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Article

Concentrations of 2, 4-Dichlorophenol and 2, 5-Dichlorophenol in Urine of Korean Adults

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Abstract: Humans are exposed to the environmental pollutants 2, 4-dichlorophenol (2, 4-DCP) and 2, 5-dichlorophenol (2, 5-DCP) through air, use of water and consuming products. In this study, we evaluated the urinary concentrations of these compounds in Korean people from the age of 18 to 69 years by making use of the data from the Korean National Human Biomonitoring Survey that was completed in 2009. Of 1,865 representative Koreans, 63.4% and 97.9% were found to have concentrations of 2, 4-DCP and 2, 5-DCP > 0.05 μg/L (limit of detection) in their urine. The geometric mean urinary concentrations were 0.14 μg/L (confidence interval of 95% = 0.13–0.16) and 0.44 μg/L (confidence interval = 0.41–0.48), respectively. It was fond that the adjusted proportional changes in 2, 4-DCP concentrations were significantly associated with body mass index, whereas those of 2, 5-DCP concentrations were influenced by place of residence. From these findings, it is evident that most adults in Korea have levels of 2, 4-DCP and 2, 5-DCP that are detectable in their urine and burden of these compounds on their bodies varies depending on numerous demographic factors.

Keywords: Human urine; biomonitoring; chlorophenol; demographic characteristics

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1. Introduction

The presence of toxic chemicals in consumer products, water and air media pose a wide range of health hazards to the general population. Therefore, biomonitoring studies of potentially toxic substances are very crucial for establishing the level of exposure of a population to these substances, and identifying groups that are at high-risk, describing the differences in geography, and evaluating health risks that a population faces [1]. It is for these purposes that many countries, including the U.S.A and Germany, have carried out national biomonitoring studies including the analyses of organochlorine compounds. 2,4-dichlorophenol (2,4-DCP) and 2,5-dichlorophenol (2,5-DCP) are the most common organochlorine compounds that are easily found in soils and waste streams [2,3].

2,4-DCP is a key component in the production of phenoxy acid herbicides and is also used in the synthesis of antiseptics and pharmaceuticals [3]. This substance can also find its way into the environment as a product of degradation of an antiseptic agent known as triclosan [4]. Furthermore, 2,5-DCP acts as a key metabolite of 1,4-dichlorobenzene (1,4-D), which forms from water and wastewater treatment, wood pulp processing, incineration processes, and the degradation/metabolism of 1,4-D. 2,5-DCP has also been applied as a chemical intermediate in the production of pharmaceutical and agricultural products, and dyes. Both 2,4-DCP and 2,5-DCP in drinking and waste water result as byproducts of water treatment by chlorination [3].

Exposure to chlorinated phenols induces toxic effects in many animals as well as humans [5–7]. Epidemiologic studies suggest that exposure to dichlorophenol increases morbidity due to asthma and total serum levels of immunoglobulin E (IgE) in atopic wheezers, and contributes to the increasing incidence of food allergies [8,9]. Furthermore, exposure to 2,5-DCP causes metabolic syndrome, diabetes, and obesity, while concentrations of 2,4-DCP in urine are reportedly significantly associated with olfactory dysfunction [10–14].

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According to previously conducted biomonitoring surveys of phenolic compounds, urinary concentrations vary significantly depending on the population sub-groups. This finding reflects the differences in the burdens these compounds have in the bodies, which vary with geographical region [15,16]. In addition, epidemiological studies have demonstrated factors that are relevant to the body burdens after exposure to phenolic compounds. These factors include age, household income, and cigarette smoking [16,17]. In the current study, we have used nation-wide biomonitoring data to estimate concentrations of 2,4-DCP and 2,5-DCP in the urine of adults from Korea, and we also investigated the demographic factors that determine the concentrations of these substances.

2. Materials and Methods

2.1. Study population

The data used in this study was obtained from the Korean National Human Biomonitoring Survey (KNHBS). The KNHBS surveys and gathers population-based information on body burden of hazardous chemicals of Korean adult population in the age bracket of 18–69 years. The World Health Organization (WHO) recommends exclusion of participants in case a sample is too dilute or too concentrated. According to WHO, creatinine concentrations of < 30 mg/dL are considered too dilute, while creatinine concentrations of > 300 mg/dL are considered too concentrated [18]. A total of 1,865 participants completed interviews by providing the required data and produced urine samples that were used in this study. The review and approval of the study was conducted by the Asan Medical Center Institutional Review Board. The ethical principles for medical research involving human subjects were used to guide the study as provided by the Declaration of Helsinki. All the participants provided an informed written consent.

2.2. Source of data

Data was acquired from participants through in-person interviews. The information collected included: age, sex, income, education level, cigarette smoking, and the geographical place of residence. There were four groups in the category of income with regard to monthly household income. The level of education had three classifications: less than high school, high school, and college or above. Cigarette smoking was classified as never, current, and former. Body mass index (BMI) was categorized based on the WHO's criteria for Asian populations: underweight (BMI < 18.5 kg/m2), normal weight (BMI 18.5–22.9 kg/m2), overweight (BMI 23.0–25.0 kg/m2), or obese (BMI ≥ 25.0 kg/m2) [19]. Samples of spot urine were receive from all the participants through the day. Using urine creatinine concentrations, urinary dilutions of the samples were adjusted. Analysis of the samples was performed by liquid-liquid extraction and gas chromatography-mass spectrometry (GC-MS). Details of this method have been described elsewhere [20]. To perform recovery tests, known amounts of standards were added into the samples, and values of 89.9–105.0% were obtained for 2,4-DCP and 90.5–105.5% for 2,5 DCP. The inter-day and intra-day accuracy and precision were approximated by the analysis of four analytes in seven replicates on a single day, for five consecutive days. For 2,4-DCP, the intra-day accuracy was at about 98.6–108.2% with a precision of 1.9–10.6%, while its inter-day accuracy was at about 97.2–103.0% with a precision of 3.6–6.0%. The intraday accuracy of 2,5-DCP was 97.1–110.6% with a precision of 2.9–10.0%, while the inter-day accuracy was about 97.5–104.2%, and a precision of 2.6–15.4%. Linearity was checked from limit of quantification (LOQ) of 0.1 to 200 μg/L, with correlation coefficients of 0.9982 for 2,4-DCP, and 0.9998 for 2,5-DCP. The limit of detection (LOD) and the LOQ for analytes within the chromatographic conditions were obtained at signal-to-noise ratios of 3 and 10 respectively. The LOD and LOQ for 2,4-DCP and 2,5-DCP were 0.05 μg/L and 0.10 μg/L, respectively. Participants whose concentration of urine was found to be below the LOD were assigned with a value equivalent to LOD/2 [21]. The levels of creatinine in the urine samples were measured by a kinetic Jaffé method that employs the use of a Hitachi 7600 auto-analyzer (Hitachi, Tokyo, Japan).

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2.3. Statistical analyses

The distribution levels of 2,4-DCP and 2,5-DCP were described using selected maximum values and percentiles. To determine geometric means for the concentrations of 2,4-DCP and 2,5-DCP in urine samples with confidence intervals of 95%, the antilog values of the means were calculated from the natural log-transformed values. Adjusting for unequal selection probabilities was performed by using sample weights of participants to calculate weighted geometric means. Linear regressions of log-transformed concentrations were calculated using the sample weights in order to obtain predictor variables. The interpretation of the exponentiated model coefficients can be taken as proportional changes in the value of mean that is associated with each predictor level relative to a reference level, making the required adjustments for other predictors within the model. A t-test was used to analyze the difference between two means obtained from two different groups, and to test for linearity among the groups and the significance of a liner contrast in the linear models. All statistical analyses were completed using the SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

A total of 1, 865 subjects were selected to participate in the study with a participation rate of 87.1%. The average age of the participants was 45.5 years, with 57.0% comprising of women. Table 1 presents the percentiles of the levels of 2,4-DCP in the urine samples collected from participants. From these results, it is evident that 63.4% of the samples had levels of 2,4-DCP above the LOD – ranging from above 0.05 µg/L to 83.6 µg/L. Females had a slightly lower concentration compared to those of male participants at most percentile points. It is however, noted that the creatinine-adjusted levels were significantly higher for females compared to males at all percentile points. It is also noted that the concentration of subjects in the age bracket of 60-69 were lower compared to those of other age brackets at most of the percentile points. However, there was no significant difference in the creatinine adjusted concentrations for this particular age group at most percentile points in comparison to other age groups.

Table 1. Selected concentration percentiles of 2,4-dichlorophenol in the urine collected from the Korean population aged between 18 and 69 years by sex and age sub-groups

Variable	N	% > LOD*	Percentile				Max
			50th	75th	90th	95th	
Total	1865	63.4	0.08 (0.11)	0.56 (0.58)	1.66 (1.75)	3.32 (4.11)	83.6 (249.5)
Gender							
Men	802	63.1	0.09 (0.10)	0.58 (0.48)	1.90 (1.51)	3.52 (3.60)	72.0 (34.5)
Women	1063	63.7	0.08 (0.13)	0.55 (0.64)	1.48 (1.85)	2.97 (4.20)	83.6 (249.5)
Age (years)							
< 30	247	62.8	0.08 (0.09)	0.56 (0.50)	2.53 (1.77)	4.26 (4.71)	58.4 (65.2)
30–39	412	64.1	0.08 (0.12)	0.52 (0.48)	1.54 (1.40)	3.23 (3.27)	72.0 (37.3)
40–49	454	63.9	0.09 (0.12)	0.59 (0.58)	1.71 (2.13)	4.48 (4.77)	62.8 (155.9)
50–59	430	63.5	0.16 (0.17)	0.68 (0.70)	1.70 (1.78)	3.30 (4.06)	83.6 (249.5)
≥ 60	322	62.4	0.08 (0.10)	0.48 (0.61)	1.30 (1.40)	2.20 (2.74)	21.0 (62.1)

*Limit of detection (LOD) = 0.05 µg/L. The expression of percentiles is based on the volume concentrations of samples (µg/L), and concentrations adjusted for creatinine (µg/g creatinine) are shown in parentheses.

In table 2, selected percentiles of levels of 2,5-DCP in the urine sample of participants are shown by sex and age. 2,5-DCP was detected to be above 0.05 µg/L (LOD) in 97.9% of participants. The total concentration fell in the range between 0.05 and 63.0 µg/L. Even though no apparent difference was noted between the males and females, females recorded a significantly higher creatinine-adjusted concentrations compared to males. There was no obvious relation between the concentration and age.

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Table 2. Selected concentration percentiles of 2,5-dichlorophenol in the urine collected from the Korean population aged between 18 and 69 years by sex and age sub-groups

Variable	N	% > LOD*	Percentile					Max
			25th	50th	75th	90th	95th	
Total	1865	97.9	0.11 (0.13)	0.40 (0.38)	0.98 (1.05)	3.20 (3.69)	6.70 (7.43)	63.0 (100.2)
Gender								
Men	802	98.0	0.12 (0.11)	0.42 (0.32)	0.97 (0.86)	3.04 (3.02)	6.96 (6.14)	49.1 (41.9)
Women	1063	97.8	0.10 (0.15)	0.39 (0.44)	0.99 (1.19)	3.30 (4.22)	6.50 (8.04)	63.0 (100.2)
Age (years)								
< 30	247	98.4	0.17 (0.11)	0.44 (0.38)	1.14 (0.94)	3.02 (2.47)	6.36 (6.44)	46.3 (50.8)
30–39	412	98.5	0.16 (0.15)	0.43 (0.41)	0.98 (1.09)	3.25 (3.94)	7.53 (6.46)	38.2 (40.9)
40–49	454	98.2	0.08 (0.14)	0.41 (0.40)	0.97 (1.11)	3.20 (3.43)	6.00 (6.32)	34.0 (100.2)
50–59	430	97.4	0.08 (0.12)	0.35 (0.33)	0.92 (0.98)	3.70 (4.21)	8.20 (9.72)	23.0 (36.1)
≥ 60	322	96.9	0.08 (0.12)	0.37 (0.40)	1.00 (1.08)	2.90 (3.06)	5.70 (6.51)	63.0 (79.3)

* LOD = 0.05 μg/L. The expression of percentiles is based on the volume concentrations of samples (μg/L), and concentrations adjusted for creatinine (μg/g creatinine) are shown in parentheses.

From table 3, the weighted geometric mean for concentrations of 2,4-DCP in in the samples of urine at confidence interval of 0.13–0.16 was 0.14 μg/L. There was no significant relation between the concentrations of 2,4-DCP and the demographic factors studied. There was a significant difference in the adjusted proportional changes in the levels of mean 2,4-DCP as indicated by BMI (p=0.025) after necessary adjustments were made for potential covariates. However, the concentrations were not significantly correlated with the demographic factors such as age, sex, level of education, household income, smoking status, or geographical residence.

Table 3. Population-weighted geometric means and adjusted proportional changes in concentrations of 2,4-DCP with regard to demographic factors in the Korean adult population aged between 18 and 69 years

Variable	N	Geometric mean (95% CI), μg/L	*p*-value[a]	Adjusted proportional change (95% CI)[b]	*p*-value
Total		0.14 (0.13–0.16)		–	
Gender					
Men	802	0.14 (0.12–0.16)	0.400	1.01 (0.76–1.34)	0.960
Women	1063	0.15 (0.13–0.17)		1.00 (reference)	
Age (years)					
< 30	247	0.16 (0.12–0.21)	0.784	1.00 (reference)	0.263
30–39	412	0.12 (0.10–0.15)		0.80 (0.58–1.11)	
40–49	454	0.13 (0.11–0.16)		0.90 (0.64–1.27)	
50–59	430	0.16 (0.14–0.20)		1.08 (0.74–1.58)	
≥ 60	322	0.13 (0.11–0.16)		0.89 (0.59–1.33)	
Body mass index					
< 18.5	56	0.16 (0.08–0.32)	0.296	1.00 (reference)	0.025
18.5–22.9	816	0.16 (0.14–0.19)		1.03 (0.51–2.08)	
23.0–24.9	453	0.14 (0.12–0.17)		0.89 (0.44–1.80)	
≥ 25.0	540	0.11 (0.10–0.14)		0.72 (0.36–1.46)	
Educational level					
< High school	529	0.16 (0.13–0.19)	0.533	1.00 (reference)	0.416
High school	705	0.13 (0.11–0.15)		0.83 (0.64–1.10)	
> High school	631	0.15 (0.12–0.17)		0.88 (0.63–1.24)	
Average income (US$/month)					
< 900	399	0.13 (0.11–0.16)	0.944	1.00 (reference)	0.652
900–2699	894	0.15 (0.13–0.17)		1.19 (0.91–1.57)	
2700–4500	423	0.14 (0.11–0.17)		1.14 (0.82–1.58)	
> 4500	149	0.14 (0.10–0.20)		1.10 (0.72–1.68)	
Cigarette smoking					
Never	1232	0.15 (0.13–0.17)	0.863	1.00 (reference)	0.132
Former	228	0.11 (0.09–0.15)		0.79 (0.56–1.11)	
Current	405	0.15 (0.12–0.18)		1.09 (0.79–1.49)	
Residential location					
Rural	448	0.15 (0.13–0.18)	0.468	1.10 (0.88–1.37)	0.389
Urban	1417	0.14 (0.13–0.16)		1.00 (reference)	

[a]*p* is determined by either linear trend test or survey *t*-test. [b]The exponentiated *β*-coefficient from a multiple regression of log-linear that included all covariates and creatinine concentrations in the urine samples.

From table 4, the population-weighted geometric mean concentration of 2,5-DCP in urine samples was 0.44 μg/L at 95% (CI = 0.41–0.48). There was no significant relation between the mean concentrations and BMI, age, sex, level of education, household income, cigarette smoking, or the geographical residence of the participants. Furthermore, adjusted proportional changes in levels did not significantly differ with demographic factors, in exception of the place of residence (p = 0.045).

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Table 4. Population-weighted geometric means and adjusted proportional changes in concentrations of 2,5-DCP with regard to demographic factors in the Korean adult population aged between 18 and 69 years

Variable	*N*	Geometric mean (95% CI), μg/L	*p*-value[a]	Adjusted proportional change (95% CI)[b]	*p*-value
Total		0.44 (0.41–0.48)		–	
Gender					
Men	802	0.44 (0.39–0.49)	0.871	1.07 (0.86–1.33)	0.547
Women	1063	0.44 (0.40–0.49)		1.00 (reference)	
Age (years)					
< 30	247	0.48 (0.40–0.59)	0.087	1.00 (reference)	0.365
30–39	412	0.45 (0.39–0.53)		0.88 (0.68–1.14)	
40–49	454	0.42 (0.36–0.49)		0.79 (0.60–1.03)	
50–59	430	0.41 (0.35–0.48)		0.76 (0.56–1.04)	
≥ 60	322	0.40 (0.33–0.47)		0.73 (0.53–1.01)	
Body mass index					
< 18.5	56	0.33 (0.21–0.53)	0.247	1.00 (reference)	0.432
18.5–22.9	816	0.45 (0.40–0.51)		1.38 (0.86–2.23)	
23.0–24.9	453	0.42 (0.36–0.49)		1.33 (0.82–2.16)	
≥ 25.0	540	0.45 (0.39–0.53)		1.46 (0.90–2.37)	
Educational level					
< High school	529	0.41 (0.36–0.47)	0.422	1.00 (reference)	0.560
High school	705	0.45 (0.40–0.52)		1.04 (0.83–1.30)	
> High school	631	0.44 (0.39–0.50)		0.94 (0.71–1.23)	
Average income (US$/month)					
< 900	399	0.43 (0.36–0.51)	0.993	1.00 (reference)	0.939
900–2699	894	0.44 (0.39–0.49)		1.00 (0.80–1.26)	
2700–4500	423	0.46 (0.39–0.55)		1.07 (0.80–1.41)	
> 4500	149	0.41 (0.32–0.54)		0.99 (0.70–1.40)	
Cigarette smoking					
Never	1232	0.45 (0.40–0.49)	0.569	1.00 (reference)	0.730
Former	228	0.41 (0.34–0.51)		0.90 (0.68–1.18)	
Current	405	0.44 (0.38–0.52)		0.96 (0.75–1.22)	
Residential location					
Rural	448	0.46 (0.40–0.54)	0.461	1.09 (0.90–1.30)	0.045
Urban	1417	0.43 (0.40–0.47)		1.00 (reference)	

[a]*p* is determined by either linear trend test or survey *t*-test. [b]The exponentiated β-coefficient from a multiple regression of log-linear that included all covariates and creatinine concentrations in the urine samples.

4. Discussion

In the current study, 2,4-DCP was detected in 63.4% of participants, while 2,5-DCP was detected in 97.9% of participants. These results indicate that there is a wide exposure to these chemicals in the Korean adult population. The geometric mean level of 2,4-DCP concentration in the urine of Korean adults was 0.14 μg/L. According to the US National Health and Nutrition Examination Survey (NHANES) that was conducted between 2009 and 2010, a value of 0.80 μg/L was reported in the population aged 6 years and above [22]. A study conducted in Germany reported a level of 0.54 μg/L in Germans aged 18–69 years [23]. Given that the levels of 2,4-DCP do not significantly vary with age, the body burden of 2,4-DCP is assumed to be lower in the Korean population compared to the U.S. or German population.

The geometric mean concentration level of 2,5-DCP in the urine of Korean adults was 0.44 μg/L. This value is markedly lower compared to that obtained in the U.S. population. According to the NHANES 2009–2010, a concentration of 6.07 μg/L was reported in the US population aged 6 years and over [22]. The German Environmental Survey reported a level of 1.85 μg/L [23]. Both levels are way higher than that reported in the current study. Dichlorophenols remain in use in many countries worldwide. Some countries have attempted to decrease the production and import of these chemicals

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and their precursors [22]. Therefore, the different body burdens of 2,4-DCP and 2,5-DCP among the Korean, US, and German populations may be attributable to differences in exposure levels. In the NHANES, dichlorophenol concentrations were reported to be significantly lower in non-Hispanic whites compared to Hispanics or non-Hispanic blacks [11,22]. Therefore, ethnicity may also be related to the differences in urinary concentrations of dichlorophenols among populations.

Demographic factors, including place of residence and smoking, are reportedly related to urinary levels of some phenolic compounds [24–28], although the causal nature of these associations is unclear. In the current study, the adjusted proportional changes indicated that there was a significant correlation between BMI and levels of 2,4-DCP in the urine. In addition, subjects who resided in the rural areas reported a higher level of 2,5-DCP concentration as opposed to the subjects who resided in urban areas. The geographical place of residence and obesity had influence the level of concentration levels of 2,4-DCP and 2,5-DCP, suggesting that variations in the concentration of these chemicals was possibly influenced by place of residence and food intake.

The strength associated with this study is that it was possible to obtain concentration levels of 2,4-DCP and 2,5-DCP in the urine samples of participants, and establish how these concentrations were related to different demographic factors among adults from Korea using nationally representative data. Furthermore, urinary concentrations of these chemicals in the population were assessed using sample weights, which may have increased the accuracy of the national data. One limitation of this study was the use of a single spot-urine sample. There is a possibility that there was variation in the concentration of the 2,4-DCP and 2,5-DCP within a person over variation in time. However, it is known that approximation of mean population levels by use of a single spot sample for each participant is a more reliable approach in cross-sectional studies [15]. Future studies should focus on identifying sources of exposure to these toxic chemicals and assess the potential effects on human health.

5. Conclusions

A considerable percentage of the Korean adults aged 18–69 years old has urinary levels of 2,4-DCP and 2,5-DCP above 0.05 μg/L. The geometric mean levels were 0.14 μg/L (95% CI = 0.13–0.16) and 0.44 μg/L (95% CI = 0.41–0.48), respectively. Among the demographic characteristics studied, BMI and place of residence were significantly associated with the adjusted proportional changes in 2,4-DCP and 2,5-DCP levels, respectively. These findings suggest the need for policies to reduce exposure to these chemicals to prevent adverse effects in high-risk groups.

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