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Health risk assessment on mercury, cadmium and lead in marketed cigarettes

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ABSTRACT — The Hg, Cd, and Pb concentrations in marketed cigarettes from South Korea, Vietnam, Japan, Indonesia, Taiwan, Thailand, United Kingdom (UK), Belgium, Italy, Finland, and France were investigated. The average Hg concentration in cigarettes marketed in Vietnam and Thailand had the highest trend. Meanwhile, there was more Cd found in cigarettes from Thailand, UK, and Belgium. The Pb concentrations in cigarettes from Belgium, UK, and Korea were higher than in others. In the health risk assessment in this study, the significant non-carcinogenic health risk (HI) values of Hg, Cd, and Pb were investigated. The results showed that the HI of Hg, Cd, and Pb were 4.12×10^{-2}, 4.07×10^{1}, and 9.78×10^{0}, respectively. It indicated that only Cd and Pb had a significant HI. When the incremental lifetime cancer risk (ILCR) was estimated, the ILCRs for both Cd (7.32×10^{-4}) and Pb (0.88×10^{-5}) in cigarettes were higher than the acceptable limit. The acceptable and significant cancer risks for Pb and Cd, respectively were evaluated in cigarettes used in this study.

Key words: Marketed cigarettes, Health risk, Mercury, Cadmium, Lead

INTRODUCTION

It is well-known that tobacco and its smoke contain more than 4000 different substances, including various carcinogens and toxic metals (Stration *et al.*, 2001). Around 6.5 trillion cigarettes are sold worldwide each year, which translates to roughly 18 billion cigarettes per day (Martin, 2019). Furthermore, it is considered that tobacco becomes the cause of death of more than 7–8 million people each year, while around 1.2 million nonsmokers die as a result of being exposed to secondhand smoke (World Health Organization, 2020). Particularly, Cd in tobacco leaf is suggested as one of the major sources of exposure to humans (Wu *et al.,* 2016). In addition, it was reported that Pb from cigarette smoke (including second- and third-hand tobacco smoke exposures) increases the blood Pb levels in children (Agency for Toxic Substances and Disease Registry, 2019). On the other hand, it is suggested that Hg inhalation causes severe damage to the body (Fresquez *et al.,* 2015; United Nations Environment, 2019), however, the research data on Hg in cigarettes are still limited.

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Aside from polycyclic aromatic hydrocarbons, the metals in cigarette smoke also have a potential risk to human health. Based on human health risk assessments of Pb, Cd, and Cr concentrations in tobacco products from Bangladesh, all smoke-based tobacco products and most smokeless tobacco products have high concentrations of heavy metals, such as Pb, Cd, and Cr (Hossain *et al.,* 2018). In health risk assessments of various metals, including Cd and Pb, in tobacco products from Malaysia, both the significant non-carcinogenic and carcinogenic health risks were evaluated (Ismail *et al.*, 2017). Cigarettes from Nigeria (Benson *et al.*, 2017) possibly had both significant carcinogenic and non-carcinogenic health effects associated with inhalation exposure. However, in the literature of health risk assessments, almost all studies reported the heavy metal contents by the unit of cigarette leaves (mg/g cigarette). Therefore, a risk assessment of Hg, Cd, and Pb to human health based on the heavy metal contents of smoke and smoke exposures via inhalation is necessary.

In a previous study, Dinh *et al*. (2021) conducted an evaluation of Hg, Cd, and Pb in commercial cigarettes from many regions and countries in 2019. The data showed that a large part of Hg, Cd, and Pb existed in the mainstream, and even active carbon is added to the filters. This was followed by a study on human health risks based on the non-carcinogenic and the carcinogenic effects via inhalation, which may be caused by the Hg, Cd and Pb contents of cigarettes (tobacco leaf, roll paper, and filter).

MATERIALS AND METHODS

Samples and cigarette properties

The detailed material properties and pretreatments of cigarette samples are described in a previous study by Dinh *et al*. (2021). Sixty-seven samples of marketed cigarettes were collected from several countries in 2019 (Korea: $n = 10$, Vietnam: $n = 9$, Japan: $n = 10$, Indonesia: $n = 13$, Thailand: $n = 4$, Taiwan: $n = 6$, Belgium: $n = 3$, France: $n = 3$, Italy: $n = 3$, Finland: $n = 3$, and UK: $n = 3$). The Hg, Cd, and Pb contents in cigarettes used in this health risk assessment were obtained from a previous study by Dinh *et al*. (2021).

Health risk assessment

To understand the health risk assessment of toxic heavy metals, including Hg, Cd, and Pb, a health risk assessment model was used to calculate their health risk to humans. Benson *et al*. (2017), Ismail *et al*. (2017), and Freitas *et al*. (2011), applied the US EPA model for inhalation route to estimate the carcinogenic and the non-carcinogenic human health risk of heavy metals in cigarette. Many studies which estimated the human health risk of heavy metals in cigarettes used their concentrations in cigarettes based on the unit of tobacco leaf (mg/g cigarette). In this study, the human health risk of Hg, Cd, and Pb were estimated using the concentrations of these metals in the entire cigarette (mg/cigarette: tobacco leaf, rolling paper, and filter).

Based on a study by Rodgman and Green, (2003), the average daily concentration (ADC: μg/m^3), non-cancer health effects (HI), lifetime ADC (ADC_{life}, μg/m^3), and incremental life cancer risk (ILCR) were evaluated using formulas (1) to (4).

$$ADC\ (\mu g/m^3) = [C_m\ (\mu g/\text{cigarette}) \times SF\ (\text{cigarette/day})] / VB\ (m^3 \text{ of air breathed/day}) \quad (1)$$

Where C_m (μg/cigarette) is the Hg, Cd, and Pb contents; C_m was derived from the total content of each metal per cigarette (tobacco leaf, roll paper, and filter). SF (cigarettes/day) is the daily smoking frequency (packed-a-day smoker = 20 cigarettes/day), and VB (m^3/day) is the daily volume of air breathed by adults (20 m^3/day).

The potential non-cancer health effect (HI) was evaluated using formula (2). RfC is the reference concentration (mg/m^3) (RfC for Hg = 3.0×10^{-4}, Cd = 2.0×10^{-5}, and Pb = 1.5×10^{-4}).

$$HI = ADC\ (\mu g/m^3 \times mg/1000) \times RfC\ (mg/m^3) \quad (2)$$

An HI value ≥ 1 suggests a potential for adverse health effects, while an HI value < 1 suggests no health effects (Vorhees *et al.*, 1997). In this study, only Cd and Pb were considered for their carcinogenic health effects because Hg is not known to be carcinogenic, hence has no cancer risk factor. The ADC_{life} (μg/m^3) was calculated using formula (3). Then, the ILCR values were estimated based on formula (4).

$$ADC_{life}\ (\mu g/m^3) = (ADC \times \text{number of years for smoking}) / LT\ (70 \text{ years}) \quad (3)$$

$$ILCR = ADC_{life} \times IUR \quad (4)$$

Where IUR is the inhalation unit risk factor (Cd: 1.8×10^{-3} per μg/m^3; Pb: 8.0×10^{-5} per μg/m^3) (US EPA, 2012), and LT is the average lifetime (70 years). The ADCs are the same as the calculated one in formula (1). Based on the US EPA's carcinogenic risk assessment (US EPA, 2012), an ILCR between 1×10^{-6} and 1×10^{-4} is considered acceptable. An ILCR > 1×10^{-4} is a significant cancer risk, while an ILCR < 1×10^{-6} poses an insignificant cancer risk.

RESULTS AND DISCUSSION

Cigarette properties

Sixty-seven filtered cigarettes had three main parts: tobacco leaf, cigarette filter, and roll paper. From the data on a previous report (Dinh *et al.,* 2021), there was an average of 0.829 g/cigarette (tobacco leaf: 0.633 g/cigarette; filter: 0.158 g/cigarette; and roll paper: 0.038 g/cigarette). The tobacco leaf, filter, and roll paper, averagely accounted for 76.36%, 19.06%, and 4.58% respectively of the total weight of a filtered cigarette.

The mercury, cadmium, and lead contents of cigarettes

The mean of total Hg, Cd, and Pb contents (C_m) in each cigarette was 0.012 ± 0.004, 0.814 ± 0.501, and 1.467 ± 2.244 µg/cigarette, respectively. The average values of C_m in tobacco were in the order: Pb > Cd > Hg (Table 1). The Hg content in cigarettes was much lower than the Cd and Pb contents. The range of detected Hg, Cd, and Pb concentrations in cigarettes used in this study were approximately the same as that in US cigarettes (Fresquez *et al.,* 2013).

In this study, the cigarette samples collected from Korea, Vietnam, Indonesia, UK, and Belgium contained higher C_m of Pb than that of Cd. However, the cigarettes collected from Japan, Taiwan, Thailand, Italy, Finland, and France had higher C_m of Cd than that of Pb. For Cd, the highest C_m in cigarettes was found in cigarettes from Thailand (1.811 ± 0.885 µg/cigarette), followed by those from UK (1.379 ± 0.525 µg/cigarette), Belgium (1.318 ± 0.632 µg/cigarette), and France (1.134 ± 0.588 µg/cigarette). The lower C_m of Cd was found in cigarettes from Japan (0.448 ± 0.109 µg/cigarette) and Italy (0.462 ± 0.082 µg/cigarette). In contrast, the highest C_m of Pb was found in cigarettes from Belgium (6.085 ± 0.936 µg/cigarette), followed by those from UK (4.025 ± 0.548 µg/cigarette) and Korea (2.592 ± 1.422 µg/cigarette). On the other hand, the C_m of Pb from Japan (0.297 ± 0.138 µg/cigarette), Italy (0.355 ± 0.099 µg/g cigarette), Finland (0.397 ± 0.020 µg/g cigarette), France (0.457 ± 0.132 µg/g cigarette), and Taiwan (0.474 ± 0.138 µg/cigarette) had low levels of the metals. The C_m of Hg in cigarettes was much lower than that of Cd and Pb. The average Hg content in cigarettes was 1%–1.5% of the Cd and Pb contents. A higher C_m of Hg was found in cigarettes from Thailand (0.018 ± 0.002 µg/cigarette), Vietnam (0.015 ± 0.007 µg/cigarette), and Belgium (0.015 ± 0.006 µg/cigarette); the C_m of Hg in cigarettes from the other countries were 0.008–0.012 µg/cigarette (Dinh *et al*., 2021).

Health risk assessment

Estimation of non-carcinogenic health risk of Hg, Cd, and Pb in cigarette

The ADCs (µg/m^3) were calculated using formula (1), and the estimated non-carcinogenic health risk (HI) values of Hg, Cd, and Pb were calculated using formula (2). Both data are shown in Table 1. The ADCs of Hg, Cd, and Pb were evaluated by C_m, SF (cigarette/day), and VB (m^3 of air breathed/day). Therefore, ADC and C_m had the same numerical value because of SF (20 cigarette/day) and VB (20 m^3 of air breathed/day); however, its unit was different (mg/m^3).

The average HI values of Hg, Cd, and Pb were 0.0412, 40.7, and 9.78, respectively. Based on these HI values, a significant non-carcinogenic health risk was associated with Cd and Pb but not Hg (Table 1, Fig. 1).

The order of HI levels in cigarettes from highest to lowest was Cd > Pb > Hg. The HI values of Cd and Pb were >1, and the HI values of Cd were > 20 and higher than those of Pb. The higher HI values of Cd in cigarettes were found in cigarettes from Thailand (9.06 × 10^1), UK (6.90 × 10^1), Belgium (6.59 × 10^1), and France (5.67 × 10^1). The lower HI values of Cd were found in cigarettes from Japan (2.24 × 10^1) and Italy (2.31 × 10^1). The HI values of Pb in cigarettes from Belgium (4.06 × 10^1), UK (2.68 × 10^1), Korea (1.73 × 10^1), and Indonesia (1.02 × 10^1) were > 10. On the other hand, the HI values of Pb in cigarettes from France (3.05 × 10^0), Taiwan (3.16 × 10^0), Finland (2.65 × 10^0), Italy (2.37 × 10^0), and Japan (1.98 × 10^0) were < 10. In this study, it was shown that the HI of Cd was extremely higher than that of Pb and Hg, indicating the highest potential for non-carcinogenic health risk of Cd in cigarettes that may affect both primary and second-hand smokers. The HI values of Pb in cigarettes from Belgium, UK, Korea, and Indonesia suggested that the cigarette smoke had health risk due to Pb. Although the HI values of Hg in cigarettes investigated in this study were relatively lower than those of Cd and Pb, the health of smokers should still be of concern because of the direct and long-term inhalation exposure.

Estimation of carcinogenic health risk of Cd and Pb in cigarettes

In this study, the ILCRs of Cd and Pb contents in cigarettes were also estimated by the ADC_{life} (µg/m^3) and IUR using formulas (3) and (4). The smoking years (35 years) and average lifetime (70 years) were used for ADC_{life} estimation. As a result, ADC_{life} was estimated as the half of the ADC value calculated for non-carcinogen-

Table 1. Estimation of non-carcinogenic health risk of Hg, Cd, and Pb in cigarettes.

Country	Metal	C_m (μg/cigarette) Mean ± SD	ADC (μg/m³) Mean ± SD	HI Mean ± SD
Korea (n = 10)	Hg	0.011 ± 0.003	0.011 ± 0.003	$3.79 \times 10^{-2} \pm 9.15 \times 10^{-3}$
	Cd	0.604 ± 0.353	0.604 ± 0.353	$3.02 \times 10^{1} \pm 1.77 \times 10^{1}$
	Pb	2.592 ± 1.422	2.592 ± 1.422	$1.73 \times 10^{1} \pm 9.48 \times 10^{0}$
Vietnam (n = 9)	Hg	0.015 ± 0.007	0.015 ± 0.007	$5.11 \times 10^{-2} \pm 2.37 \times 10^{-2}$
	Cd	0.696 ± 0.297	0.696 ± 0.297	$3.48 \times 10^{1} \pm 1.48 \times 10^{1}$
	Pb	0.994 ± 0.624	0.994 ± 0.624	$6.63 \times 10^{0} \pm 4.16 \times 10^{0}$
Japan (n = 10)	Hg	0.011 ± 0.002	0.011 ± 0.002	$3.67 \times 10^{-2} \pm 6.81 \times 10^{-3}$
	Cd	0.448 ± 0.109	0.448 ± 0.109	$2.24 \times 10^{1} \pm 5.44 \times 10^{0}$
	Pb	0.297 ± 0.138	0.297 ± 0.138	$1.98 \times 10^{0} \pm 9.21 \times 10^{-1}$
Indonesia (n = 13)	Hg	0.012 ± 0.004	0.013 ± 0.004	$4.16 \times 10^{-2} \pm 1.35 \times 10^{-2}$
	Cd	0.700 ± 0.279	0.700 ± 0.279	$3.50 \times 10^{1} \pm 1.39 \times 10^{1}$
	Pb	1.528 ± 3.741	1.528 ± 3.741	$1.02 \times 10^{1} \pm 2.49 \times 10^{1}$
Taiwan (n = 6)	Hg	0.011 ± 0.002	0.011 ± 0.002	$3.71 \times 10^{-2} \pm 6.73 \times 10^{-3}$
	Cd	0.903 ± 0.289	0.903 ± 0.289	$4.52 \times 10^{1} \pm 1.44 \times 10^{1}$
	Pb	0.474 ± 0.138	0.474 ± 0.138	$3.16 \times 10^{0} \pm 9.23 \times 10^{-1}$
Thailand (n = 4)	Hg	0.018 ± 0.002	0.018 ± 0.002	$5.91 \times 10^{-2} \pm 7.49 \times 10^{-3}$
	Cd	1.811 ± 0.885	1.811 ± 0.885	$9.06 \times 10^{1} \pm 4.43 \times 10^{1}$
	Pb	0.728 ± 0.268	0.728 ± 0.268	$4.85 \times 10^{0} \pm 1.79 \times 10^{0}$
UK (n = 3)	Hg	0.011 ± 0.001	0.011 ± 0.001	$3.47 \times 10^{-2} \pm 2.93 \times 10^{-3}$
	Cd	1.379 ± 0.525	1.379 ± 0.525	$6.90 \times 10^{1} \pm 2.62 \times 10^{1}$
	Pb	4.025 ± 0.548	4.025 ± 0.548	$2.68 \times 10^{1} \pm 3.65 \times 10^{0}$
Belgium (n = 3)	Hg	0.015 ± 0.006	0.015 ± 0.006	$5.13 \times 10^{-2} \pm 1.93 \times 10^{-2}$
	Cd	1.318 ± 0.632	1.318 ± 0.632	$6.59 \times 10^{1} \pm 3.16 \times 10^{1}$
	Pb	6.085 ± 0.936	6.085 ± 0.936	$4.06 \times 10^{1} \pm 6.24 \times 10^{0}$
Italy (n = 3)	Hg	0.008 ± 0.0005	0.008 ± 0.0005	$2.65 \times 10^{-2} \pm 1.53 \times 10^{-3}$
	Cd	0.462 ± 0.082	0.462 ± 0.082	$2.31 \times 10^{1} \pm 4.12 \times 10^{0}$
	Pb	0.355 ± 0.099	0.355 ± 0.099	$2.37 \times 10^{0} \pm 6.59 \times 10^{-1}$
Finland (n = 3)	Hg	0.011 ± 0.001	0.011 ± 0.001	$3.81 \times 10^{-2} \pm 3.71 \times 10^{-3}$
	Cd	0.883 ± 0.131	0.883 ± 0.131	$4.42 \times 10^{1} \pm 6.55 \times 10^{0}$
	Pb	0.397 ± 0.020	0.397 ± 0.020	$2.65 \times 10^{0} \pm 1.31 \times 10^{-1}$
France (n = 3)	Hg	0.011 ± 0.002	0.011 ± 0.002	$3.56 \times 10^{-2} \pm 6.64 \times 10^{-3}$
	Cd	1.134 ± 0.588	1.134 ± 0.588	$5.67 \times 10^{1} \pm 2.94 \times 10^{1}$
	Pb	0.457 ± 0.132	0.457 ± 0.132	$3.05 \times 10^{0} \pm 8.83 \times 10^{-1}$
Average (n = 67)	Hg	0.012 ± 0.004	0.012 ± 0.004	$4.12 \times 10^{-2} \pm 1.37 \times 10^{-2}$
	Cd	0.814 ± 0.501	0.814 ± 0.501	$4.07 \times 10^{1} \pm 2.51 \times 10^{1}$
	Pb	1.467 ± 2.244	1.467 ± 2.244	$9.78 \times 10^{0} \pm 1.50 \times 10^{1}$

HI ≥1 indicates significant potential for adverse health effects. HI less than 1 suggests insignificant health effects.
ADC (average daily concentration) (μg/m³) = C_m (content of cigarette (μg/cigarette) × SF (cigarette/day)/VB (m³/day).
SF is the number of smoke; 20 cigarette/day), VB is the volume of air breath; 20 (m³/day).
HI (non-carcinogenic hazard index) = ADC (μg/m³) × mg/1000)/RfC.
RfC (mg/m³): Hg = 3.0×10^{-4}, Cd = 2.0×10^{-5}, Pb = 1.5×10^{-4}.

ic health risks.

The average ILCR of both Cd (7.32×10^{-4}) and Pb (0.88×10^{-5}) in cigarettes were higher than the acceptable limit of 1×10^{-6} (above the US EPA target range of insignificant cancer risk) (Table 2). The ILCR of Cd ranged from 4.03×10^{-4} (Japan) to 16.30×10^{-4} (Thailand). These values were > 1×10^{-4}, hence the Cd concentrations in cigarettes evaluated in this study may have significant cancer risks. Although the ILCR of Pb ranged from 0.18×10^{-5} (Japan) to 3.95×10^{-5} (Belgium), the Pb contents in cigarettes evaluated in this study may have acceptable cancer risk.

In conclusion, in this study, the non-carcinogenic health effects of Cd, Pb, and Hg from cigarette smoke were estimated. The high-potential non-carcinogenic health risks of both Cd and Pb in cigarettes were also

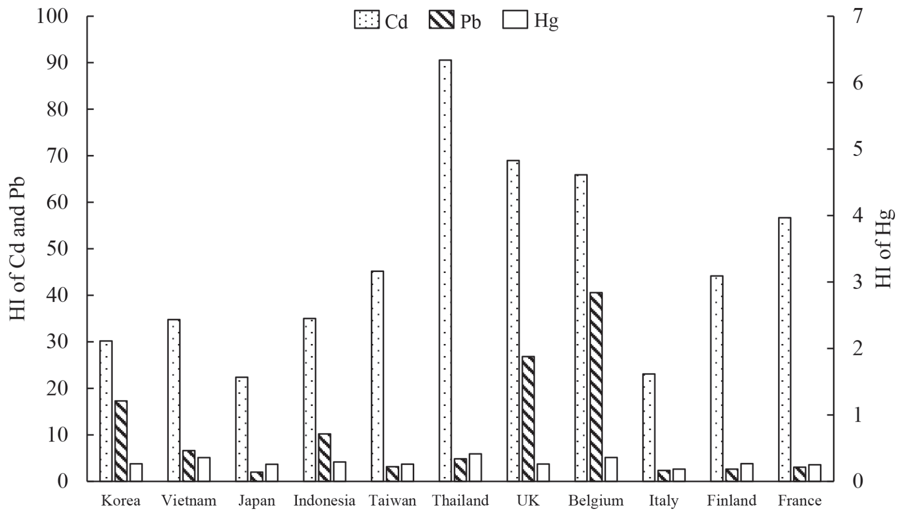

Fig. 1. The hazard index (HI) of Hg, Cd, and Pb in cigarettes.

Table 2. Estimation of carcinogenic health risk of Cd and Pb in cigarettes.

Country	Metal	ADC (μg/m^3) Mean ± SD	ADC_{Life} (μg/m^3) Mean ± SD	ILCR Mean ± SD
Korea	Cd	0.604 ± 0.353	0.302 ± 0.176	$5.44 \times 10^{-4} \pm 3.18 \times 10^{-4}$
(n = 10)	Pb	2.592 ± 1.422	1.926 ± 0.711	$1.55 \times 10^{-5} \pm 0.85 \times 10^{-5}$
Vietnam	Cd	0.696 ± 0.297	0.348 ± 0.149	$6.26 \times 10^{-4} \pm 2.67 \times 10^{-4}$
(n = 9)	Pb	0.994 ± 0.624	0.994 ± 0.624	$0.60 \times 10^{-5} \pm 0.37 \times 10^{-5}$
Japan	Cd	0.448 ± 0.109	0.224 ± 0.055	$4.03 \times 10^{-4} \pm 0.98 \times 10^{-4}$
(n = 10)	Pb	0.297 ± 0.138	0.149 ± 0.069	$0.18 \times 10^{-5} \pm 0.083 \times 10^{-5}$
Indonesia	Cd	0.700 ± 0.279	0.350 ± 0.140	$6.30 \times 10^{-4} \pm 2.51 \times 10^{-4}$
(n = 13)	Pb	1.528 ± 3.741	0.764 ± 1.871	$0.92 \times 10^{-5} \pm 2.24 \times 10^{-5}$
Taiwan	Cd	0.903 ± 0.289	0.452 ± 0.145	$8.13 \times 10^{-4} \pm 2.60 \times 10^{-4}$
(n = 6)	Pb	0.474 ± 0.138	0.237 ± 0.069	$0.284 \times 10^{-5} \pm 0.08 \times 10^{-5}$
Thailand	Cd	1.811 ± 0.885	0.906 ± 0.443	$16.30 \times 10^{-4} \pm 7.97 \times 10^{-4}$
(n = 4)	Pb	0.728 ± 0.268	0.364 ± 0.134	$0.43 \times 10^{-5} \pm 0.16 \times 10^{-5}$
UK	Cd	1.379 ± 0.525	0.190 ± 0.263	$12.41 \times 10^{-4} \pm 4.73 \times 10^{-4}$
(n = 3)	Pb	4.025 ± 0.548	2.013 ± 0.274	$2.42 \times 10^{-5} \pm 0.33 \times 10^{-5}$
Belgium	Cd	1.318 ± 0.632	0.659 ± 0.316	$11.86 \times 10^{-4} \pm 5.69 \times 10^{-4}$
(n = 3)	Pb	6.085 ± 0.936	3.043 ± 0.468	$3.95 \times 10^{-5} \pm 0.56 \times 10^{-5}$
Italy	Cd	0.462 ± 0.082	0.231 ± 0.041	$4.16 \times 10^{-4} \pm 0.74 \times 10^{-4}$
(n = 3)	Pb	0.355 ± 0.099	0.178 ± 0.050	$0.21 \times 10^{-5} \pm 0.06 \times 10^{-5}$
Finland	Cd	0.883 ± 0.131	0.442 ± 0.066	$7.94 \times 10^{-4} \pm 1.18 \times 10^{-4}$
(n = 3)	Pb	0.397 ± 0.020	0.199 ± 0.010	$0.24 \times 10^{-5} \pm 0.00 \times 10^{-5}$
France	Cd	1.134 ± 0.588	0.567 ± 0.294	$10.21 \times 10^{-4} \pm 2.94 \times 10^{-4}$
(n =3)	Pb	0.457 ± 0.132	0.229 ± 0.066	$0.27 \times 10^{-5} \pm 0.08 \times 10^{-5}$
Average	Cd	0.814 ± 0.501	0.407 ± 0.251	$7.32 \times 10^{-4} \pm 4.51 \times 10^{-4}$
(n = 67)	Pb	1.467 ± 2.244	0.733 ± 1.122	$0.88 \times 10^{-5} \pm 1.35 \times 10^{-5}$

ADC_{Life} (μg/m^3) = (ADC × smoking years: 35 years) / average lifetime: 70 years)
ILCR = (ADC_{Life} (μg/m^3) × URF(μg/m^3)$^{-1}$) /1000 URF(μg/m^3)$^{-1}$: Cd = 1.8; Pb = 0.012.

estimated. In addition, the significant cancer risk of Cd and acceptable cancer risk of Pb in cigarettes were evaluated by ILCR assessment. Exposure to Hg, Cd, and Pb through inhalation of cigarette smoke should be of primary concern due to the detrimental effects of these heavy metals on human health. Moreover, a consideration should be given to their presence in tobacco products as a source of human exposure through different pathways from the living environment, food, and beverages.

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Conflict of interest---- The authors declare that there is no conflict of interest.

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