as estimated BOEL, even if provisional one, would be beneficial for occupational health services, as the reference will be a starting point for the future improvement.

3.7 | Limitation in the present study

The paucity in available basic data is the fundamental problem. In practice, full data sets are available only for six solvents (Table 3), posing severe limitation in generalization of the study conclusion. Wide use of biological monitoring by means of un-metabolized solvent in end-of-shift urine samples is positively encouraged, because urine sampling is not invasive and methods for urinalysis are well established.[6,7,11,13]

The constant ratio between solvent exposure and urinary excretion across individuals has been empirically approved, but theoretical consideration is yet to be made. The development of the theory on this point deserves further study.

4 | CONCLUSIONS

The acceptable calculation of SLOPE from the [U-gm/A-GM] substantially simplified the procedures to estimate BOEL.

TABLE 3 The ratio of estimated BOELs over existing BOELs

Solvents	Men or Women	JSOH's BOEL or ACGIH's BEI (mg/l)	Estimated BOEL or BEI (mg/l)	Ratio[1]
[A] Calculation with JOH' OEL (n = 11)				
Acetone	M	40	38.8	0.97
Dichloromethane	M	0.2	0.08	0.41
Methyl alcohol	M	20	20.4	1.02
Methyl ethyl ketone	M	5	7	1.40
Methyl isobutyl ketone	M	1.7	0.6	0.38
Toluene	M	0.06	0.04	0.65
Acetone	W	40	64.9	1.62
Methyl alcohol	W	20	11.7	0.58
Methyl ethyl ketone	W	5	9.9	1.98
Methyl isobutyl ketone	W	1.7	0.5	0.32
Toluene	W	0.06	0.04	0.66
Geometric mean				0.77
Geometric standard deviation				1.84
Minimum				0.32
Maximum				1.98
[B] Calculation with ACGIH's TLV (n = 11)				
Acetone	M	25	48.5	1.94
Dichloromethane	M	0.3	0.08	0.27
Methyl alcohol	M	15	20.4	1.36
Methyl ethyl ketone	M	2	7	3.49
Methyl isobutyl ketone	M	1	0.3	0.26
Toluene	M	0.03	0.02	0.52
Acetone	W	25	81.2	3.25
Methyl alcohol	W	15	11.7	0.78
Methyl ethyl ketone	W	2	9.9	4.94
Methyl isobutyl ketone	W	1	0.22	0.22
Toluene	W	0.03	0.02	0.51
Geometric mean				0.93
Geometric standard deviation				3.10
Minimum				0.22
Maximum				4.94
[C] Combination (n = 22)				
Geometric mean				0.85
Geometric standard deviation				2.44
Minimum				0.22
Maximum				4.94

[1]The ratio of the estimated BOEL over the existing BOE.

The estimated BOELs correlate closely with existing BOELs such as JSOH's BOELs and ACGIH's BEI. Practical application of estimated BOELs in occupational health is discussed in case when BOEL is yet to be exist for the solvent in concern.

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DISCLOSURE

Approval of the research protocol: N/A. *Informed consent:* N/A. *Registry and the registration no. of the study/trial*: N/A. *Animal studies:* N/A. *Conflict of interest:* None.

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