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Original Research

Assessment of Multipathway Lifetime Risks of Cancer and Non-Cancerous Diseases Associated with Trihalomethanes in Drinking Water in Petropavlovsk City, Kazakhstan

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Abstract

Chlorine (Cl^-) is used as a disinfectant of drinking water and drinking water distribution networks in Petropavlovsk, Kazakhstan. The disinfectant, interacting with fulvic and humic acids, forms disinfection by-products (DBPs), particularly, trihalomethanes (THMs). THMs might be harmful to the population, as it may cause cancer and non-cancerous diseases. As a result, the current study was focused on the assessments of the lifetime risk of cancer and non-cancerous diseases associated with THMs in Petropavlovsk community. To calculate multipathway lifetime risks of cancer and non-cancerous diseases associated with THMs we used combined United States Environmental Protection Agency (US EPA) and scientific methods. The mean concentrations of $CHCl_3$, $CHBr_3$, and $CHCl_2Br$ in drinking water were 18.41 µg/L, 48.7 µg/L, and 6.15 µg/L, respectively. The mean lifetime risk of cancer associated with THMs in drinking water was 3.83×10^{-5}. The total lifetime risk of non-cancerous diseases associated with THMs was 2.13×10^{-1}. The total lifetime risks for cancer from the three routes for the three THMs at 50th and 95th percentile scenarios were higher than the risk of the US EPA recommendation of 1.00×10^{-6}, while the total lifetime risks of non-cancerous diseases associated with THMs were lower than the US EPA recommendation of 1.

Keywords: cancer risk, drinking water, hazard index, trihalomethane

Introduction

Safe drinking water is one of the most essential rights of human beings. A variety of conventional and modern purification and disinfection methods are used to meet nowadays' drinking water quality requirements. Chlorination is a low-cost and widely used method of water disinfection [1-3]. Chlorination has been identified as the most effective method for removing microorganisms and preventing the regrowth of viruses, bacteria, and protozoa in water distribution networks [4, 5, 6]. However, chlorine interacts with natural organic

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substances, particularly, humic, and fulvic acids, resulting in 600 to 700 different disinfection by-products (DBPs) [7, 8]. Trihalomethanes (THMs) are among the most fundamental DBPs [9-11, 12]. THMs are classified into four main species: chloroform ($CHCl_3$), bromodichloromethane ($CHBrCl_2$), dibromochloromethane ($CHBr_2Cl$), and bromoform ($CHBr_3$) [13, 14]. To control concentrations of contaminants in drinking water the World Health Organization (WHO) and the United States Environmental Protection Agency (US EPA) have set safety limits. In addition, US EPA has developed the guidelines for carcinogen risk assessment of individual THMs and classified them by a carcinogenic group. Guideline values for $CHCl_3$, $CHBr_3$, $CHBr_2Cl$ and $CHBrCl_2$ are 300 µg/L, 100 µg/L, 100 µg/L, and 60 µg/L, respectively, which are set in WHO guidelines for drinking water quality [15]. According to US EPA drinking water regulations, total THMs are regulated at a maximum allowable annual average level of 80 µg/L, but there is no collective maximum contaminant level goal (MCLG) for total THMs below which there is no known or expected risk to health. However, there are individual MCLGs for the individual contaminants: $CHCl_3$ (70 µg/L), $CHBr_3$ (zero), $CHBr_2Cl$ (60 µg/L), and $CHBrCl_2$ (zero) [16]. In addition, all the four agents are considered as possible human carcinogen by US EPA [17]. Many previous studies on deterministic lifetime multipathway cancer and non-cancerous diseases risks associated with THMs in drinking water showed that THMs in drinking water may pose higher risk of cancer than the negligible cancer risk and hazardous index of US EPA of 1×10^{-6} and 1×10^{1}, accordingly. Basu and colleagues reported that the lowest total THMs concentration of 18.9 µg/L was associated with cancer risk of 6.02×10^{-5}, exceeding the US EPA limit of 1×10^{-6}. This study revealed that the hazard index exceeds non-cancer risk limit for total THMs of 1×10^{1} for the majority of drinking water supplies by ingestion exposure route [18]. Pentawma et al. discovered that cancer risk from THMs in drinking water in 6 out of 17 drinking water supplies exceeds the negligible cancer risk of US EPA by ingestion [4]. Other studies have also shown a higher cancerogenic risk associated with total THMs in drinking water than the US EPA limit. Zhang et al. estimated and compared cancer risks from THMs and low-level arsenic in drinking water based on disability-adjusted life years in Xi'an city, Northwest China and found that the cancer risk at 50th and 95th percentile scenarios were 8.54×10^{-6} and 2.77×10^{-5}, respectively [19]. Meanwhile, Lee and colleagues in a similar study on multipathway risk assessment on DBPs of drinking water in Hong-Kong found that the risk was 9.76×10^{-5} and 9.60×10^{-5} for males and females, respectively [20]. Pardakhti et al. studying comparative cancer risk of THMs in drinking water from well water sources and surface water sources in Tehran found that the lifetime cancer risk from THMs was 7.19×10^{-5} in a district where mostly surface water sources are used to supply drinking water and it was 9.38×10^{-6} in a district which is mainly supplied with well water sources [21]. Kujlu and colleagues found that cancer risk from THMs in drinking water via the highest route of exposure of inhalation was 1.78×10^{-4} and 6.40×10^{-6} for males and 1.83×10^{-4} and 6.59×10^{-5} for females in dormitory and school, respectively [22]. The US EPA hazard index limit was only exceeded in the study by Basu and colleagues, with the highest index for THMs of 6.93×10^{1}. The concentrations of THMs in drinking water were lower than the WHO guideline values in most of the previous studies, however, the lifetime multipathway cancer risk was higher than the US EPA standard. Several epidemiological studies have recently reported that the consumption and interaction with drinking water containing THMs is associated with increased risk of various diseases [23-25] and is linked to adverse reproductive and developmental outcomes [26, 27]. A multicase-control study in Spain found that estimated THM exposure may be involved in inflammation processes [28]. A study conducted in 28 European countries assessed THM levels in drinking water and estimated the population-attributable fraction (PAF) of bladder cancer. The findings of this study showed that the estimated bladder cancer PAF was 4.9 % (95% CI 2.5-7.1) overall, accounting for 6561 (95% CI 3389-9537) bladder cancer cases per year [29]. Rahman et al. found that exposure to $CHBr_3$ was associated with colon cancer in men [30]. In Petropavlovsk, drinking water and municipal water supply systems are disinfected using chlorine [31]. As a result, the consumers who are drinking or interacting with tap water without further home filtering, are likely to be exposed to THMs by oral, inhalation, and dermal routes throughout their lives. However, as the authors are aware of, no local cancer risk assessment has been performed for THMs. Thus, the initial deterministic multipathway risks of cancer and non-cancerous diseases associated with THMs in drinking water were calculated and compared in this article. This research will be beneficial in comparing risks and prioritizing dangers in drinking water.

Material and Methods

Sampling

During the period from January 24, 2020 to September 23, 2020, tap water samples were collected in each season of the year from 5 sites (located around 5, 10, 15, 20, and 25 km away from the plant), representing Petropavlovsk city (54°53′N 69°10′E), and were then measured for THMs concentrations. The average of each THM value was used for further analysis and calculations. In total, 20 samples were gathered during the study period. All samples were put into dark glass vessels of 1 L volume, which were washed with distilled water beforehand. During the collection of the samples,

faucets were turned on and allowed to run for about 5 min to obtain water from the water distribution system. All samples were kept in a dark fridge-case at the temperature of 4-6ºC until transported to the National Expertise Laboratory in Petropavlovsk. The sampling was carried out according to previous THM studies of Chowdhury and colleagues [32] and Grazuleviciene and colleagues [26]. The laboratory workers were able to analyze samples only for three THMs: $CHCl_3$, $CHBr_3$, and $CHCl_2Br$. THMs were detected using a gas chromatograph-mass spectrometer (GC-MS 7890B, Agilent Technologies, USA) equipped with a DB-624 capillary column (60 m × 0.32 mm × 1.80 mm) and an electron capture detector (ECD) after liquid-liquid extraction by methyl *tert*-butyl ether (MTBE). The limit of detection (LOD) was determined to be 0.1 μg/L for each THM species.

Cancer Risk Estimation

The health risk assessment was carried out in compliance with the recommendations of the US EPA [33, 34] and a strategy that has recently been used by a number of studies [1, 18, 19, 20, 21, 22]. The source, routes, extent, duration, and frequency of exposure to THMs for each exposed group were established based on the lifestyle of the residents and the contaminant concentrations in drinking water. Potency factors (PF) and unit risk estimates were used to evaluate the carcinogenic effects. The estimations of cancer risks through ingestion, dermal absorption, and inhalation exposure are as follows (Eq. 1, Eq. 2, Eq. 3) [34, 35, 36]:

$$CR_{oral} = CDI_{oral} \times PF_{oral} \quad (1)$$

$$CR_{dermal} = CDI_{dermal} \times PF_{dermal} \quad (2)$$

$$CR_{inhalation} = CDI_{inhalation} \times PF_{inhalation}, \quad (3)$$

where PF_{oral} is the potential factor or slope factor of a specific cancer substance. CDI_{oral}, CR_{dermal}, *and* $CR_{inhalation}$ indicate the chronic daily intake (CDI) of a particular compound under study through specific exposure pathways. CDI for each exposure route was calculated according to the following equations (Eq. 4, Eq. 5, Eq. 6):

$$CDI_{oral} = \frac{(CW \times IR \times EF \times ED)}{(BW \times AT)} \quad (4)$$

$$CDI_{dermal} = \frac{(CW \times SA \times PC \times ET \times EF \times ED)}{(BW \times AT)} \quad (5)$$

$$CDI_{inhalation} = \frac{(C_{air} \times IR \times ET \times EF \times ED)}{(BW \times AT)} \quad (6)$$

where CDI_{oral}, CDI_{dermal}, and $CDI_{inhalation}$ are CDI values through oral ingestion, dermal absorption and inhalation, respectively (mg/kg/day); *CW* is the concentration of the chemical in drinking water (mg/L); IR_w is the ingestion rate (L/day); *EF* is exposure frequency (day/year); *ED* is exposure duration (year); *BW* is body weight (kg); *AT* is average time (day); *SA* is skin area (cm^2); *F* is the fraction of surface skin in contact with water (dimensionless); *PC* is the permeability constant (cm/h); *ET* is exposure time (h/day); C_{air} is the concentration of the studied THM species in air (mg/L); and IR_a is inhalation rate (m^3/h). The inhalation exposure model developed by Little [37] was used in this study to calculate THMs volatilized from the drinking water into the shower room. For inhalation intake, C_{air} was calculated as follows (Eq. 7, Eq. 8, Eq. 9, Eq. 10, Eq. 11):

$$C_{air} = \frac{(C_t + C_0)}{2} \quad (7)$$

and

$$C_t = [1 - exp(-bt)](a/b) \quad (8)$$

$$b = \frac{\{(Q_L/H)\,[1 - \exp(-N)] + Q_G\}}{V_S} \quad (9)$$

$$a = \frac{\{Q_L C_W\,[1 - exp(-N)]\}}{V_S} \quad (10)$$

$$N = \frac{K_{OL}A}{Q_L} \quad (11)$$

where C_t is THM concentration at time t (mg/L); C_0 is the initial THM concentration (assumed as 0 mg/L); Q_L is water flow rate (L/min); V_s is bathroom volume (m^3); H is Henry's law constant (dimensionless); Q_G is air flow rate (L/min); and $K_{OL}A$ is the overall mass transfer coefficient (L/min). The necessary input parameters and references are provided in Table 1 and Table 2.

Estimation of The Risk of Non-Cancerous Diseases

The reference doses (RfDs) were used to calculate hazard indices for the evaluation of noncarcinogenic and developmental effects in humans (Table 2). The calculation of hazard indices for oral ingestion and dermal absorption routes was as follows (Eq. 12, Eq. 13):

Hazard index (HI) for THMs of the oral ingestion route

$$= CDI_{oral}/RfD_{oral} \quad \text{and} \quad (12)$$

Hazard index for THMs of the dermal absorption route

$$= CDI_{dermal}/RfD_{dermal} \quad (13)$$

Table 1. Input parameters used for the estimation of THM-related cancer risk.

Input parameters	Units	Values	References
Oral ingestion			
Concentration of the chemical in water (CW)	mg/L	See Table 3	This study
Ingestion rate (IR)	L/day	3	18, 32
Exposure frequency (EF)	days/year	365	38
Exposure duration (ED)	years	65.76 (males) 76.46 (females)	39
Dermal absorption			
Skin-surface area (SA)	m^2	1.94 (males) 1.69 (females)	18
Chemical-specific dermal permeability constant (PC)	m/h	0.000089 ($CHCl_3$) 0.000058 ($CHCl_2Br$) 0.000026 ($CHBr_3$)	18
Inhalation exposure			
Contaminant concentration in air (C_{air})	mg/L	Model calculations	37
Inhalation rate (IR)	m^3/h	0.84 (males) 0.66 (females)	43
Bathroom volume (V_s)	m^3	5	43
Water flow rate (Q_L)	L/min	5	43
Air flow rate (Q_G)	L/min	50	43
Dimensionless Henry's law constants (H)		0.12 ($CHCl_3$) 0.0656 ($CHCl_2Br$) 0.0219 ($CHBr_3$)	18
Overall mass transfer coefficient ($K_{OL}A$)[a]	L/min	7.4 ($CHCl_3$) 5.9 ($CHCl_2Br$) 3.7 ($CHBr_3$)	43
Exposure time (ET)	h/event	0.2	20
Exposure frequency (EF)	days/year	365	43
Exposure duration (ED)	years	65.76 (males) 76.46 (females)	39
Body weight (BW)	kg	67.2 (males) 63.9 (females)	40
Average time (AT)	days	65.76×365 (males) 76.46×365(females)	45

Statistical Analysis

The descriptive statistical analysis as mean, standard deviation, minimum, maximum, percentiles, and 95% confidence intervals were performed using Statistical Package for the Social Sciences 26 software for Windows (SPSS Inc., Chicago, IL, USA).

Results and Discussion

THMs Concentrations in Drinking Water

The concentration of three THMs in drinking water samples are given in Table 3. The annual doses of $CHCl_3$, $CHBr_3$, and $CHCl_2Br$ ranged from, respectively, 18.4 µg/L to 32 µg/L (mean: 18.41 µg/L), from below the detection limit (BDL) to 98 µg/L (mean: 48.7 µg/L), and from BDL to 28 µg/L (mean: 6.15 µg/L). The highest concentration of THMs was observed in winter (99.4 µg/L), while the lowest concentration was found in spring (58 µg/L). The annual concentration of the three THMs was 73.26 µg/L. The highest annual concentrations of the contaminants were observed in a study conducted by Basu and colleagues [18], while the lowest concentrations of the contaminants were found in studies conducted by Iszatt and colleagues [38], Chowdhury and colleagues [21], and Grazuleviciene and colleagues [26].

Table 2. Potency factor (PF) and reference doses (RfD) of THMs for risk calculation.

Parameters	Potency factor (mg/kg-day)			RfD [(mg/kg/day)$^{-1}$]	
	Oral	Dermal	Inhalation	Oral	Dermal
$CHCl_3$	6.10E-03[a]	3.05E-02[b]	8.05E-02[a]	1.00E-02[c]	2.00E-03[c]
$CHCl_2Br$	6.20E-02[a]	6.33E-02[b]	6.20E-02	2.00E-02[c]	2.00E-02
$CHBr_3$	7.90E-03[a]	1.32E-02[b]	3.85E-03[a]	2.00E-02[c]	1.20E-02[c]

[a]As provided in H. Zhang et al. 2018
[b]As provided in H. Zhang et al. 2018
[c]As provided in US EPA

Table 3. THM concentrations in drinking water, µg/L.

Agent	Mean	SD[a]	Max	Min	95% CI[b]
$CHCl_3$	18.41	7.08	32	18.4	15.1-21.7
$CHBr_3$	48.7	31.35	98	BDL[c]	34.02-63.4
$CHCl_2Br$	6.15	9.31	28	BDL	1.8-10.5
TTHMs	73.26	24.48	113	40	61.79-84.71

[a]SD = standard deviation; [b]CI = confidence interval; [c]BDL = below the detection limit.

The levels of the studied parameters were below the guideline values according to the WHO and US EPA [37, 38]. The annual concentrations of the contaminants in drinking water could be arranged in the following order: $CHBr_3$>$CHCl_3$>$CHCl_2Br$. $CHBr_3$ and $CHCl_3$ were the two dominant THM species that accounted for 66.5% and 25.1%, respectively. The higher proportion of $CHBr_3$ may be due to the higher concentration of bromine in the raw water [42].

THMs Exposures Through Different Routes

Exposure to THMs levels was calculated according to equations 4, 5, and 6. The level of exposure was considered in two scenarios based on the 50th and the 95th percentiles for males, females, and both sexes. The calculated CDI of THMs is shown in Fig. 1. The total CDI of the three THMs of the 50th and the 95th percentiles scenarios was 1.97 x 10^{-3} and 3.74 x 10^{-3} in males, respectively, while in females, it was 2.20 x 10^{-3} and 4.17 x 10^{-3}, respectively.

The highest proportion of the total CDI of THMs was those of $CHBr_3$ and $CHCl_3$. The $CHBr_3$ and $CHCl_3$ accounted for 61% and 30% of CDI in males and 62% and 29% of CDI in females, respectively. The lowest proportion of the total CDI of THMs was that of $CHBrCl_2$ - 9% in both males and females (see Fig. 2 (a, b)).

Oral ingestion was the most prevalent route of exposure for the three THMs, accounting for 79.7% and 83.3% of the overall exposure in males and females, respectively. The next most prevalent exposure route

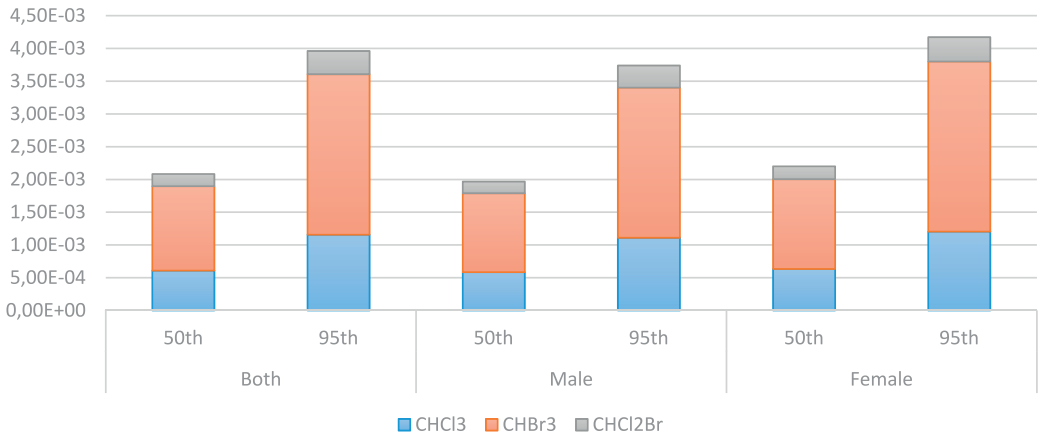

Fig. 1. The 50th and 95th percentiles of CDIs of the THMs through all the three exposure routes by sex.

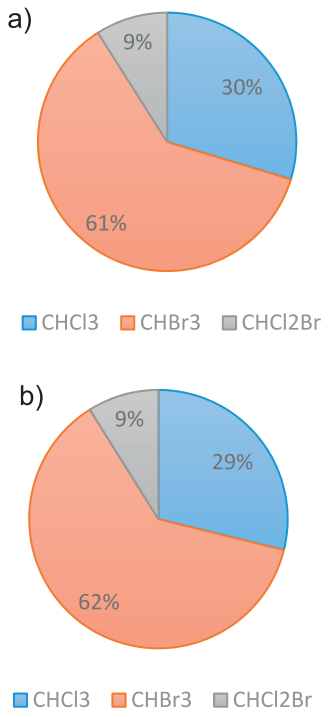

Fig. 2. Daily intake shares of trihalomethanes by each species in males a) and females b).

was inhalation, which accounted for 20.3% and 17.7% of THMs intake in males and females, respectively. Exposure to THMs through dermal absorption was found to be very low (see Fig. 3(a, b)).

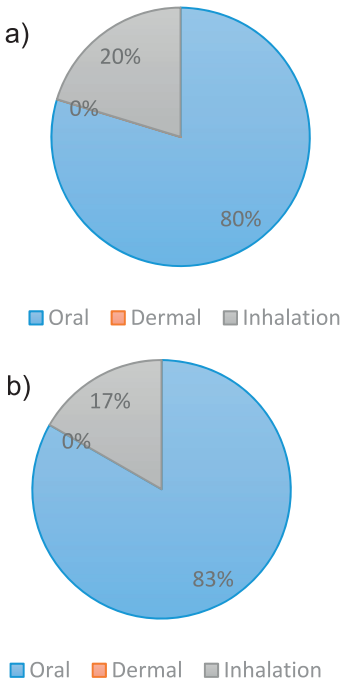

Fig. 3. Trihalomethane intake shares by exposure routes in males a) and females b).

THM-Related Lifetime Risks of Cancer with Respect to Different Routes of Exposure

The lifetime risk of cancer associated with THMs was estimated using 1, 2, and 3 equations based on THM concentration measured in the tap water samples. The cancer risks were assessed at the 50th and 95th percentiles for males and females as well as for both sexes for oral intake, dermal absorption, and inhalation.

Cancer risk related to oral ingestion is provided in Fig. 4. The 50th and 95th percentiles of the total THM-related risk of cancer in case of the oral route of exposure were 2.04 x 10^{-5} and 3.88 x 10^{-5} (males: 1.88 x 10^{-5} and 3.58 x 10^{-5}; females: 2.20 x 10^{-5} and 4.17 x 10^{-5}), respectively. The values of total risk were higher than negligible risk as defined by the US EPA (1.00 x 10^{-6}). The highest 50th and 95th percentiles of oral ingestion-related risk were found for $CHBr_3$ and were 8.93 x 10^{-6} and 1.70 x 10^{-5} (males: 8.24 x 10^{-6} and 1.57 x 10^{-5}; females: 9.62 x 10^{-6} and 1.83 x 10^{-5}), respectively. The lowest risk associated with the oral route of exposure was observed for $CHCl_3$, its 50th and 95th percentiles were 2.61 x 10^{-6} and 4.95 x 10^{-6} (males: 2.41 x 10^{-6} and 4.57 x 10^{-6}; females: 2.81 x 10^{-6} and 5.33 x 10^{-6}), respectively. Oral ingestion was the dominant route and accounted for 53.3% of the total cancer risk.

The risk of cancer associated with dermal absorption is shown in Fig. 5. The 50th and 95th percentiles of THM-related lifetime risk of cancer for the dermal absorption route were 2.50 x 10^{-10} and 4.74 x 10^{-10} (males: 2.47 x 10^{-10} and 4.70 x 10^{-10}; females: 2.52 x 10^{-10} and 4.77 x 10^{-10}), respectively. The values of total risk were considerably lower than the negligible risk level defined by the US EPA (1.00 x 10^{-6}). The highest 50th and 95th percentiles of the risk were found for $CHCl_3$ and were 1.40 x 10^{-10} and 2.65 x 10^{-10} (males: 1.38 x 10^{-10} and 2.63 x 10^{-10}; females: 1.41 x 10^{-10} and 2.67 x 10^{-10}), respectively. Dermal absorption had the lowest contribution to the total risk of cancer and accounted only for 0.0007% of the risk.

Inhalation-related risk of cancer is shown in Fig. 6. The 50th and 95th percentiles of THM-related lifetime risk of cancer for the inhalation route were 1.79 x 10^{-5} and 3.41 x 10^{-5} (males: 1.88 x 10^{-5} and 3.56 x 10^{-5}; females: 1.72 x 10^{-5} and 3.26 x 10^{-5}), respectively. The values of total risk were higher than the negligible risk level defined by the US EPA (1.00 x 10^{-6}). The highest 50th and 95th percentiles of inhalation-related risk were seen for $CHCl_3$ and were 1.46 x 10^{-5} and 2.78 x 10^{-5} (males: 1.53 x 10^{-5} and 2.90 x 10^{-5}; females: 1.40 x 10^{-5} and 2.66 x 10^{-5}), respectively. Inhalation was the second highest contributor to the total risk, accounting for 46.7% of the total risk of cancer.

THM-Related Total Lifetime Risks of Cancer

The 50th and 95th percentiles of the total lifetime risk of cancer associated with exposure to THMs via

Fig. 4. The 50th and 95th percentiles of THM-related lifetime risk of cancer for the oral ingestion route.

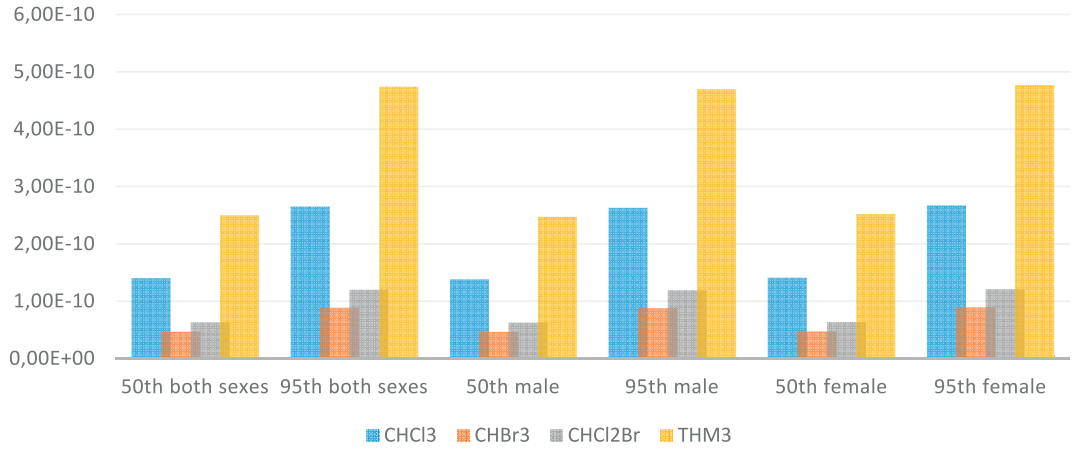

Fig. 5. The 50th and 95th percentiles of THM-related lifetime risk of cancer for the dermal absorption route.

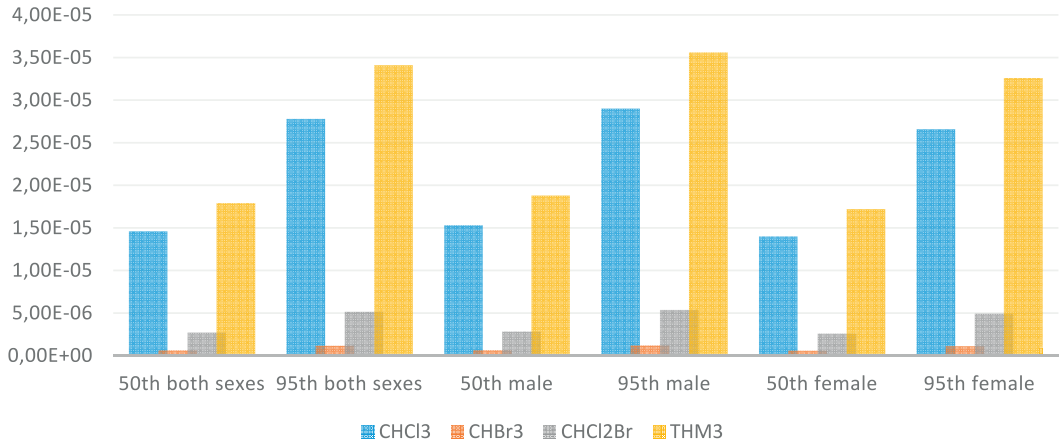

Fig. 6. THM-related lifetime risk of cancer for the inhalation route.

the three routes for both sexes were 3.83 x 10^{-5} and 7.28 x 10^{-5} (males: 3.76 x 10^{-5} and 7.13 x 10^{-5}; females: 3.91 x 10^{-5} and 7.44 x 10^{-5}), respectively (see Table 4). The 95th percentile of the risk was higher than the acceptable risk set in the US EPA recommendations (5.31 x 10^{-5}), while the value of the 50th percentile of the risk was higher than the negligible risk as defined by the US EPA (1.00 x 10^{-6}). The results were higher than those reported in the previous study of Zhang and colleagues [20]. The 50th percentile of the risk for both sexes in our study was considerably lower than the highest values and was similar to the lowest values found in a study

Table 4. The 50th and 95th percentile values of the total lifetime risk of cancer for the public associated with exposure to the three THMs via the three exposure routes (inhalation, oral ingestion, and dermal absorption).

Pollutant	Both		Males		Females	
	50th	95th	50th	95th	50th	95th
THMs	3.83E-05	7.28E-05	3.76E-05	7.13E-05	3.91E-05	7.44E-05
$CHCl_3$	1.72E-05	3.28E-05	1.77E-05	3.36E-05	1.68E-05	3.19E-05
$CHBr_3$	9.54E-06	1.82E-05	8.87E-06	1.69E-05	1.02E-05	1.94E-05
$CHCl_2Br$	1.16E-05	2.19E-05	1.10E-05	2.09E-05	1.21E-05	2.30E-05

by Basu and colleagues [18]. In addition, it was slightly lower than the lifetime risk of cancer found in a study by Kujlu and colleagues [22].

The 50th percentile scenario of the total lifetime risk of cancer associated with exposure to $CHCl_3$, $CHBr_3$, and $CHCl_2Br$ in drinking water was found to be 1.72×10^{-5} (males: 1.77×10^{-5}; females: 1.68×10^{-5}), 9.54×10^{-6} (males: 8.87×10^{-6}; females: 1.02×10^{-5}), and 1.16×10^{-5} (males: 1.10×10^{-5}; females: 1.21×10^{-5}), respectively, while the 95th percentile scenario was 3.28×10^{-5} (males: 3.36×10^{-5}; females: 3.19×10^{-5}), 1.82×10^{-5} (males: 1.69×10^{-5}; females: 1.94×10^{-5}), and 2.19×10^{-5} (males: 2.09×10^{-5}; females: 2.30×10^{-5}), respectively. The contribution of the contaminants to the risk was as follows: $CHCl_3$ (44.9%), $CHCl_2Br$ (30.2%), and $CHBr_3$ (24.9%). Oral ingestion was found to be the most substantial route of exposure (53.3%), followed by inhalation (46.7%), whereas dermal absorption showed an extremely negligible share of the risk (0.0007%). The lifetime risk of cancer associated with exposure to THMs for females was higher than that for males in case of oral ingestion and dermal absorption. The values of 50th percentile exposure scenario of total, oral ingestion-related, and dermal absorption-related risk of cancer for females were higher by, respectively, 3.84%, 14.55%, and 1.98% than that for males. Meanwhile, males had a 9.3% higher risk of cancer associated with exposure to THMs via inhalation compared to females because of a higher inhalation rate.

THM-Related Lifetime Risks of Non-Cancerous Diseases Depending on Different Routes of Exposure

The hazard indices of exposure to the three THMs via various routes were also calculated to determine the noncarcinogenic risks associated with the compounds using equations 11 and 12. The total hazard index was calculated by summing up each of the THMs indices from both routes (oral and dermal). The risks of the 50th and 95th percentile exposure scenarios were 1.07×10^{-1} (males: 9.80×10^{-2}; females: 1.15×10^{-1}) and 2.02×10^{-1} (males: 1.86×10^{-1}; females: 2.19×10^{-1}), accordingly.

The highest mean hazard index for the three THMs was observed for the oral ingestion route, and it was 1.07×10^{-1} (males: 9.80×10^{-1}, females: 1.15×10^{-1}). The route was also dominant and accounted for 99.99% of the total hazard index. Pollutants that contributed the most to the total hazard index were $CHBr_3$ and $CHCl_3$ (53.03% and 40.24%, respectively). The exposure in females was a 14.78% higher than in males. The results of the hazard indices of THMs in drinking water were lower than those reported in a study by Basu and colleagues [18] and higher than those found in the study by Kujlu and colleagues [22].

The aim of this study was to assess the multipathway risks of cancer and non-cancerous diseases associated with THMs ($CHCl_3$, $CHBr_3$, and $CHBrCl_2$) in drinking water for the residents of Petropavlovsk city. We first estimated the average annual concentrations of each THM in drinking water. Then, using the average concentration of each organochlorine compound and the total concentration of the three THMs, we calculated the individual and total carcinogenic and non-carcinogenic risks for two exposure scenarios (50th and 95th percentiles) for male and female groups as well as the average combined risk (for both sexes) by the three exposure routes (inhalation, oral ingestion, and dermal adsorption). In addition to assessing the risks by the compounds and by the three routes, the risk levels were calculated for each exposure route separately for total and individual THM species. It should be noted that the total carcinogenic risk posed by the three THMs from the three exposure routes exceeded the negligible risk as defined by the US EPA in both exposure scenarios. Hence, people who use tap drinking water in Petropavlovsk city may be at a greater-than-negligible risk of developing a carcinogenic disease if they do not apply an additional home filter system. Meanwhile, the non-carcinogenic risks posed by THMs in the tap water did not exceed the limits set by the US EPA [34].

Similar studies have been performed in several Asian countries, including China [19, 40, 41], Iran [21, 22], Pakistan [44], and Thailand [4]. Now, owing to the current research, data on carcinogenic and non-carcinogenic threats posed by THMs are for the first time available from Kazakhstan. The findings for one city are rather unrepresentative, leaving it to the local academics to assess the risks for other cities in Kazakhstan in future studies. In addition, the risk estimates in this study were only assessed for the three THMs ($CHCl_3$, $CHBr_3$, and $CHBrCl_2$), and thus

the concentrations and risks for the fourth species of THMs ($CHBr_2Cl$) should still be studied in order to obtain a holistic understanding of multipathway lifetime risk of cancer and non-cancerous diseases associated with exposure to total THMs in drinking water of Petropavlovsk city, Kazakhstan.

Conclusions

The total lifetime risk of cancer associated with exposure to the three THMs via the three studied routes for the 50th and 95th percentiles scenarios for the Petropavlovsk community was higher that the negligible risk defined in the US EPA recommendations (1.00×10^{-6}), while the total THM-related lifetime risk of non-cancerous diseases was lower than the value indicated in the US EPA guidelines. The highest risks were associated with oral ingestion. Females had a higher total lifetime risk of cancer and non-cancerous diseases compared to males.

Conflict of Interest

The authors declare no conflict of interest.

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