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Exposure and carcinogenic risk assessment of trihalomethanes (THMs) for water supply consumers in Addis Ababa, Ethiopia

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ABSTRACT

Background: Trihalomethanes (THMs), a class of DBPs (disinfection byproducts) that includes chloroform, bromodichloromethane (BDCM), chlorodibromomethane (CDBM), and bromoform. To the best of authors' knowledge, no study has addressed the relationship between the concentration of THMs and lifetime cancer risks (LCR) in drinking water supply system in Addis Ababa, Ethiopia. Therefore, this study aimed to determine the lifetime cancer risks of exposure to THMs in Addis Ababa, Ethiopia.
Method: A total of 120 duplicate water samples were collected from 21 sampling points in Addis Ababa, Ethiopia. The THMs were separated by a DB-5 capillary column and detected by an electron capture detector (ECD). Cancer and non-cancer risk assessments were performed.
Results: The average total THMs (TTHMs)concentration in Addis Ababa, Ethiopia, was 76.3 μg/L. Chloroform was the most dominant THM species identified. The total cancer risk for males was higher than that for females. The average LCR for TTHMs via ingestion in drinking water in this study was unacceptably high risk(93.4×10^{-2}). An average LCR through dermal routes was also of unacceptably high risk(4.3×10^{-2}). The LCR by chloroform contributes the highest (72%) of the total risk, followed by BDCM (14%), DBCM (10%) and bromoform (4%).
Conclusions: The cancer risk of drinking water due to THMs in Addis Ababa was higher than the level recommended by the USEPA. The total LCR from the targeted THMs was higher via the three exposure routes. Males were at higher THM cancer risk than females. The hazard index (HI) indicated that the dermal route caused higher HI values than the ingestion route. It is essential to apply alternatives to chlorine, i.e., chlorine dioxide (ClO_2), ozone and ultraviolet radiation, in Addis Ababa, Ethiopia. The monitoring and regulation of the THMs is required on a regular basis to analyse the trends and guide the water treatment and distribution system.
Availability of data and materials: The datasets generated for this analysis are available from the corresponding author upon reasonable request.

1. Introduction

1.1. Background

Chlorination is the most frequently used disinfection method to destroy pathogenic microorganisms in drinking water [1,2]. Although disinfection of drinking water lowers the risk of pathogenic infection, when organic and inorganic precursors are present in water, disinfection residues and their byproducts can constitute a chemical threat to human health [3].

Disinfection byproduct (DBP) creation varies widely depending on the quality of the source water, including natural organic matter (NOM) concentrations and characteristics (as organic precursors) and levels of bromide (as an inorganic precursor), chlorine dose, chlorine contact

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time with the water, temperature, and pH of the reaction solution [4–6]. Chlorination has been a popular method of water disinfection due to its effectiveness in removing contaminants and its affordability. The most often utilized disinfectants at the municipal level are chlorine (Cl_2), chloramines (NH_2Cl, $NHCl_2$), chlorine dioxide (ClO_2), ozone (O_3), and ultraviolet (UV) radiation [1].

When the naturally occurring organic matter present in raw water reacts with chlorine, a variety of DBPs are created, such as trihalomethanes (THMs), haloacetic acids (HAAs), and halogenated acetonitrile (HAN), which may have detrimental effects on human health [7,8]. Since the discovery of THMs, the first DBPs in 1972 during the chlorination of drinking water, major efforts have been made to explore the formation mechanism, toxicity, mitigation measures, and incidence of DBPs [8,9].

THMs, a class of DBPs that includes chloroform, BDCM, CDBM and bromoform, are among the most common DBPs. Even at very low doses, these DBPs are detrimental to human health. These health hazards could include different malignancies, reproductive issues, birth deformities, and miscarriage [10–13]. THMs are regularly considered as indicative of DBPs in human health risk assessments [14].

THMs were regulated soon after they were found in drinking water that had been treated, and their maximum contaminant limit (MCL) was set at 100 μg/L for TTHMs [15]. The Stage 1 D-DBP Rule [16] decreased the MCL for TTHMs to 80 μg/L. The maximum allowable concentrations (MAC) for total THMs and other DBPs are not specified by Ethiopia's water quality standards.

Health risk assessments of THMs have been investigated by many researchers worldwide. In Tehran's drinking water, Iran, THMs appear to provide the greatest risk through inhalation, followed by ingestion and dermal contact [6]. Similarly, in a study of multipath modelling for exposure in lifetime human health risk of THMs in the tap water of Karachi, Pakistan, it was discovered that it was mainly caused by the inhalation route [17]. In addition, in 10 regions of Fortaleza, Brazil, due to exposure to tap water, cancer risk increased by inhalation compared with oral ingestion and cutaneous absorption[18]. In Abadan, Iran, inhalation was the main route of exposure, with an approximately 80–90% cancer risk [19].

Furthermore, a study comparing the cancer risk of THMs in drinking water extracted from two different water supply sources, surface water, and well water, was carried out in Tehran. Drinking water extracted from surface water had a higher cancer risk than water extracted from other sources [6]. However, a study performed in Dhaka City, Bangladesh, showed that the carcinogenic risk via ingestion was higher than the USEPA acceptable limit of 10^{-6}. Carcinogenic risk via inhalation and dermal absorption was lower according to the USPEA acceptable limit [20].

The aim of this study was to assess cancer and non-cancer risk from lifetime exposure to THMs via inhalation, drinking water ingestion, and dermal contact from twenty-one sampling points in Addis Ababa, Ethiopia. Furthermore, this study also aimed to evaluate the health risks of THMs via a multi-exposure route in both males and females. To accomplish this, the concentrations of THMs in the drinking water of the twenty-one sampling points in the drinking water systems in Addis Ababa, Ethiopia were investigated. Therefore, this study could help water treatment utilities to monitor and regulate THMs in drinking water in Ethiopia.

2. Methods

2.1. Study setting and period

Ethiopia's capital is Addis Ababa. The city is situated 9°01′29″ to the north and 38°44′48″ to the east. 38°44′48″. Both surface water and groundwater are used in the city of Addis Ababa's water supply. There are three primary dams for collecting and storing run-off that are used as sources of water supply. The three dams are the Gefersa dam (18 km west of Addis Ababa), Legedadi dam (25 km east of Addis Ababa), and Dre dam (10 km north of Legedadi dam), as well as the Akaki groundwater (Akaki well field) [21].

For surface water sampling, a total of seven surface water reservoirs, two surface water sources, and 70 households (36 HHs and 34 HHs from the Gefersa and Legedadi water supplies, respectively) were chosen. Five boreholes and 35 homes were selected for groundwater sampling (Figs. 1, 2). Since the water sources are used just once a year and are distributed through a closed system, the samples taken at any time are believed to be consistent throughout the year. Samples were collected from June 1 to July 30, 2022.

2.2. Study design

A cross-sectional study design was used in the water supply networks of the Addis Ababa municipal water system.

2.3. Sample size determination

Twenty-one (21) sampling stations were used to gather 120 drinking water samples. The Legedadi, Gefersa, and groundwater sources were the three areas for sampling. From Legedadi, Gefersa, and groundwater supply networks, 33, 36 and 35 households respectively were selected for tapwater collection. Each sampling location produced forty water samples. Samples were collected from several points of use throughout the distribution network, as well as from the raw water source (Fig. 2).

2.3.1. Location of sampling points

The primary requirements for choosing the sampling points were distances from the treatment facility, representiveness to the distribution system's, water supplied directly by the municipal water treatment plant itself, and the absence of the influence of any re-chlorination facilities. Uniqueness of each locality were taken into account when choosing sampling places. Besides the following standard criteria were used [22].

- Selected sampling stations were representative of the various sources from which the general public acquires water.
- A piped distribution system's number of links or branches and the population distribution were considered when determining the number of sampling locations.
- The convenience of reservoirs for water sampling sites.

For a systems with more than one water source, the placements of the sampling points were take into consideration in relation to number of residents supplied by each source [23].

2.4. Sample collection and storage

Sample collection and handling procedures were carried out in strict and precise accordance with the US EPA [24]. Duplicate water samples were taken from the raw water sources immediately following chlorination, several points of the distribution system, and household taps. Each sample bottle contained 125 mL, and the screw caps had silicon septa with Teflon faces. Na2SO3 (0.5% w/v) solution was added to the sample containers to quench residual chlorine. Before sampling, water was allowed to run through the pipe outlets for three to five minutes to ensure that the water came directly from the distribution system.

The sample bottles were fully filled to minimize headspace and prevent the formation of air bubbles. The bottle was then properly sealed. In addition to the samples that would be examined, a sampling blank was also added. The THM-free reagent water was placed in one of the sampling containers, which was then carried to the sampling site, back to the site where the samples were stored, and then back again. In an ice bag, samples were brought to the lab and kept there until analysis at 4 °C.

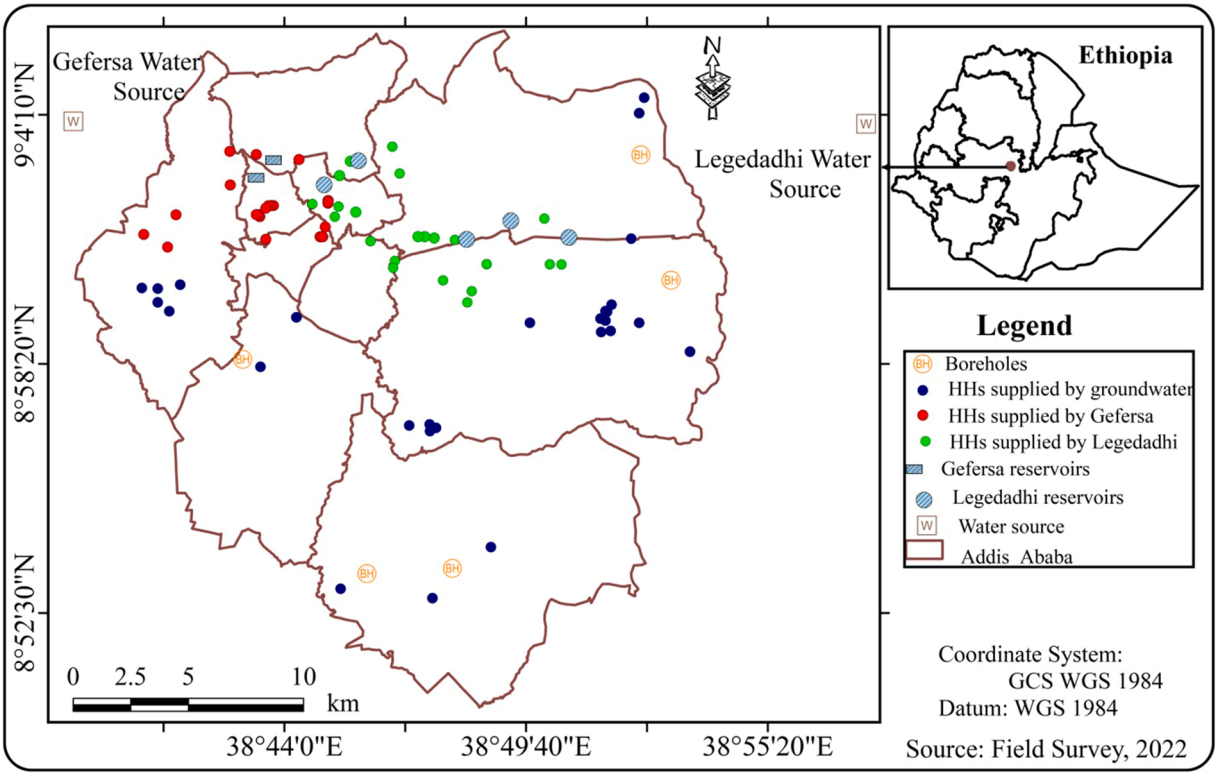

Fig. 1. Sampling points of the water samples in Addis Ababa, Ethiopia, 2022.

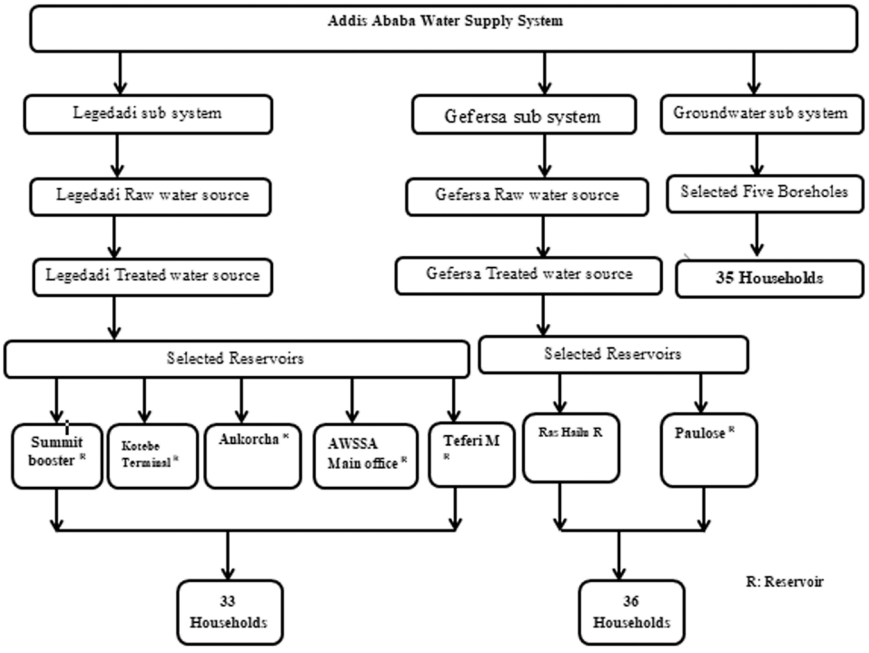

Fig. 2. Selected sampling points for water collection, Addis Ababa, 2022.

2.5. Sample analysis

With a few adjustments, EPA method 551.1 [25] was used to determine the THM values in the samples. To extract the THMs, 10 mL of the sample was briskly agitated with 2 mL of pentane. After that, 2 μL of the extract was carefully transferred to a 2 mL glass vial and put in a Varian auto-injector model CP 8400 before being injected into a Varian CP-3800 gas chromatograph (GC). The injector was used in split mode at 220 °C (split ratio 25:1).

Using split mode, the injector was run at 220 °C (split ratio 25:1). The THMs were separated by the capillary Agilent 122–5032 - GC Column DB-5 (30 m 0.25 mm × 0.25 m) column and were discovered using an electron capture detector (ECD) set to 290 °C. The makeup gas was nitrogen, with the carrier gas set to flow at 1.5 mL/min and 40–60 mL/min. The temperature of the oven was set to 40 °C for 5 min, and then it was raised to 250 °C at a rate of 15 °C and maintained there for 2 min.

The aforementioned standard combination of THMs was used to calculate the concentrations of THMs using the matrix matched calibration method. With the aforementioned configuration, the GC ran for more than 12–14 h, and the background was checked often. The detector current was first set to 0.0 nA; then, when the baseline had stabilized, it was adjusted to 0.5–1.0 nA, depending on the signal. Upon stabilization of the GC signal, the blank was run (several times) without any injection, and following an increase in baseline stability, 1 μL of pentane was injected.

2.6. Chemicals

The EPA 501/601 THMs calibration mix (CRM48746) certified reference material (200 μg/mL of each of the components chloroform, CDBM, BDCM, and bromoform in methanol) was acquired from Sigma—Aldrich in Germany. Sigma—Aldrich in Germany also provided GC grade pentane. The purity of Chloroform, CDBM, BDCM and bromoform were 100, 98.6, 97.2, and 96.1% respectively. Similarly, the purity level of pentane solvent was 99.0%.

2.7. Quality control and assurance

According to the Eurachem guide, the applied analytical method was verified prior to the analysis of the collected samples in terms of linearity, recovery, method detection limit (MDL), and repeatability [26]. The limit of detection (LOD) is the minimum concentration of trihalomethanes that can be detected at a specified level of confidence. To determine the LOD, a concentration of 10 μg/L (one tenth of MAC) of matrix-matched samples of the four mixed standards was prepared in seven different replicates. Then, independent measurements of each sample were taken seven times, their standard deviation (SD) was calculated, and the LOD was determined as LOD = 3 X SD. During sample analysis, blank samples, duplicates, and spiked sample recovery were carried out for each batch [27].

During method verification, as internal quality controls, blank samples and water samples fortified with THM compounds of interest at six working ranges were prepared as matrix-matched calibrants. Hence, three batches of matrix-matched calibrants were prepared over three different days (Day 1, Day 2 and Day 3). For determination of recovery and precision, nine (9) spiked samples each in triplicate were prepared by spiking blank samples at 0.5, 1.0 and 1.5 times concentrations of the MACs. Together with each batch of verification samples, matrix-matched reference standards fortified at the MAC level post spiked on the water matrix (after sample underwent all preparative steps) and a true blank, reagent blank, which does not contain any analytes of interest to eliminate false positives and ensure that the system is under control. In this study, quality control samples were prepared in triplicate, whereas the test samples were prepared and analysed in duplicate (Table 1).

Table 1
Method Verification parameters, Addis Ababa, Ethiopia, 2022.

Parameter	Trihalomethanes (THMs)			
	CHCl3	CHCl2 Br	CHBr2 Cl	CHBr3
Retention time (min.± 5%)	4.21	5.48	7.55	9.95
correlation coefficients (r^2)	0.99	0.99	0.99	0.99
Recovery (%)	88.4–109.6	90.8–109.6	85.6–112.4	99.3–114.1
MDL[a] or LOD (μg/L)	1.37	1.73	1.92	1.67
Repeatability[a] (%)	6.18	3.58	6.79	6.41

MDL, Method Detection Limit; [a] for seven replicates.

2.8. Cancer risk assessment

A cancer risk assessment evaluates the likelihood that a person will develop cancer as a result of pollutant exposure over the course of their lifetime. There are four steps in this process: assessing exposure and toxicity, gathering and analyzing data, characterizing risks, and managing risks [28]. THMs were evaluated for their potential to cause human cancer using Equation [1]and three different exposure methods: oral ingestion, skin absorption, and inhalation [10].

$$\textbf{\textit{Cancer risk}} = \textbf{\textit{CSF}} \times \textbf{\textit{CDI}} \tag{1}$$

where CSF is the cancer slope factor and CDI (mg/kg/day) is the chronic daily intake. The following formulae were used to determine the CDI for each of the exposure routes:

$$CDI_{Oralingestion} = \frac{C_W \times IR \times EF \times ED \times CF}{BW \times AT} \tag{2}$$

$$CDI_{Absorption} = \frac{C_W \times SA \times F \times PC \times ET \times EF \times ED \times CF}{BW \times AT} \tag{3}$$

$$CDI_{Inhalation} = \frac{C_{Air} \times VR \times AE \times ET \times EF \times CF}{BW \times AT} \tag{4}$$

where AT is the average lifespan (days), BW is the body weight (kg), CF is the mass conversion factor from μg to mg (0.001), SA is the surface area of the skin exposed to water (m^2), F is the fraction of skin in contact with water (%), PC is the permeability coefficient (cm/h), and C_W is the concentration of THM species or TTHMs in the collected drinking water samples. where IR is the rate of water ingestion (L/day), EF is the exposure frequency (days/year), ED is the exposure duration (years), ET is the exposure time (min/day), and VR is the ventilation rate (m^3/h), AE is the absorption efficiency. Based on Eq.[5 −9], C_{air} is the concentration of THMs in the air that was calculated using the Little model [29]. According to Eq. [10]the LCR estimate from multiple exposure routes was calculated by adding the cancer risks from numerous exposure routes for each species of THM. C air is determined by using the following formula:

$$C_{air} = \left(Y_{s(t)} + Y_{si}\right) \tag{5}$$

Where.

Ysi is the initial THM concentration in the shower room (assumed as 0 mg/l).

Ys(t) is the THM concentration in the shower room at time t (min) assumed to be 30 min in this study.

$$Y_{(s(t))} = [1 - \exp(-bt)](a/b) \tag{6}$$

$$b = \{(Q_1/H)[1 - \exp(-N)] + Q_G | V_s\} \tag{7}$$

$$a = \{Q\_1 \cdot C\_w\ [1\text{-}\exp(\text{-}N)]\} / V\_s \tag{8}$$

$$N = ((K\_OL\ A)) / Q\_L \tag{9}$$

Where N is a dimensionless coefficient which is calculated from K_OL A

$$\textbf{Total risk} = (\textbf{CDI}_{\textbf{Oral}} \times \textbf{CSF}_{\textbf{Oral}}) + (\textbf{CDI}_{\textbf{Inhalation}} \times \textbf{CSF}_{\textbf{Inhalation}}) + (\textbf{CDI}_{\textbf{Dermal}} \times \textbf{CSF}_{\textbf{Dermal}}) \tag{10}$$

In this work, THMs volatilized from the drinking water into the shower room were calculated using the inhalation exposure model developed on the basis of Little's [29] two-resistance theory.

2.9. Non-cancer risk assessment

The hazard index (HI) of THMs was calculated using Eqs. (11) and (12) to assess the non-cancer risk,

$$HIforTHMs(Oral) = CDI_{Oral} / R_f D_{THMs} \tag{11}$$

$$HIforTHMs(Dermal) = CDI_{Dermal} / R_f D_{THMs} \quad (12)$$

where RfD is the reference dose (mg/kg/day). The input parameters utilized in the risk assessment studies for cancer and non-cancer are displayed in Table 2. Cancer risk is defined into four classes: negligible$(CR < 10^{-6})$, acceptable low risk$(1 \times 10^{-6} \leq CR < 5.1 \times 10^{-5})$, acceptable high risk $(5.1 \times 10^{-5} \leq CR < 10^{-4})$ and unacceptable risk$\geq 10^{-4}$.

3. Results and discussion

3.1. Method performance

The standard chromatogram depicts a sharp well-separated and resolved peak for each of the THM compounds (S1). The matrix-matched calibrations were constructed for six points (S1–4). The method detection limit (MDL) was 1.67 μg/L. This value is compatible with the USEPA detection limits (ranging from 0.1 to 2.5 μg/L for the THMs), which vary across laboratories and time [42]. The correlation coefficients (r) were higher than 0.99 for all standards, which signifies a good linear response for the different THM compounds in the concentration range. The mean recovery ranged from 85.6% to 114.1%, which falls in the acceptable range (80–120%) set by EPA method 551.1 [43] and showed good accuracy of the method. Similarly, the method repeatability (3.58–6.79%) ranges were within the EPA method 551.1 guideline (<15%) [43] and indicated good precision of the method.

Table 2
Input parameters of cancer and non-cancer risk estimation, Addis Ababa, Ethiopia, 2022.

Parameter	Value	Reference
Body weight(BW, kg)	70(male) 60(female)	[10,30,31]
Concentration of THMs in water	See Table 3	This study
Average lifetime (AT, days)	67.46 × 365(male) 72.61 × 365(female) 70 × 365	[32–34]
Exposure frequency (EF, days/year)	365	[30,31]
Exposure duration (ED, year)	30	[10,32,35]
Ingestion rate (IR, L/day)	2	[30,31,33]
Exposure time(min/*day*)	35	[36]
Skin surface area (SA, m2)	1.8	[33]
Fraction of skin in contact with water (F, %)	90	[36]
Permeability coefficient (PC, cm/h)	Chloroform: 0.00683 BDCM: 0.00402 CDBM: 0.00289 Bromoform: 0.0026	[6,17]
Carcinogenic slope factor (CSF, (mg/kg/day)− 1	Oral/dermal Chloroform: 0.031 BDCM: 0.062 CDBM: 0.084 Bromoform: 0.0079 Inhalation Chloroform: 8.05 × 10–5 BDCM: 0.13 CDBM: 0.095 Bromoform: 0.00385	[6] [6]
THM concentration in air (C air, mg/L)	Little's model	[29]
Reference dose (RfD, mg/kg/day	Chloroform: 0.01 BDCM: 0.02 DBCM: 0.02 Bromoform: 0.02	[37]
Inhalation rate (IR, m3/h	0.84(male) 0. 66 (Female)	[38]
Bathroom volume (Vs, m3)	2–18	[39]
Water flow rate (QL, L/min)	5	[29]
Air flow rate (QG, L/min)	50	[29]
Dimensionless Henry's law constants (H)	0.12 (CHCl3) 0.0656 (CHCl2Br) 0.0321 (CHClBr2) 0.0219(CHBr3)	[40]
Overall mass transfer coefficient (KOLA, L/min)*	7.4 (CHCl3) 5.9 (CHCl2Br) 4.6 (CHClBr2) 3.7 (CHBr3)	[29]

* KOLA for the other three THMs was calculated according to Wang et al.[41], and the KOLA of chloroform was from Little[29].

3.2. Levels of trihalomethanes in drinking water

The average values of the acquired data are displayed in Table 3 compared with the World Health Organization's (WHO) recommended limits (200, 60, 100, and 100 μg/L for $CHCl_3$, $CHCl_2$ Br, $CHClBr_2$, and $CHBr_3$, respectively) [44]. The total THMs in this study was 76.3 μg/L, which was lower than the prescribed USEPA standards of 80 μg/L [45]. This finding is also lower than those of other studies [10,19,46]. However, it is higher than a study report from Southern Mauritius and Iran [46,47]. Chloroform was the most dominant DBP recorded in this study. Other studies reported similar pattern of findings [17,40].

3.3. Cancer risk analysis of THMs through different routes

3.3.1. Ingestion route

The total THMs LCR was calculated using Eq. (1) for all possible exposure routes using the input values indicated in Table 2 and the average concentration of TTHMs observed in this study. The average LCR for TTHMs via ingestion in drinking water samples in this study was unacceptably high risk(93.4×10^{-2}), which was higher than the unacceptable risk$(\geq 10^{-4})$. The following was the order in which the risk contribution was noted:*Chloroform* > *BDCM* > *DBCM* > *Bromoform* (Table 4).

The risk was higher among males than females, and the oral route was the most common risk factor. Among the four THMs, chloroform showed an acceptable low oral cancer risk $(2.9 \times 10^{-4})$for males and $(2.5 \times 10^{-4})$for females. This is comparable with the results reported by [48], [49] and [50]. According to their findings, chloroform's percentage contribution to overall risks was the highest. However, other studies [36] and [10] reported that BDCM had the highest percentage contributions.

3.3.2. Lifetime cancer through dermal absorption

THMs can pass into the body through contact with chlorine-treated water while swimming, cleaning dishes, and handling water; therefore, taking a shower and a bath are particularly important[51]. The average lifetime risk through dermal routes was also unacceptably high(4.3×10^{-2}), which was above the unacceptable risk. The mean skin surface areas for females and males are 1.53 and 1.7m^2, respectively [45]. The following was the order in which the risk contribution was recorded:*Chloroform* > *DBCM* > *BDCM* > *Bromofor*(Table 5). The

Table 3
Total trihalomethanes and drinking water supplies in Addis Ababa, Ethiopia, 2022.

	Mean Concentration μg/L (95% CI)	Min (μg/L)	Max (μg/L)	WHO Guideline (μg/L)
CHCl3	54.93(50.97–58.53)	4.33	79.40	200
CHCl2 Br	10.66(9.74–11.53)	2.42	19	60
CHBr2 Cl	7.70(6.83–8.53)	2.22	13.12	100
CHBr3	3.02(2.83–3.21)	2.71	3.21	100
TTHMs	**76.31**			

Table 4
Chronic Daily Intake of Trihalomethanes through oral ingestion, Addis Ababa, Ethiopia, 2022.

Parameters	Percentage of $CDI_{Oral\ ingestion}$	$CDI_{Oral\ ingestion\ male}$	$CDI_{Oral\ ingestion\ in\ Female}$
Chloroform	6.73×10^{-8}	2.9×10^{-4}	2.5×10^{-4}
BDCM	1.31×10^{-8}	5.71×10^{-5}	4.86×10^{-5}
DBCM	9.4×10^{-5}	4.11×10^{-5}	3.49×10^{-5}
BF	3.96×10^{-5}	1.72×10^{-5}	1.46×10^{-5}
THMs	9.34×10^{-4}	40.7×10^{-5}	35×10^{-5}

Table 5
Chronic Daily Intake of Trihalomethanes through Dermal contact, Addis Ababa, Ethiopia, 2022.

Parameters	$CDI_{Absorption}$	$CDI_{Absorption\ in\ Male}$	$CDI_{Absorption\ in\ Female}$
Chloroform	6.46×10^{-5}	13.54×10^{-6}	14.65×10^{-6}
BDCM	1.5×10^{-3}	5.16×10^{-5}	16.8×10^{-4}
DBCM	2.67×10^{-4}	80.2×10^{-5}	30.1×10^{-2}
BF	11.2×10^{-2}	30.3×10^{-5}	12.6×10^{-2}
TTHMs	4.3×10^{-2}	44.91×10^{-2}	48.69×10^{-2}

cancer hazards of THMs via dermal contact for females and males were (48.69×10^{-2}) and (44.91×10^{-2}), respectively, higher than the unacceptable risk (1×10^{-4}). Although the surface area of skin in males is higher, females have the highest cancer risk through the dermal route, in contrast with other studies [36]. On the other hand, some other studies are found to have similar results as the present study [19,46].

3.3.3. Cancer risk from inhalation

Inhalation was the major route of exposure contributing approximately 80–90% of cancer risk mainly due to $CHCl_3$ because this compound is highly volatile with a low boiling point [17,19,52]. The findings of cancer risk via inhalation are shown in Table 6 and Fig. 2. LCRs due to inhalation exposure were (54.41×10^{-2}) for males and (46.31×10^{-2}) for females. The LCR due to TTHMs via the inhalation route was higher than the USEPA unacceptable risk (1×10^{-4}) in the drinking water. That means approximately 1 in every 10,000 individuals in Addis Ababa, Ethiopia, could get cancer from the daily intake of water in their life. The major contributor through inhalation was $CHCl_3$, with a value of 86.5%, followed by $BDCM > BF > DBCM$. A related study reported similar findings [19].

3.3.4. Average life time cancer risks

The average LCR estimate of THMs via three exposure routes in this work showed that ingestion is the most common route of exposure (Fig. 3). A consistent pattern of exposure routes was reported from the Ivedik Water Treatment Plant, Ankara Turkey [53], depicting that one of the five million residents of Ankara could develop cancer every year by drinking water on a regular basis. In addition, inhalation was the second most common route of exposure in this work. A similar finding was also reported in other studies in which inhalation were the major route of exposure to THMs [52,54,55]. A recent related study also signified that

Table 6
Chronic Daily Intake of Trihalomethanes through Inhalation, Addis Ababa, Ethiopia, 2022.

Parameters	Percentage of $CDI_{Inhalation}$	$CDI_{Inhalation\ in\ Male}$	$CDI_{Inhalation\ in\ Female}$
Chloroform	18.0×10^{-2}	23.8×10^{-2}	20.3×10^{-2}
BDCM	1.58×10^{-2}	24.3×10^{-3}	5.9×10^{-3}
DBCM	2.69×10^{-5}	1.17×10^{-5}	9.98×10^{-6}
BF	31.5×10^{-4}	13.7×10^{-4}	11.7×10^{-4}
TTHMs	125.3×10^{-2}	54.41×10^{-2}	46.31×10^{-2}

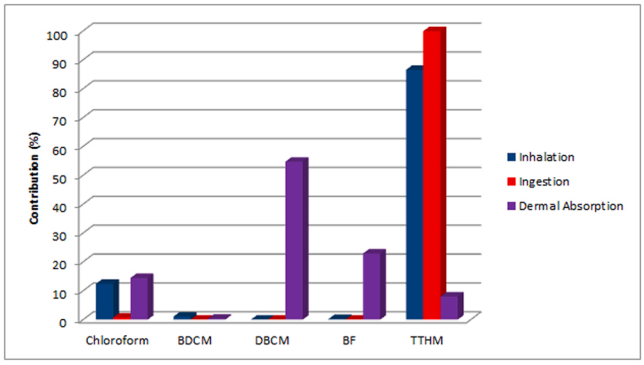

Fig. 3. The percentage contribution of each of the THMs to cancer risk via the three exposure routes, Addis Ababa, Ethiopia, 2022.

the utilization of hot water for showering was a risk factor for colorectal cancer that might be due to exposure to THMs, as the volatility of the THMs is higher in hot water [6,56].

3.3.5. Contribution of each trihalomethane

The average percentage of each THM species contribution to the TTHMs (Fig. 4) depicted that the LCR by chloroform contributes the highest percentage (72%) of the total risk, followed by BDCM (14%), DBCM and bromoform. A similar pattern of THM species and LCR was reported in India [50]. Although the concentrations of BDCM and CDBM were significantly lower than that of chloroform, they posed a higher LCR. These findings are because BDCM and CDBM have potency factors that are ten times greater than those of chloroform and bromoform [36, 57–60]. The bromoform concentration was very low in Addis Ababa, Ethiopia. This could be because bromoform was detected only from groundwater sources, which could be due to the presence of natural bromide. Further investigation of brominated THMs in the drinking water supply of Addis Ababa, Ethiopia, is required.

3.3.6. Total cancer risk and trihalomethanes by sex

The risk analysis in this study indicated that the total LCR from the targeted THMs was higher via the three exposure routes than the negligible risk levels (1×10^{-6}). The findings also showed that males were at higher THM cancer risk than females (Fig. 5). Other findings reported from other studies showed that males are more susceptible to this cancer [61,62].

3.3.7. Trihalomethanes and non-cancer risk

The hazard index (HI) of THMs was calculated using Eqs. (11) and (12) to assess the non-cancer risk. The hazard index (HI) findings in this study showed that the dermal route caused higher HI values than the ingestion route and that chloroform had the greatest contribution to the HI value. The remaining THM species contributions were below unity, signifying that there would be negligible non-cancer risk (Fig. 6).

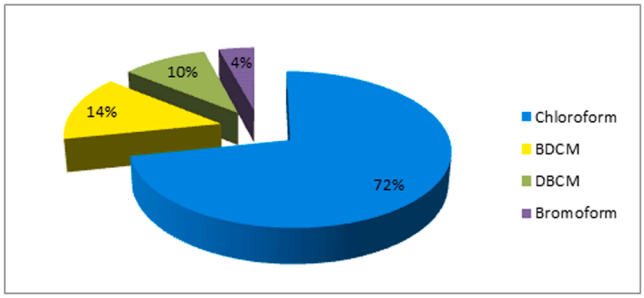

Fig. 4. Percentage contribution of each THM species to the average TTHMs lifetime cancer risk in Addis Ababa, Ethiopia, 2022.

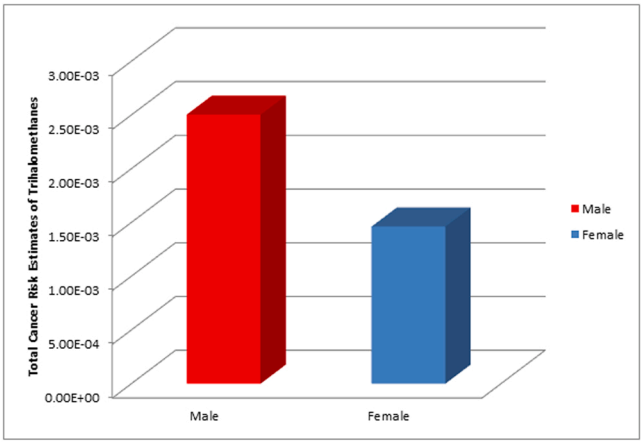

Fig. 5. Total risk estimates of trihalomethanes by sex in Addis Ababa, Ethiopia, 2022.

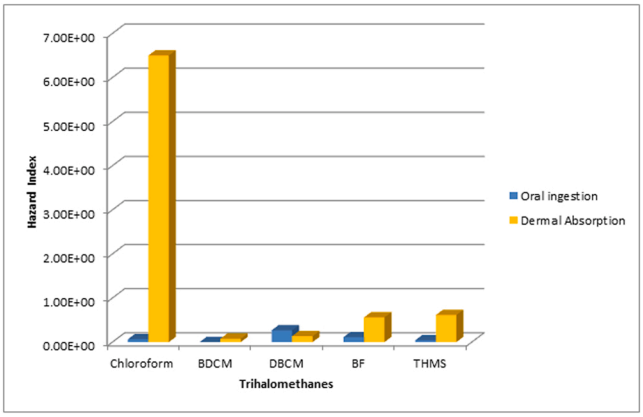

Fig. 6. Hazard index values of total and individual THM average concentrations for oral and dermal exposure routes, Addis Ababa, Ethiopia, 2022.

4. Conclusions

This study is the pioneer in its kind to determine the concentration of THMs and their cancer risk investigation through inhalation, dermal absorption and ingestion exposure routes in Addis Ababa, Ethiopia. The findings showed that the THMs concentration in the drinking water of Addis Ababa, Ethiopia, was lower than the US EPA limit. $CHCl_3$ had the highest concentration, and $CHBr_3$ had the lowest concentration. The LCRs caused by all pathways were higher than 10^{-6} (negligible risk level defined by the USEPA).

The ingestion route carried the greatest lifetime cancer risk for all THMs, followed by inhalation and dermal contact. Chloroform was linked to an increased risk of developing cancer through dermal contact. Males had a higher overall cancer risk than females. On the other hand, the hazard index value was below unity, indicating that adverse non-cancer health effects were negligible. In Addis Ababa, Ethiopia, it is crucial to use chlorine dioxide (ClO_2), ozone, and ultraviolet (UV) radiation as alternatives to chlorine. Recently, ClO_2 has been linked to reduced THMs formation. The THMs concentrations are below the US EPA limit level. However, more attention is required to BDCM and DBCM because they cause high cancer risk even at low levels. The monitoring and regulation of the THMs is required on a regular basis to analyse the trends and guide the water treatment and distribution system.

Ethics approval and informed consent

The Ethical Review Board of Addis Ababa University, Ethiopia, granted the study ethical approval (CNSDO/499/10/2018).

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Consent for publication

Not applicable.

CRediT authorship contribution statement

Nebiyou Tafesse conceived the study and was involved in the study design, reviewed the article, analysed and reported the writing, and drafted and revised it. Massimiliano Porcelli, Belachew Bacha Hirpessa, Janvier Gasana, R.K. Padhi, Sirak Robele Garie, and Argaw Ambelu contributed to data analysis and report writing, drafted and revised the manuscript, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Authors Statement

All authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript.

Declarations

none.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.toxrep.2023.02.004.

References

[1] A.L. Srivastav, N. Patel, V.K. Chaudhary, Disinfection by-products in drinking water: Occurrence, toxicity and abatement, Environ. Pollut. 267 (2020), 115474.
[2] M.A. Mazhar, N.A. Khan, S. Ahmed, A.H. Khan, A. Hussain, F. Changani, et al., Chlorination disinfection by-products in municipal drinking water–a review, J. Clean. Prod. 273 (2020), 123159.
[3] H.R. Mian, G. Chhipi-Shrestha, K. Hewage, M.J. Rodriguez, R. Sadiq, Predicting unregulated disinfection by-products in small water distribution networks: an empirical modelling framework, Environ. Monit. Assess. 192 (8) (2020) 1–20.
[4] R. Sadiq, M.J. Rodriguez, Disinfection by-products (DBPs) in drinking water and predictive models for their occurrence: a review, Sci. Total Environ. 321 (1–3) (2004) 21–46.
[5] N.Y. Salih, M.N. Al-Azzawi, Human health risk assessment of trihalomethane through multi-pathway exposure from drinking water of Baghdad, Iraq. J. Int. Environ. Appl. Sci. 11 (3) (2016) 294–302.
[6] A.R. Pardakhti, G.R.N. Bidhendi, A. Torabian, A. Karbassi, M. Yunesian, Comparative cancer risk assessment of THMs in drinking water from well water sources and surface water sources, Environ. Monit. Assess. 179 (1) (2011) 499–507.
[7] C. Liu, M.S. Ersan, M.J. Plewa, G. Amy, T. Karanfil, Formation of regulated and unregulated disinfection byproducts during chlorination of algal organic matter extracted from freshwater and marine algae, Water Res. 142 (2018), 313-24.
[8] Hamid A, Riaz A, Mohsin A. A REVIEW PAPER ON DISINFECTION BY-PRODUCTS FORMATION DURING DRINKING WATER TREATMENT.
[9] Z. Wang, M. Li, Y. Liao, Y. Pan, C. Shuang, J. Li, et al., Formation of disinfection byproducts from chlorinated soluble microbial products: Effect of carbon sources in wastewater denitrification processes, Chem. Eng. J. 432 (2022), 134237.
[10] E.-S.I. Mishaqa, E.K. Radwan, M. Ibrahim, T.A. Hegazy, M.S. Ibrahim, Multi-exposure human health risks assessment of trihalomethanes in drinking water of Egypt, Environ. Res. 207 (2022), 112643.
[11] B.-F. Hwang, J.J. Jaakkola, Risk of stillbirth in the relation to water disinfection by-products: a population-based case-control study in Taiwan, PLoS One 7 (3) (2012), e33949.
[12] T.A. McDONALD, H. Komulainen, Carcinogenicity of the chlorination disinfection by-product MX, J. Environ. Sci. Health Part C. 23 (2) (2005) 163–214.
[13] S.H. Ewaid, A.M. Rabee, S.K. Al-Naseri, Carcinogenic risk assessment of trihalomethanes in major drinking water sources of Baghdad City, Water Resour. 45 (5) (2018), 803-12.
[14] D. Loomis, N. Guha, A.L. Hall, K. Straif, Identifying occupational carcinogens: an update from the IARC Monographs, Occup. Environ. Med. 75 (8) (2018) 593–603.
[15] R.A. Li, J.A. McDonald, A. Sathasivan, S.J. Khan, A multivariate Bayesian network analysis of water quality factors influencing trihalomethanes formation in drinking water distribution systems, Water Res. 190 (2021), 116712.
[16] S. Chowdhury, I.R. Chowdhury, M.A.J. Mazumder, M.S. Al-Suwaiyan, Predicting risk and loss of disability-adjusted life years (DALY) from selected disinfection byproducts in multiple water supply sources in Saudi Arabia, Sci. Total Environ. 737 (2020), 140296.
[17] A. Siddique, S. Saied, M. Mumtaz, M.M. Hussain, H.A. Khwaja, Multipathways human health risk assessment of trihalomethane exposure through drinking water, Ecotoxicol. Environ. Saf. 116 (2015) 129–136.
[18] R.B. Viana, R.M. Cavalcante, F.M. Braga, A.B. Viana, J.C. De Araujo, R. F. Nascimento, et al., Risk assessment of trihalomethanes from tap water in Fortaleza, Brazil, Environ. Monit. Assess. 151 (1) (2009) 317–325.
[19] R. Kujlu, M. Mahdavianpour, F. Ghanbari, Multi-route human health risk assessment from trihalomethanes in drinking and non-drinking water in Abadan, Iran, Environ. Sci. Pollut. Res. 27 (34) (2020), 42621-30.
[20] F. Ahmed, T.A. Khan, A.N.M. Fakhruddin, M.M. Rahman, R.M. Mazumdar, S. Ahmed, et al., Estimation and exposure concentration of trihalomethanes (THMs) and its human carcinogenic risk in supplied pipeline water of Dhaka City, Bangladesh, Environ. Sci. Pollut. Res. 26 (16) (2019), 16316-30.
[21] M.C.E. NrbZAa. Alternative power source for pumping stations at the reservoirs and wells existing assessment report, addis ababa, 2015.
[22] Kirmeyer G.J., Martel K. Pathogen intrusion into the distribution system: American Water Works Association; 2001.
[23] Organization W.H. Drinking water quality, 2010.
[24] USEPA. Quick Guide to Drinking Water Sample Collection, 2016.
[25] M. Yang, H.K. Liberatore, X. Zhang, Current methods for analyzing drinking water disinfection byproducts, Curr. Opin. Environ. Sci. Health 7 (2019) 98–107.
[26] Bertil M., Örnemark U. The fitness for purpose of analytical methods: a laboratory guide to method validation and related topics. A laboratory guide to method validation and related topics, LGC, Teddington, Middlesex, UK, 2014.
[27] Magnusson B. The fitness for purpose of analytical methods: a laboratory guide to method validation and related topics, 2014. Eurachem; 2014.
[28] Y. Wang, G. Zhu, B. Engel, Health risk assessment of trihalomethanes in water treatment plants in Jiangsu Province, China, Ecotoxicol. Environ. Saf. 170 (2019), 346-54.
[29] J.C. Little, Applying the two-resistance theory to contaminant volatilization in showers, Environ. Sci. Technol. 26 (7) (1992) 1341–1349.
[30] E.K. Radwan, M. Ibrahim, A. Adel, M. Farouk, The occurrence and risk assessment of phenolic endocrine-disrupting chemicals in Egypt's drinking and source water, Environ. Sci. Pollut. Res. 27 (2) (2020), 1776-88.
[31] E.K. Radwan, M.H. Barakat, M.B. Ibrahim, Hazardous inorganic disinfection by-products in Egypt's tap drinking water: Occurrence and human health risks assessment studies, Sci. Total Environ. 797 (2021), 149069.
[32] C. Legay, M.J. Rodriguez, R. Sadiq, J.B. Sérodes, P. Levallois, F. Proulx, Spatial variations of human health risk associated with exposure to chlorination by-products occurring in drinking water, J. Environ. Manag. 92 (3) (2011) 892–901.
[33] Health USEPAOo, Group EAEA. Exposure factors handbook: Office of Health and Environmental Assessment, US Environmental Protection …; 1989.
[34] M. UmakantKori, A. Chandra, XVIII■ SOUTH ASIA, Tarascon Glob. Health Pocketb. (2010) 291.
[35] Emergency USEPAOo, Response R. Risk Assessment Guidance for Superfund: Interim Final: Office of Emergency and Remedial Response, US Environmental Protection Agency; 1989.
[36] S. Lee, H. Guo, S. Lam, S. Lau, Multipathway risk assessment on disinfection by-products of drinking water in Hong Kong, Environ. Res. 94 (1) (2004) 47–56.
[37] H. Amjad, I. Hashmi, M.S.U. Rehman, M.A. Awan, S. Ghaffar, Z. Khan, Cancer and non-cancer risk assessment of trihalomethanes in urban drinking water supplies of Pakistan, Ecotoxicol. Environ. Saf. 91 (2013) 25–31.
[38] EPA A. Risk assessment guidance for superfund. Volume I: human health evaluation manual (part a). EPA/540/1–89/002; 1989.
[39] M. Chen, K. Wu, L. Chang, A new approach to estimating the volatilization rates of shower water-contained volatile organic compounds during showering, Atmos. Environ. 37 (31) (2003), 4325-33.
[40] M. Basu, S.K. Gupta, G. Singh, U. Mukhopadhyay, Multi-route risk assessment from trihalomethanes in drinking water supplies, Environ. Monit. Assess. 178 (1) (2011) 121–134.
[41] G.-S. Wang, Y.-C. Deng, T.-F. Lin, Cancer risk assessment from trihalomethanes in drinking water, Sci. Total Environ. 387 (1–3) (2007) 86–95.
[42] J.A. Kaufman, J.M. Wright, A. Evans, Z. Rivera-Núñez, A. Meyer, M.G. Narotsky, Disinfection by-product exposures and the risk of musculoskeletal birth defects, Environ. Epidemiol. 4 (2020) 1.
[43] A.D. Nikolaou, T.D. Lekkas, S.K. Golfinopoulos, M.N. Kostopoulou, Application of different analytical methods for determination of volatile chlorination by-products in drinking water, Talanta 56 (4) (2002) 717–726.
[44] Nottle C.E. Advanced water treatment technologies to minimise the formation of emerging disinfection by-products in potable water: Curtin University; 2013.
[45] J. Moya, L. Phillips, Overview of the use of the US EPA exposure factors handbook, Int. J. Hyg. Environ. Health 205 (1–2) (2002) 155–159.
[46] A. Nadali, A. Rahmani, G. Asgari, M. Leili, H.A. Norouzi, A. Naghibi, The assessment of trihalomethanes concentrations in drinking water of Hamadan and Tuyserkan Cities, Western Iran and its health risk on the exposed population, J. Res. Health Sci. 19 (1) (2019), e00441.
[47] A. Uppeegadoo, N.C.K. Yive, K. Gopaul, Determination of trihalomethanes in drinking water in southern Mauritius, Univ. Maurit. Res. J. 3 (1999) 109–114.
[48] C.-H. Hsu, W.-L. Jeng, R.-M. Chang, L.-C. Chien, B.-C. Han, Estimation of potential lifetime cancer risks for trihalomethanes from consuming chlorinated drinking water in Taiwan, Environ. Res. 85 (2) (2001) 77–82.
[49] W. Lahey, M. Connor, The case for ocean waste-disposal, Technol. Rev. 86 (6) (1983) 60–68.
[50] M. Mazhar, S. Ahmed, A. Husain, R. Uddin, Monitoring of Trihalomethanes and its Cancer Risk Assessment in Drinking Water of Delhi City, India Pollut. 8 (3) (2022) 830–843.
[51] Arman K., PARDAKHTI A., Osoleddini N., Leili M. Cancer risk assessment from multi-exposure to chloroform in drinkingwater of Ilam City, Iran, 2016.
[52] A.A. Babaei, N. Alavi, G. Hassani, F. Yousefian, M. Shirmardi, L. Atari, Occurrence and related risk assessment of trihalomethanes in drinking water, Ahvaz, Iran, Fresenius Environ. Bull. 24 (12c) (2015) 4807–4815.
[53] B. Tokmak, G. Capar, F.B. Dilek, U. Yetis, Trihalomethanes and associated potential cancer risks in the water supply in Ankara, Turkey, Environ. Res. 96 (3) (2004) 345–352.
[54] J. Lee, E.-S. Kim, B.-S. Roh, S.-W. Eom, K.-D. Zoh, Occurrence of disinfection by-products in tap water distribution systems and their associated health risk, Environ. Monit. Assess. 185 (9) (2013) 7675–7691.
[55] M. Mosaferi, M. Asadi, H. Aslani, A. Mohammadi, S. Abedi, S. Nemati Mansour, et al., Temporospatial variation and health risk assessment of trihalomethanes (THMs) in drinking water (northwest Iran), Environ. Sci. Pollut. Res. 28 (7) (2021), 8168-80.
[56] N. Tafesse, M. Porcelli, S. Robele Gari, A. Ambelu, Drinking Water Source, Chlorinated Water, and Colorectal Cancer: A Matched Case-Control Study in Ethiopia, Environ. Health Insights 16 (2022), 11786302211064432.
[57] Y. Du, L. Zhao, J. Ban, J. Zhu, S. Wang, X. Zhu, et al., Cumulative health risk assessment of disinfection by-products in drinking water by different disinfection methods in typical regions of China, Sci. Total Environ. 770 (2021), 144662.
[58] L. Semerjian, J. Dennis, Multipathway risk assessment of trihalomethane exposure in drinking water of Lebanon, J. Water Health 5 (4) (2007) 511–522.
[59] J.C. Bare, Risk assessment and life-cycle impact assessment (LCIA) for human health cancerous and noncancerous emissions: integrated and complementary with consistency within the USEPA, Hum. Ecol. Risk Assess. 12 (3) (2006) 493–509.
[60] M. Kumari, S. Gupta, B. Mishra, Multi-exposure cancer and non-cancer risk assessment of trihalomethanes in drinking water supplies–a case study of Eastern region of India, Ecotoxicol. Environ. Saf. 113 (2015) 433–438.
[61] B.K. Mishra, S.K. Gupta, A. Sinha, Human health risk analysis from disinfection by-products (DBPs) in drinking and bathing water of some Indian cities, J. Environ. Health Sci. Eng. 12 (1) (2014) 1–10.
[62] N. Tafesse, M. Porcelli, S.R. Gari, A. Ambelu, Prevalence and Trends of Drinking Water Disinfection Byproducts-Related Cancers in Addis Ababa, Ethiopia, Environ. Health Insights 16 (2022), 11786302221112569.