

# Cancer Risk Assessment From Multi-Exposure to Chloroform in Drinking Water of Ilam City, Iran

Kamyar Arman,<sup>1\*</sup> Ali Reza Pardakhti,<sup>1</sup> Noushin Osoleddini,<sup>2</sup> and Mostafa Leili<sup>3</sup>

<sup>1</sup>Environmental Engineering Department, Faculty of Environment, University of Tehran, Tehran, IR Iran

<sup>2</sup>Applied Chemistry Department, Faculty of Pharmaceutical Chemistry, Pharmaceutical Sciences Branch, Islamic Azad University, Tehran, IR Iran

<sup>3</sup>Department of Environmental Health Engineering, School of Public Health and Research Center for Health Sciences, Hamadan University of Medical Sciences, Hamadan, IR Iran

\*Corresponding author: Kamyar Arman, Environmental Engineering Department, Faculty of Environment, University of Tehran, Tehran, IR Iran. Tel: +98-9393431236, E-mail: kamyar.arman@gmail.com

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## Abstract

Among various trihalomethane (THM) compounds, chloroform is considered to be the main compound and was selected as an indicator of THMs in this study. This study aims to calculate and assess the lifetime cancer risks resulting from chloroform intakes of various exposure routes in Ilam's urban drinking water. The samples were analyzed using a gas chromatograph equipped with a flame ionization detector (GC/FID). The results showed that average chloroform concentrations in different districts were between 20 and 30.3  $\mu\text{g/L}$ , and the highest concentrations were detected in district 4 with a value of 32.2  $\mu\text{g/L}$ . All water samples contained concentrations of chloroform below the standards of the world health organization (WHO) and the institute of standards and industrial research of Iran (ISIRI). Assessment of lifetime cancer risks was carried out using prediction models for different exposure routes, including ingestion, inhalation, and dermal routes for people living in Ilam city. The highest risk from chloroform seems to be from the oral ingestion route, followed by inhalation and dermal absorption. The maximum and minimum lifetime cancer risks were  $6.59 \times 10^{-6}$  and  $5.95 \times 10^{-6}$  in districts 4 and 3, respectively. It was also concluded that the average lifetime cancer risk was  $6.26 \times 10^{-6}$  in all districts. Based on the population data, the total number of expected lifetime cancer cases from exposure to chloroform is 1 for Ilam city.

**Keywords:** Cancer Risk Assessment, Chloroform, Trihalomethanes, Drinking Water, Ilam

## 1. Introduction

Disinfectants such as chlorine are used in municipal water treatment in order to protect public health from water-related diseases. The disinfectants are used to prevent microorganism growth and profanations in drinking water treatment plants and distribution networks. Water chlorination is the most common and economic disinfection method due to its high oxidation potential, low cost, and ease of use. Although chlorination is widely used as a disinfection process, it produces a number of disinfection byproducts (BDPs) (1-3). Disinfection byproducts and trihalomethanes (THMs) are produced due to reactions between chlorine and natural organic matter (NOM) in water resources, particularly surface water. Production of THMs depends on several factors such as pH, exposure duration, residual chlorine, bromide concentration, and water temperature (4). Chloroform, bromodichloromethane (BDCM), dibromochloromethane (DBCM), and bromoform are the four main compounds of THMs. Disinfection byproducts in drinking water have been a concern since 1974 due to probable cancer and non-cancer risks to human health (5). Trihalomethanes were the most prob-

able carcinogenic agent among all disinfection byproducts because carcinogenic effects of chloroform on animals were observed earlier (6). Clinical and epidemiological studies have shown that multiple clinical symptoms such as high rates of bladder cancer, rectal cancer, colon cancer, and brain cancer are due to direct exposure to disinfection byproducts (5). The US environmental protection agency (EPA) has placed chloroform, bromodichloromethane, and bromoform in class B2 (probable human carcinogen with sufficient animal data), and dibromochloromethane in class C (possible human carcinogen) (7). Moreover, the concentration of chloroform in total trihalomethanes (TTHMs) is higher than other compounds (2, 8-11). Studies have been conducted by various organizations to determine maximum contaminant levels (MCLs) of disinfection byproducts in water. For example, the world health organization (WHO) has determined maximum contaminant levels of total THMs in drinking water to less than 100 micrograms per liter of water (12). The EPA established the maximum contaminant level for total THMs in 1998. In stage I, the MCL for total THMs was set at 80  $\mu\text{g/L}$ ; in stage II, the maximum contaminant level goal (MCLG) is expected to further decrease to 40  $\mu\text{g/L}$  (6).

An individual may be exposed to disinfection byproducts such as THMs like chloroform over his/her lifetime through multiple pathways such as drinking water, regular and continuous breathing, and inhalation, as well as dermal exposure through showering, bathing, and cooking. Chronic exposure to chloroform is a risk factor for human health. Several studies have assessed the cancer risk posed by trihalomethanes in chlorinated drinking water. It was reported that exposure to chloroform poses a higher cancer risk than other THM compounds (10, 13-15). Most studies have only evaluated the cancer risk caused by gastrointestinal (oral) exposure to chloroform. However, recent scientific studies have considered other exposure pathways to disinfectants for health risk assessment (16). The cancer risk posed by various exposure pathways to disinfectants in drinking water in Hong Kong was assessed in 2004 (17). In this study, it was reported that the risk of gastrointestinal exposure to disinfectants was higher than skin absorption and inhalation of disinfectants (17). The cancer risk posed by exposure to THMs was also assessed in other studies (13, 18). They showed that the risk of gastrointestinal exposure to disinfectants was higher than other cases.

Surface water is the main source of drinking water supply in Ilam. Water chlorination is performed at the urban water treatment plant, which in turn increases the potential of trihalomethane formation. Therefore, this study aims to calculate the numeric value of cancer risk caused by exposure to chlorinated drinking water in terms of various exposure pathways in Ilam. Chloroform concentrations in the drinking water distribution network were obtained from four districts in Ilam.

## 2. Materials and Methods

### 2.1. Sample Collection and Analysis

According to the 2012 population and housing census by the statistics center of Iran (19), Ilam city has a population of 177,988 people, and is located in the northwestern province of Ilam. The main sources of drinking water in Ilam city are spring, wells, and the Cham Gardalan dam, with the latter supplying about 55% of the total water needs of the city. After passage to the water treatment plant, water undergoes a treatment process for removing contaminants, which mainly includes physical processes such as settling and filtration, and chemical processes such as disinfection and coagulation. The following processes are used at the Ilam municipal drinking water treatment plant: aeration along with pre-chlorination, coagulation and flocculation, sedimentation, filtration using sand filters, and finally disinfection using multioxidants such as

chlorine, chlorine dioxide, ozone, and oxygen. The system in which these oxidants are produced is called REDO® disinfection systems. They are produced through electrolysis of water and pure salt. The disinfected water is stored in water reservoirs, then released into the urban water distribution network. Samples were taken from tap water across the four different districts during the period July 2014 to February 2015. The positions of the four districts and the water treatment plant of Ilam are shown in Figure 1.



Figure 1. Map of the Study Area Showing Sampling Locations

The samples were taken directly from the taps of consumers. A sample volume of 40 mL was collected in clean glass vials, and then sodium thiosulfate was added to it as a de-chlorination agent. The glass vials were fully filled with water, leaving no headspace, and were stored in the dark at temperature  $< 40^{\circ}\text{C}$  for further analysis. The chloroform concentrations in water samples were measured using EPA method 551.1 (20, 21). A gas chromatograph equipped with a flame ionization detector (Acme 6000 GC/FID, Young Lin Co., Korea) (13, 15, 22) was used for the determination and quantification of chloroform. A 30 m TRB-5 capillary column with a 0.32 mm ID and 1  $\mu\text{m}$  film thickness (Teknokroma, Spain) was used for chromatography. The flame ionization detector was used for identification and quantification of eluting peaks.

### 2.2. Exposure Assessment

In total, the risk assessment process consists of four steps: hazard identification, exposure assessment, dose-response assessment, and risk assessment. At first, risk factors should be identified in order to assess the cancer risk. Considering that THMs such as chloroform were identified as carcinogens and classified in the B2 group by the EPA (23), the presence of these compounds in drinking water in Ilam city could be a cancer risk. As a result, the present study evaluated the cancer risk of exposure to chloroform

among people in Ilam based on measurement of chloroform concentrations in drinking water. The rate of daily exposure to trihalomethane compounds such as chloroform through oral, dermal, and inhalation pathways for every individual in a lifetime in the study area can be determined according to integrated risk information system (IRIS) (7), EPA and other authorities, given the amount of water consumed per day, the volume of breathed air inside the bathroom, the level of dermal contact with water, and other factors such as average human weight, human lifetime, absorption coefficients, and frequency of bathing. Exposure assessments of Ilam's population were conducted based on the measured concentration of chloroform in drinking water and was performed on oral ingestion, inhalation, and dermal absorption routes. Showers were considered a major route for inhalation and dermal absorption (24). Past studies have shown that inhalation exposure to chloroform in cooking was lower when compared to inhalation exposure during showers (25).

An exposure assessment of chloroform via ingestion, inhalation, and dermal routes was carried out using chronic daily intake (CDI) estimation. The equations for calculation of chronic daily intakes are shown below (17, 18):

$$\begin{aligned} \text{Oral ingestion} \left( \frac{\text{mg}}{\text{kg.day}} \right) \\ = \frac{[CW \times IR \times EF \times ED \times CF]}{BW \times AT} \end{aligned} \quad (1)$$

$$\begin{aligned} \text{Dermal absorption} \left( \frac{\text{mg}}{\text{kg.day}} \right) \\ = \frac{[CW \times SA \times F \times PC \times ET \times EF \times ED \times CF]}{BW \times AT} \end{aligned} \quad (2)$$

$$\begin{aligned} \text{Inhalation absorption} \left( \frac{\text{mg}}{\text{kg.day}} \right) \\ = \frac{[C_{\text{air}} \times VR \times AE \times ET \times EF \times ED \times CF]}{BW \times AT} \end{aligned} \quad (3)$$

The inhalation exposure model theory that was proposed by Little in 1992 has been used in this study to calculate the THM concentration in a shower room.  $C_{\text{air}}$  was estimated as follows:

$$C_{\text{air}} = \frac{[Y_{s(t)} + Y_{s(i)}]}{2} \quad (4)$$

$Y_{s(i)}$  is the initial THM concentration in the shower room (assumed as 0 mg/L).

$Y_{s(t)}$  is the THM concentration in the shower room at time t (minute).

$$Y_{s(t)} = [1 - \exp(-bt)] \times \left( \frac{a}{b} \right) \quad (5)$$

$$b = \frac{\left\{ \left( \frac{QL}{H} \right) [1 - \exp(-N)] + QG \right\}}{VS} \quad (6)$$

$$a = \frac{\{QL \times CW [1 - \exp(-N)]\}}{VS} \quad (7)$$

$$N = \frac{K_{OLA}}{QL} \quad (8)$$

Where N is a dimensionless coefficient that was calculated from  $K_{OL}$ . The input parameters for the exposure assessment and risk calculations are summarized in Table 1.

### 2.3. Risk Calculation

The lifetime cancer risk of chloroform was calculated by incorporating exposure assessment and toxicity values (cancer slope factors). The equations for calculation of lifetime cancer risk are shown in Equations 9 and 10:

$$\text{Total cancer risk} = \Sigma [CDI \times SF] \quad (9)$$

$$TCR = CR_{\text{Oral}} + CR_{\text{Dermal}} + CR_{\text{Inhalation}} \quad (10)$$

Where  $CR_{\text{Oral}}$  is cancer risk from the ingestion route,  $CR_{\text{Dermal}}$  is cancer risk from the dermal route, and  $CR_{\text{Inhalation}}$  is cancer risk from the inhalation route. The primary source of the slope factors was the risk assessment information system (23). Table 2 summarizes the cancer slope factors (CSF) for oral, dermal, and inhalation used for chloroform via different routes. These values were taken from the RAIS (23).

An exposure assessment of Ilam's population was performed on the oral ingestion, inhalation, and dermal absorption routes. In this study, the average adult body weight was 80 kg, the average lifespan was 70 years, and the average water consumption per adult person was 2.5 liters per day according to a 2011 EPA report (20). Daily exposure to trihalomethane compounds through oral, dermal, and inhalation pathways was multiplied by toxicity or cancer slope factors in order to calculate cancer risk (CR) from chloroform through different exposure pathways. According to Equation 10, the sum of chloroform-induced cancer risk through oral exposure ( $CR_{\text{Oral}}$ ), chloroform-induced cancer risk through dermal exposure ( $CR_{\text{Dermal}}$ ), and chloroform-induced cancer risk through inhalation ( $CR_{\text{Inhalation}}$ ) gives the total cancer risk (TCR).

**Table 1.** Input Parameters for Calculating Exposure and Intake

Input parameters	Unit	Values (for Adult)	Reference
Concentration in water (CW)	$\mu\text{g/L}$	$\mu\text{g/L}$	This Study
Ingestion rate (IR)	L/day	2.5	(20)
Concentration in air ( $C_{\text{air}}$ )	mg/L	Little's model	(26)
Ventilation rate (VR)	$\text{m}^3/\text{hour}$	0.84 (male)	(21)
Absorption efficiency in alveoli (AE)	-	50%	(27)
Water flow rate (QL)	L/minute	5	(26)
Air flow rate (QG)	L/minute	50	(26)
Dimensionless Henry's law constants (H)	-	0.15	(23)
Water temperature (T)	44	$^{\circ}\text{C}$	(27)
Overall mass transfer coefficient (KOLA)	L/minute	7.4	(26)
Skin surface area (SA)	$\text{m}^2$	2.0	(20)
Fraction of skin in contact with water (F)	Percent	80	(27)
Permeability coefficient (PC)	cm/hour	0.00683	(23)
Exposure time (ET)	minute/day	35	(23)
Conversion factor (CF)	$\text{L}/\text{cm}^3$	0.001	-
Exposure duration (ED)	year	26	(20)
Exposure frequency (EF)	day/year	350	(21)
Mean exposure time (AT)	day	$70 \times 365$	(25)
Body weight (BW)	kg	80	(20)

**Table 2.** Carcinogenic Slope Factors Used for Chloroform Via Different Routes (23)

Routes	Slope Factors (SF) ( $\text{mg}/\text{kg}\cdot\text{day}$ ) <sup>1</sup>
Ingestion	6.10E-03
Dermal	3.05E-02
Inhalation	8.01E-02

### 3. Results and Discussion

#### 3.1. Concentrations of Chloroform in Different Districts

Average chloroform concentrations varied between 20 and 30.3  $\mu\text{g/L}$  in the water samples collected from sampling locations. The results also showed that the highest concentration, 32.2  $\mu\text{g/L}$ , was detected in district 4. Furthermore, the average concentration of chloroform in the sampling location was 25.2  $\mu\text{g/L}$ , which was well below the standards of WHO and the Institute of standards and industrial research of Iran (ISIRI) of 200  $\mu\text{g/L}$  (28). These values were lower than the values reported in the studies (13, 14); for example, Yazdanbakhsh et al. (22) reported that the total average concentration of chloroform in Tehran's drinking water distribution network was 36.5  $\mu\text{g/L}$ .

#### 3.2. Multi-Pathway Valuations of Lifetime Cancer Risks for Chloroform

##### 3.2.1. Ingestion Route

The cancer risks from the oral route for all districts were calculated by incorporating chronic daily intake (CDI) and cancer slope factors (SF).

As seen in Table 3, the maximum and minimum cancer risks from the ingestion route ( $CR_{\text{oral}}$ ) were  $5.07 \times 10^{-6}$  and  $4.57 \times 10^{-6}$  in districts 4 and 3, respectively. The average of cancer risks resulting from chloroform through the oral exposure route in drinking water in Ilam city for a lifetime of a 70-year-old individual was  $4.81 \times 10^{-6}$ , which was less than the cancer risk reported in similar studies conducted in other countries (29, 30). The average cancer risk from chloroform through oral exposure in the latter study was almost 3 times higher than the cancer risks reported

**Table 3.** Lifetime Cancer Risk From Chloroform

Route	Ingestion	Dermal	Inhalation	Total
Districts	Risk	Risk	Risk	Risk
District 1	4.84E-06	4.06E-07	1.05E-06	6.29E-06
District 2	4.76E-06	4.00E-07	1.03E-06	6.19E-06
District 3	4.57E-06	3.84E-07	9.96E-07	5.95E-06
District 4	5.07E-06	4.25E-07	1.10E-06	6.59E-06
Average cancer risk	4.81E-06	4.04E-07	1.04E-06	6.17E-06

in the study conducted by Pardakhti et al. in Tehran ( $1.49 \times 10^{-6}$ ) (10). The difference between the two aforementioned studies could be due to the difference between concentrations of chloroform in drinking water in Ilam ( $26.6 \mu\text{g/L}$ ) and Tehran ( $2.34 \mu\text{g/L}$ ).

### 3.2.2. Dermal Route

The dermal surface exposed to chloroform was assumed to be 2.0 square meters, while the duration of showering was assumed to be 30 minutes and the frequency of showering three times per week in order to estimate cancer risk resulting from chloroform through dermal exposure. The results are shown in Table 3. As can be seen, district 3 had the lowest cancer risk ( $3.84 \times 10^{-7}$ ) while district 4 had the highest risk of cancer ( $4.25 \times 10^{-7}$ ). Nevertheless, the average cancer risk through dermal exposure is less than the average cancer risk through oral exposure and inhalation. The average chloroform-induced cancer risk through dermal exposure in Ilam was  $4.04 \times 10^{-7}$ , which only constitutes 6.4% of total chloroform-induced cancer risk in drinking water in Ilam. These results are in consistent with the results obtained by Pardakhti et al. (10) in Tehran and in some studies in other countries (13, 18, 24).

### 3.2.3. Inhalation Route

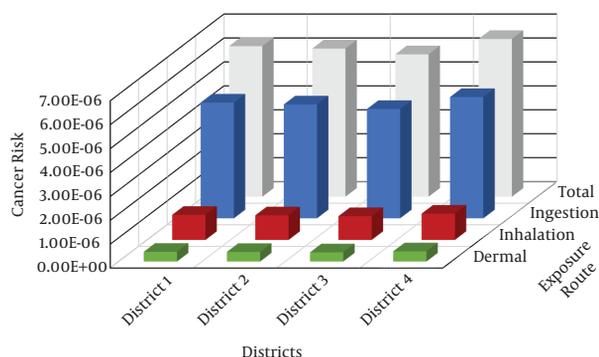
The mean showering times was three other days, while the duration of showering was 30 minutes and the volume of breathed air inside the bathroom was  $10 \text{ m}^3$  in order to estimate cancer risk resulting from chloroform through inhalation. As specified in Table 3, chloroform-induced cancer risks through inhalation in all four regions were higher than cancer risks through dermal exposure. The average chloroform-induced cancer risk through inhalation was  $1.04 \times 10^{-6}$ , which constitutes 16% of the total cancer risk from chloroform in drinking water in Ilam. The results of this study are not consistent with the results reported in the study conducted by Pardakhti et al. in 2011 (10). In the latter study, the cancer risk through inhalation ( $1.60 \times 10^{-5}$ ) was greater than the cancer risk through oral

exposure. This difference may be due to the differences between the average showering duration, the volume of breathed air inside the bathroom, and the average times of showering in Tehran and Ilam. Cancer risks through inhalation were estimated at  $1.20 \times 10^{-5}$  and  $1.24 \times 10^{-4}$  respectively in the studies conducted by Tokmark et al. in Turkey (18) and Amjad et al. in Pakistan (13). In the former studies, the chloroform-induced cancer risk through inhalation was lower than the cancer risk through oral exposure and higher than the cancer risk through dermal exposure.

### 3.2.4. Lifetime Cancer Risks for Chloroform

The lifetime cancer risks through ingestion, inhalation, and dermal routes for people living in Ilam were calculated using the input parameters in Table 1, the slope factors in Table 2, and the chloroform concentrations that were measured in sampling districts. As a result, the highest cancer risk from chloroform in Ilam is in the category of ingestion risk and was observed in district 4. The corresponding value of the ingestion cancer risk in district 4 was  $5.07 \times 10^{-6}$ . The lowest cancer risk from chloroform is dermal risk, which was observed in district 3 with the value of  $3.84 \times 10^{-7}$ . According to Figure 2, the overall cancer risks from chloroform in the city of Ilam are  $4.81 \times 10^{-6}$  via ingestion,  $1.04 \times 10^{-6}$  via inhalation, and  $4.04 \times 10^{-7}$  via the dermal route.

The induced total cancer risk from exposure to chloroform in drinking water in Ilam in a lifetime was  $6.26 \times 10^{-6}$ , which was six times higher than the negligible risk level ( $1.00 \times 10^{-6}$ ) determined by the EPA (20). Chloroform-induced cancer risk through oral exposure constitutes 76.83% of total cancer risk. The remaining total cancer risk was caused by chloroform-induced cancer risk through dermal exposure and inhalation. However, the estimated risk values reported in this study were greater than the risk values reported in the study conducted by Wang et al. in Taiwan ( $1.82 \times 10^{-6}$ ) (24). On the other hand, the risk values reported in similar studies in Iran and other countries



**Figure 2.** Comparative Risks From Ingestion, Inhalation, and Dermal Exposure to Total Chloroform in Different Districts

were lower than the risk values reported in the present study (10, 13, 18, 24). The results of the present study were compared with the results obtained by Pardakhti et al. in 2011 (10), and it was shown that the chloroform-induced cancer risk in Ilam was  $6.26 \times 10^{-6}$ , which was three times less than the calculated cancer risk reported by Pardakhti et al. ( $18.2 \times 10^{-6}$ ) for Tehran. The results showed that one individual was at risk of cancer according to the estimated chloroform-induced total cancer risk in drinking water in Ilam in a lifetime. However, many factors may prove the uncertainty of these results. For example, the cancer risk was estimated during the 70-year lifetime of an individual. Therefore, many factors could affect the estimated cancer risk in this period. Nevertheless, the possibility of increased cancer risk through exposure to chloroform in drinking water was estimated at 0.015 cancer cases per year, which was negligible compared with 359 cases of cancer in Ilam (31).

#### 4. Conclusion

The present study was conducted by taking into account a variety of chloroform exposure pathways in Ilam's drinking water, and an assessment of cancer risk from chloroform exposure was carried out. The results showed that the potential of chloroform formation in drinking water supply resources and facilities in Ilam was  $25.2 \mu\text{g/L}$ . The highest risk value of chloroform-induced cancer risk through oral exposure was ( $4.81 \times 10^{-6}$ ) and the lowest cancer risk through dermal exposure was ( $4.04 \times 10^{-7}$ ). The lifetime cancer risk assessment for chloroform indicates that ingestion is the most important route of entry, followed by inhalation and dermal exposure. The cancer risks from chloroform are  $4.81 \times 10^{-6}$  via ingestion,  $1.04 \times 10^{-6}$  via inhalation, and  $4.04 \times 10^{-7}$  via the dermal route. The results of this study show that lifetime cancer cases caused by

chloroform exposure from drinking water are  $6.26 \times 10^{-6}$  or almost one cancer case per 177,988 people living in Ilam city.

In other words, the possibility of increased cancer risk through exposure to chloroform in drinking water was estimated at 0.015 cancer cases per year, which was negligible compared with the 359 cases of cancer in Ilam.

It seems that some corrective measures such as accurately determining the optimal dose of chlorine or similar disinfectant that is used in a water treatment plant, considering, if possible, alternative or newer disinfection technologies, and considering water distribution network monitoring and maintenance measures could be useful for reducing or controlling human health cancer risks from exposure to chlorinated disinfection byproducts, such as THMs, in drinking water.

#### Footnote

**Authors' Contribution:** Kamyar Arman, as the coordinator of the study, managed sampling, data analysis, and manuscript writing; Ali Reza Pardakhti contributed in experiment design and data analysis; Noushin Osoleddini conducted experiment and data collecting; and Mostafa Leili was involved in data analysis and manuscript writing. All authors read and approved the final manuscript.

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