



Research article

Analysis of THM formation potential in drinking water networks: Effects of network age, health risks, and seasonal variations in northwest of Iran

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ABSTRACT

Various factors influence the formation of disinfection by-products (DBPs) in drinking water. Therefore, it is crucial to study the formation of DBPs and identify the associated influencing agents in water distribution networks (WDNs) to effectively prevent and control the health risks posed by DBPs. This research aimed to examine THM concentrations in the WDNs of Maragheh, Iran, focusing on seasonal variations. It also compared THM levels between new and old WDNs and assessed the health risks associated with exposure to THMs through various exposure routes. The mean concentrations of Chloroform, BDCM, DBCM, and Bromoform were 44.28 ± 18.25 , 12.66 ± 5.19 , 3.16 ± 0.89 , and 0.302 ± 0.89 $\mu\text{g/L}$, respectively. Therefore, Chloroform was the predominant compound among the THM species, accounting for over 72 % of the total THMs (TTHMs). The average TTHMs concentration in summer (69.89 $\mu\text{g/L}$) was significantly higher than in winter (50.97 $\mu\text{g/L}$) ($p < 0.05$). Except for Bromoform, concentrations of other THM species in the new WDNs were considerably lower than in the old WDN ($p < 0.05$). The mean lifetime cancer risk (LTCR) rates for oral and dermal exposure routes to THMs were negligible and within acceptable risk levels. However, the LTCR mean values for inhalation exposure routes to THMs in winter and summer were within low ($1 \times 10^{-6} \leq \text{LTCR} < 5.1 \times 10^{-5}$) and high acceptable risk levels ($5.1 \times 10^{-5} \leq \text{LTCR} < 10^{-4}$), respectively. Inhalation exposure presented the highest cancer risk among the various exposure routes. The hazard index values for oral and dermal contact with THMs were less than 1. Finally, sensitivity analysis revealed that the ingestion rate and exposure duration of THMs had the most significant positive effect on chronic daily intake (CDI) values and cancer risk. However, further comprehensive investigations are needed to develop effective solutions for reducing and controlling the precursors of DBP formation, as well as identifying suitable alternative disinfection compounds that minimize by-product formation.

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1. Introduction

Disinfection is the final stage in the water treatment process, aimed at preventing the emergence of secondary pollutants resulting from the regrowth of pathogenic microorganisms. Its primary objectives are to eliminate pathogens and ensure the safety of water within the network system [1,2]. Various disinfectants such as chlorine (Cl_2), chlorine dioxide (ClO_2), chloramines (NH_2Cl , NHCl_2), ultraviolet (UV) and ozone (O_3) are used worldwide to treat water, but chlorine remains the most widely used disinfectant for drinking water in developing countries, particularly in Iran [2–5].

Chlorine is considered the most reliable disinfectant due to its low cost, easy availability, and persistence within the water distribution network [6]. When chlorine is added to water, chlorine is produced either as hypochlorous acid (HOCl) or hypochlorite ion (OCl^-), which interact with natural organic matter (NOM) present, such as decaying vegetation or algae, leading to the formation of numerous disinfection byproducts (DBPs) [7–10]. Factors influencing the formation of DBPs depend on the quality of the source water, including the concentration of chlorine, chlorine contact time, pH, temperature, concentrations of iodide and bromide ions (as inorganic precursors), the concentrations and characteristics of NOM (as organic precursors), and the type and material of the WDN [4, 11]. However, in the presence of iodide and bromide ions in water, these ions can further increase the formation of brominated and iodinated THMs by reacting with NOM to create Br^- and I^- DBPs [10]. A variety of DBPs, such as trihalomethanes (THMs), haloacetic acids (HAAs), and halogenated acetonitriles (HANs), are formed through the reaction between chlorine and the organic matter present in raw water [4,8,12]. In drinking water networks, THMs are primarily formed during the disinfection process [13]. In surface water where bromide and iodide ions are not present, chlorinated byproducts become prevalent during disinfection using free chlorine [13–16].

THMs, a group of DBPs that includes four compounds—chloroform, dibromochloromethane (DBCM), bromodichloromethane (BDCM), and bromoform—are the most common DBPs [1]. THMs are volatile and can evaporate from water, posing potential risks through ingestion, inhalation, or skin sorption during activities like drinking, cooking, washing dishes, or swimming in pools [17–19]. Due to the adverse impacts of THMs, the WHO guidelines suggest maximum limits for chloroform, bromoform, DBCM, and BDCM at 300, 100, 100, and 60 $\mu\text{g}/\text{L}$, respectively [17]. Additionally, the US Environmental Protection Agency (EPA) and the European Union (EU) have set the maximum contaminant level (MCL) for total THMs (the sum of chloroform, bromoform, DBCM, and BDCM) in water sources at 80 $\mu\text{g}/\text{L}$ and 100 $\mu\text{g}/\text{L}$, respectively [10].

THMs are probable carcinogens, and short-term exposure can lead to adverse health effects, including reproductive and developmental issues, headaches, dizziness, and problems associated with the central nervous system (CNS) [20–22]. According to the International Agency for Research on Cancer (IARC), chloroform and BDCM are classified as possible human carcinogens, primarily associated with bladder, stomach, colon, and liver cancers. For example, in Europe, 5 % of bladder cancers are linked to THMs in water [23]. Numerous epidemiological investigations have explored the association between THM exposure and harmful health outcomes, including an increased risk of bladder cancer, birth defects, low birth weight, miscarriages, stomach and colorectal cancers, and developmental anomalies [23–27]. Animal studies have also provided valuable insights into the mechanisms through which THMs exert their toxic effects [28]. Given the potential health risks associated with THMs, proper management of distribution systems is crucial for maintaining water quality and minimizing THM levels [6]. Preventive maintenance, the use of alternative disinfectants such as ozone, monochloramines, hydrogen peroxide/ozone, UV-ozone and UV-hydrogen peroxide, along with regular flushing and controlling water residence time in the distribution network, can help reduce THM concentrations. Additionally, implementing a well-designed water quality monitoring program is essential to detect any changes in THM levels and enable prompt corrective actions [21,29,30].

Considering that the drinking water of Maragheh city is supplied through the Alaviyan Dam, located 3 km from the city, several factors could contribute to an increase in NOM. These factors include the presence of rural areas, tourism, high vegetation coverage (due to fruit orchards and various agricultural crops), the presence and decomposition of fish, and plant remnants upstream of the dam. However, no study has investigated THMs in the WDN of this city. The innovation of this study lies in comparing the effect of different parameters on the formation of THMs, particularly in the new and old WDN of Maragheh city. Thus, the aims of this study included: (i) to measure the concentrations of THMs and their seasonal variations in the drinking water network system of Maragheh city; (ii) to investigate the influence of disinfectant concentration, temperature, pH, dissolved oxygen (DO), electrical conductivity (EC), total organic carbon (TOC), bromide content, age of the WDN, and distance from water treatment plant (WTP) on THM formation; (iii) to assess the non-carcinogenic and carcinogenic risks to the population via ingestion, inhalation, or dermal absorption from exposure to THMs in the WDN.

2. Material and methods

2.1. Study area

The study was performed in Maragheh, located in the southwest region of East Azerbaijan, Iran. The city, home to approximately 185,000 residents and covering an area of 30 square kilometers, is the second largest and most populous city in the province. Maragheh is situated at an elevation of 1477 m above sea level, with coordinates spanning from $46^\circ 9'$ to $46^\circ 44'$ E longitude and $37^\circ 1'$ to $37^\circ 45'$ N latitude. The city receives an average annual rainfall of 322 mm and maintains a mean temperature of 12.5°C . The drinking water supply for Maragheh city is sourced from the Sufi Chai River and the Alavian Dam. Fig. 1 displays the sampling locations within the study area.

2.2. Water sample collection

Considering the size of Maragheh city, 21 sampling points were selected (one from the dam and 20 from the urban WDN). Information regarding the state of the city's drinking water distribution network, as well as the amount of chlorine used, is presented in Table 1. Sampling was conducted in June 2022 and January 2023, covering two seasons (summer and winter). Samples were gathered in 300-mL amber glass bottles, with sodium thiosulfate added to neutralize free residual chlorine (FRC) and prevent THM formation while stored. These samples were kept in the dark at 4 °C until analysis. Samples for TOC and bromide were collected in 250-mL plastic bottles.

2.3. THMs analysis

Firstly, to create a calibration curve, THM samples were prepared by diluting a THM standard solution in deionized water at concentrations ranging from 1 to 100 ppb. The peak curves of chloroform, DBCM, BDCM, and bromoform were obtained from Gas Chromatograph-Mass Spectrometer (GC) (Varian CP 3800, USA) analysis. Subsequently, THMs in each collected sample were analyzed using GC with an electron capture detector (ECD) and a capillary column (30 m × 0.25 m × 0.25 m). The temperatures for the injector and detector of the GC-ECD were set at 250 °C and 290 °C, respectively. Initially, the oven temperature was held at 35 °C for 11.1 min, after which it was raised to 100 °C and subsequently increased to 140 °C. In this study, water temperature, EC, free FRC, DO, pH, TOC, and bromide were also determined. To ensure quality control, both samples and blanks underwent duplicate analysis. THM samples were considered acceptable if their Relative Standard Deviation (RSD) values were below 30 %. The limits of detection (LOD) and quantitation (LOQ) were 0.1 µg/L and 0.2 µg/L, respectively. Additionally, SPSS software (version 21) was utilized to conduct statistical tests and to determine descriptive statistics such as mean, minimum, maximum, and standard deviation of input variables. The Kolmogorov-Smirnov test was employed to evaluate the normality of the variables. Due to non-normality, non-parametric statistical tests were employed. One-way ANOVA tests were applied to evaluate differences in average THM concentrations among the water sampling stations. Mann-Whitney U and Wilcoxon W tests were utilized to assess the average THM concentrations between new and old WDNs and throughout different seasons. Spearman's correlation coefficient was employed to analyze the relationship between the parameters under study. Finally, the Inverse Distance Weighted (IDW) method in ArcGIS 10 was used for spatial analysis and interpolation of THM levels in the study area.

2.4. Health risk assessment

The exposure routes for THMs include oral ingestion of drinking water, dermal absorption, and inhalation. Therefore, to estimate the cancer risk linked to THM exposure via these routes, a method developed by the USEPA can be used [31]. To determine the cancer risks posed by THMs, the Chronic Daily Intake (CDI) and its corresponding Slope Factor (SF) were employed in calculations [2,32]. Cancer risks from THMs through each exposure pathway—dermal, oral, and inhalation—were calculated using Equations (1)–(3) as follows:

$$CDI_{\text{inges},i} = \frac{C_{w,i} \times IR \times EF \times ED \times CF}{BW \times AT} \quad (1)$$

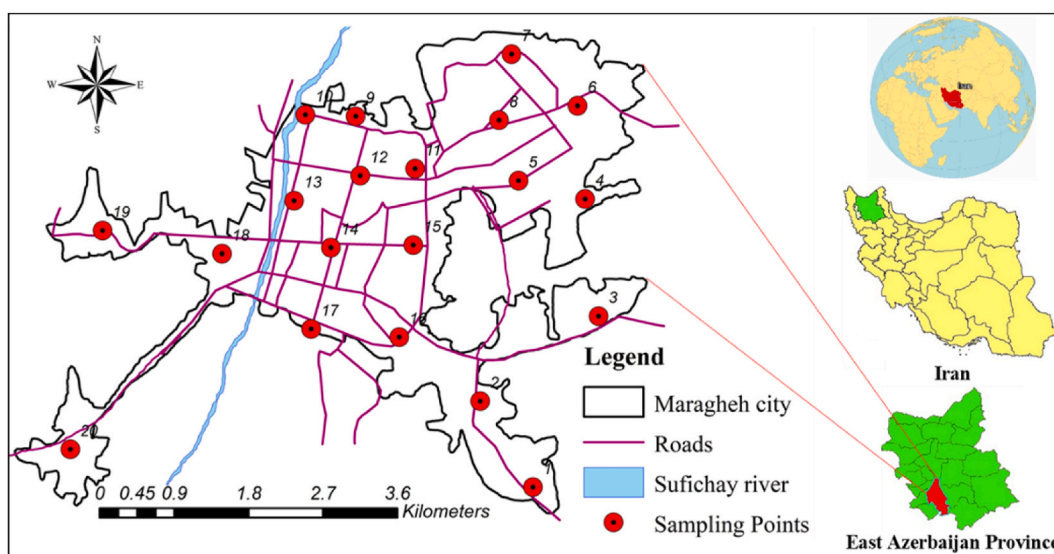


Fig. 1. The water sampling points in study area.

Table 1
Characteristics of the city's WDN and disinfectant used.

| Chlorine dose applied (ppm) | Contact time (min) | Target FRC in the WDN (mg/L) | Pipe material of WDN ^a | Pipe life of WDN (year) |
|--------------------------------------|--------------------|------------------------------|--------------------------------------|-------------------------|
| Spring/Summer: 1 Fall/Winter: 1.2 | 20 | 0.5–0.8 | Polyethylene, metal, asbestos-cement | 20 |

^a Most metal and asbestos-cement pipes have been replaced with polyethylene pipes. Currently, the distribution network is predominantly composed of polyethylene pipes.

where, $CDI_{ing,i}$ is the chronic daily intake of THMs via ingestion ($mg\ kg^{-1}\ day^{-1}$), $C_{w,i}$ is the concentration of THMs in drinking water ($\mu g\ L^{-1}$), IR is the ingestion rate of drinking water ($L\ day^{-1}$), EF is the exposure frequency ($days\ year^{-1}$), ED is the exposure duration (year), CF is the conversion factor from μg to mg (10^{-3}), BW is body weight (kg), and AT is the averaging time (days).

$$CDI_{derm,i} = \frac{C_{w,i} \times SA \times F \times PC \times ET \times EF \times ED}{BW \times AT} \quad (2)$$

where, $CDI_{derm,i}$ is the chronic daily intake of THM via dermal absorption route ($mg\ kg^{-1}\ day^{-1}$), $C_{w,i}$ is the concentration of THMs in drinking water ($\mu g\ L^{-1}$), SA is the skin surface area (m^2), PC is the permeability coefficient, ED is the exposure time ($min\ day^{-1}$), and EF is the exposure frequency ($Days\ year^{-1}$).

$$EC_i = \frac{C_{air,i} \times EF \times ET \times ED}{BW \times AT} \quad (3)$$

Where $C_{air,i}$ is the concentration of THM in shower air ($\mu g\ m^{-3}$), EC_i is the exposure concentration of THM in the air ($\mu g\ m^{-3}$), ET is the exposure time ($h\ day^{-1}$), and AT is the averaging time (h). The lifetime cancer risk (LTCR) for any THM species can be calculated using the following equation:

$$LTCR = EC_i \times IUR_i \quad (4)$$

Where IUR_i is the inhalation unit risk for any THM species ($\mu g\ m^{-3}$)⁻¹ (Table 2). $LTCR_{air-i}$ can be calculated using the following equations [33,34].

Table 2
Input parameters for the estimation of cancer and non-cancer assessment of THMs.

| Input variable | Notation | Unit | Value | References |
|--|----------------------|-------------------------|--|-------------|
| Value of THMs | $C_{w,i}$ Cair, i | $\mu g/l$ | measured | This study |
| Ingestion rate | IR | $L\ day^{-1}$ | 2 | [35] |
| Exposure frequency | EF | $Days\ year^{-1}$ | 365 | |
| Exposure duration | ED | Year | 30 | [36] |
| Conversion factor | CF | $L\ cm^{-3}$ | 0.001 | |
| Body weight | BW | Kg | 70 | |
| Average time | AT | Days | 70×365 | |
| Area of surface skin | SA | m^2 | 1.8 | |
| Fraction of skin in exposure to water | F | Percent | 90 % | [36] |
| Permeability coefficient | | | 0.00683 (Chloroform), 0.00402 (BDCM), 0.00289 (DBCM) 0.0026 (Bromoform) | [37] |
| Exposure time | ET | min/day | 35 | |
| Concentration of studied THM species in air | Ca_i | mg/l | Little's model | [33] |
| Ventilation rate | VR | $m^3\ h^{-1}$ | 0.83 | [35] |
| Absorption efficiency | AE | % | 50 | [36] |
| Reference dose | RfD | $mg\ kg^{-1}\ day^{-1}$ | 0.01 (Chloroform), 0.02 (BDCM, DBCM and Bromoform), | |
| Showering duration | t | min | 5, 10, 15 | [38] |
| Shower stall volume | V_s | L | 2000, 3500, 5000) | [38] |
| Henry's constant | H | – | Chloroform: 0.25, BDCM: 0.124, DBCM: 0.0526, Bromoform: 0.0501. | [39] |
| Water flow | Q_w | $L\ min^{-1}$ | 3, 4, 5 | [40] |
| Air flow/ventilation rate | Q_g | $L\ min^{-1}$ | 40, 50, 60 | [34,41] |
| KoLA—Overall mass coefficient of each THM | | $L\ min^{-1}$ | Chloroform: 7.4, BDCM: 5.9, DBCM: 4.6, TBM: 3.7 | [20] |
| Cancer slope factor | CSF | $mg\ kg^{-1}\ day^{-1}$ | Oral and dermal: Chloroform: 0.0061, BDCM: 0.062, DBCM: 0.084, Bromoform: 0.0079 | [34,41] |
| Inhalation unit risk | IUR | $(\mu g\ m^{-3})^{-1}$ | Chloroform: 0.000023, BDCM: 0.000037, DBCM: 0.0000024, Bromoform: 0.0000011 | [34,39, 42] |

$$C_{air,i} = \frac{C_{0,i} + C_{t,i}}{2} \tag{5}$$

where, $C_{air,i}$ is the estimated concentration of THM ($\mu\text{g L}^{-1}$), $C_{0,i}$ is the initial concentration of THMs (considered to be zero) and $C_{t,i}$ is the concentration of THMs at time t. $C_{t,i}$ is calculated as:

$$C_{t,i} = (1 - e^{-bt}) \times \left(\frac{a}{b}\right) \tag{6}$$

$$b = \frac{1}{Vs} \left\{ \left(\frac{Q_w}{H}\right) \times (1 - e^{-N}) + Q_g \right\} \tag{7}$$

$$a = \frac{1}{Vs} \left\{ Q_w \times C_w \times (1 - e^{-N}) \right\} \tag{8}$$

Where, Vs is the bathroom volume (L), Q_w is the flow rate of water in the bathroom (L min^{-1}), H is Henry's constant for any species of THMs (at 40°C), Q_g is the airflow rate in the shower (L min^{-1}), and N is the non-dimensional overall mass transfer coefficient (KoLA, L/min). Therefore, N can be calculated as [34]:

$$N = \frac{\text{KoLA}}{Q_w} \tag{9}$$

Table 2 presents the input values of variables used in estimating the risk of THMs for each exposure pathway.

2.5. Cancer risk characterization

The lifetime cancer risk (LTCR) associated with each type of THM across different exposure routes was computed using Equation (10) as outlined below:

$$\text{Total LTCR} = \text{CDI}_{\text{inges},i} \times \text{SF}_{\text{inges},i} + \text{CDI}_{\text{derm},i} \times \text{SF}_{\text{derm},i} + \text{CDI}_{\text{inhal},i} \times \text{SF}_{\text{inhal},i} \tag{10}$$

The cancer slope factor (SF (mg/kg/day)) was used to compute the probability of cancer prevalence as a result of exposure to a chemical (Table 2) [2,13]. The probability of cancer risks from exposure to THM compounds was categorized into four classes: unacceptable cancer risk ($\text{LTCR} \geq 10^{-4}$), negligible cancer risk ($\text{LTCR} < 10^{-6}$), acceptable low cancer risk ($1 \times 10^{-6} \leq \text{LTCR} < 5.1 \times 10^{-5}$), and acceptable high cancer risk ($5.1 \times 10^{-5} \leq \text{LTCR} < 10^{-4}$) [2,43].

2.6. Non-cancer risk assessment

The non-cancerous risks of THMs through ingestion and dermal exposure were assessed using the Hazard Index (HI) with Equations (11) and (12):

$$H_{\text{inges},i} = \text{CDI}_{\text{inges},i} / \text{RFD}_i \tag{11}$$

$$H_{\text{derm},i} = \text{CDI}_{\text{derm},i} / \text{RFD}_i \tag{12}$$

The CDI value indicating the risk from inhalation exposure is significantly lower than that from ingestion or dermal exposure; hence, the HI was only calculated for ingestion and dermal exposures [13]. Each THM species with a HI of 1 or greater is considered to

Table 3
Physico-chemical characteristics drinking water in both seasons (summer and winter).

| Parameters | Unit | N | Summer | | | | Winter | | | | Total mean | |
|------------------------|------------------|----|--------|-------|-------|-------|--------|-------|-------|-------|------------|-------|
| | | | Mean | SD | Max | Min | Mean | SD | Max | Min | Mean | SD |
| T | $^\circ\text{C}$ | 42 | 27.6 | 1.19 | 29.7 | 24.2 | 12.35 | 1.59 | 15.5 | 9.5 | 19.54 | 7.91 |
| EC | $\mu\text{s/cm}$ | 42 | 305 | 23.69 | 345 | 267 | 300.9 | 27.76 | 341 | 265 | 418.06 | 35.49 |
| pH | | 42 | 7.15 | 0.22 | 7.4 | 6.5 | 6.74 | 0.48 | 7.6 | 6 | 7.2 | 1.25 |
| Free residual chlorine | mg/l | 42 | 0.28 | 0.13 | 0.6 | 0.1 | 0.35 | 0.15 | 0.7 | 0.1 | 0.32 | 0.14 |
| TOC | $\mu\text{g/l}$ | 42 | 18.8 | 4.25 | 23.5 | 10.15 | 10.68 | 3.63 | 13.71 | 7.35 | 14.74 | 3.45 |
| DO | mg/l | 42 | 3.58 | 0.32 | 4 | 3.12 | 5.59 | 1.19 | 7 | 1.9 | 4.59 | 1.33 |
| Distance of WTPs | Km | 42 | 3.96 | 1.42 | 7.76 | 2.23 | 3.96 | 1.42 | 7.76 | 2.23 | 3.96 | 1.42 |
| Bromide | mg/l | 42 | 3.35 | 1.73 | 4.43 | 2.23 | 3.17 | 1.44 | 3.19 | 1.93 | 3.27 | 1.58 |
| Chloroform | $\mu\text{g/l}$ | 42 | 53.33 | 18.48 | 115.5 | 32.5 | 35.28 | 13.03 | 81.65 | 21.44 | 44.28 | 18.25 |
| BDCM | | 42 | 13.14 | 5.87 | 26.7 | 5.1 | 12.17 | 4.52 | 20.33 | 5.61 | 3.16 | 0.89 |
| DBCfM | | 42 | 3.11 | 0.79 | 4.7 | 1.75 | 3.2 | 1.01 | 5.65 | 1.58 | 12.66 | 5.19 |
| Bromoform | | 42 | <0.3 | <0.3 | <0.3 | <0.3 | 0.305 | 0.02 | 0.41 | 0.3 | 0.302 | 0.01 |
| TTHMs | | 42 | 69.89 | 23.41 | 145.3 | 42 | 50.97 | 15.23 | 94.29 | 31.07 | 60.40 | 21.75 |

be potentially toxic [44].

2.7. Sensitivity analysis

In this research, the Monte Carlo simulation method was used with Crystal Ball software (Version 11.1.2.4) to assess the risks associated with exposure to THMs and to conduct sensitivity analysis [2,13]. This technique, involving 10,000 trials, was used to create a distribution of risk probabilities, incorporating the uncertainty and variability of each variable [45]. Sensitivity analysis was conducted using Spearman's rank-order correlation to evaluate the influence of variables on the estimated health risk associated with THMs and the effect of the studied variables on THMs formation.

3. Results and discussion

3.1. Water physico-chemical characteristics in WDN

Physicochemical characteristics of tap water, including temperature, EC, pH, FRC, TOC, DO, distance from WTP, chloroform, BDCM, DBCM, bromoform, bromide, and TTHMs for both summer and winter seasons, are presented in Table 3. According to the table, the water temperature during the summer was 27.6 °C and 12.35 °C in the winter. The mean temperature in summer was significantly higher ($p < 0.001$) than in winter, indicating a significant seasonal variation in temperatures [46]. The mean EC values for both seasons were approximately the same, at about 300 mg/L. No significant seasonal variation was observed in EC, indicating that this EC level is considered acceptable according to WHO guidelines [13]. Significant differences were observed in pH values between the seasons ($p < 0.009$), with the mean pH in summer (7.4) being higher than in winter (6.74). This finding aligns with other studies, which also report higher pH values during the summer season [19,47]. In summer, favorable conditions are typically present for the growth of microorganisms such as bacteria and algae in water sources [19]. Their growth leads to the release of intracellular and extracellular organic matter [48,49]. Consequently, during summer, algae increase water pH levels by releasing hydroxyl ions through an intensified photosynthesis process [19,47]. According to Table 3, the average concentration of FRC in tap water samples was higher in winter (0.35 mg/L) than in summer (0.28 mg/L). Additionally, results from other studies indicate that higher temperatures in summer can accelerate chlorination reactions, leading to increased chlorine consumption. This results in lower concentrations of chlorine remaining in the WDN [19,50]. The average concentration of TOC in the summer was 18.8 μg/L, significantly higher ($p < 0.001$) than in winter (10.68 μg/L). This finding is supported by Shanks et al. who reported the highest levels of dissolved organic carbon (DOC) during the summer [51]. These results align with other studies indicating that higher water temperatures or increased DOC levels during the water disinfection process can lead to enhanced formation of DBPs [52,53]. According to Table 3, the mean concentration of DO in tap water samples was significantly higher in winter (5.59 mg/L) than in summer (3.58 mg/L) ($p < 0.001$). The solubility of oxygen in water sources has an inverse relationship with temperature; as temperature decreases, the DO of water

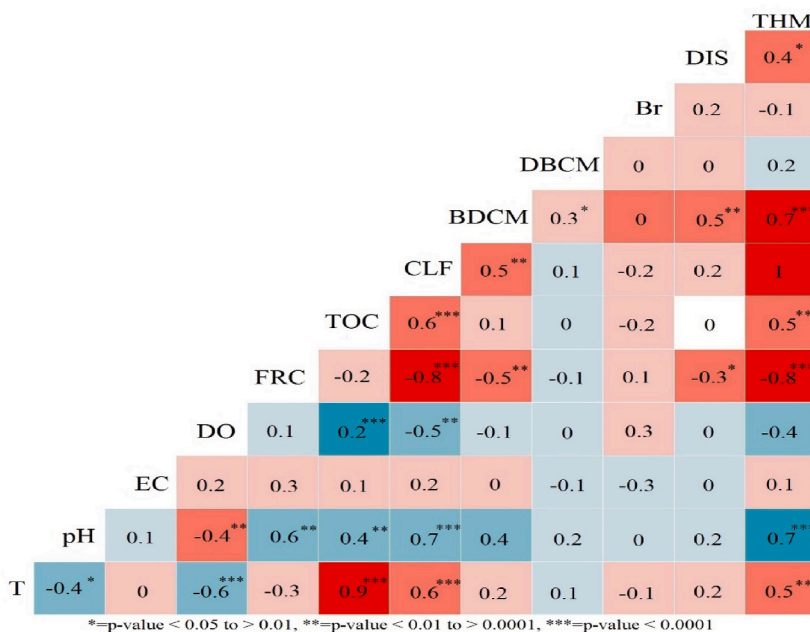


Fig. 2. The correlation of TTHMs with other water quality variables. (EC (electrical conductivity), DO (dissolved oxygen), FRC (free residual chlorine), TOC (total organic carbon), CLF (chloroform), DBCM (dibromochloromethane), BDCM (bromodichloromethane), Br (bromide), DIS (distance from water treatment plant), and THM (trihalomethanes)).

increases. Therefore, assuming other variables are constant, the concentration of DO in an aquatic system will be higher in winter than in summer [54,55]. A summary of TTHMs concentration is presented in Table 2. The minimum, maximum, and mean concentrations of TTHMs were 31.07, 145.3, and 60.43 ± 21.75 $\mu\text{g/L}$, respectively. The mean concentration of TTHMs in the present study was below the limits prescribed by USEPA (80 $\mu\text{g/L}$), WHO, and the national standard of Iran (100 $\mu\text{g/L}$) [56–58]. A comparison of the mean concentration of TTHMs in our study with those observed in similar studies reveals that the levels of TTHMs in this study were lower than those reported in Denmark, Bangladesh, Ahvaz, Tabriz, and Tehran [13,59–62] and higher than those observed in China and Yazd [2,22]. High and low THM values in these cities could be attributed to the type of water resources (i.e., dams, surface, and ground-water) and the levels of THM precursors (i.e., organic compounds). Chloroform, with a mean concentration of 44.28 ± 18.25 $\mu\text{g/L}$, was the major and dominant compound among THM species, accounting for over 72 % of TTHMs. BDCM and DBCM, with mean concentrations of 12.66 ± 5.19 and 3.16 ± 0.89 $\mu\text{g/L}$, constituted 21 % and 5 % of TTHMs, respectively. Bromoform, contributing less than 0.5 % to the total THMs, had the smallest share. Contrary to our findings, some studies have reported bromoform as the dominant THM compound owing to high concentrations of bromide in the water sources [63,64]. Finally, the order of THM compounds observed in this study was chloroform > BDCM > DBCM > bromoform, aligning with findings from other research [2,13,63,64].

3.2. Correlation of TTHMs with water quality parameters

Spearman's correlation coefficients (r) and significance level (p) were used to assess the correlation of TTHMs with water quality variables influencing TTHMs formation. According to the data presented in Fig. 2, moderate correlation was observed between water temperature ($r = 0.5$, $p = 0.001$) and TTHMs formation. This indicates that temperature is a significant factor affecting the formation of TTHMs in tap water, as seasonal variations in temperature influence the activation energy required for the reaction rate of organic matter with free residual chlorine [65–67]. Most similar research confirms that the higher temperatures in warm seasons, compared to cold seasons, create more favorable conditions for the growth of many microorganisms, especially bacteria, which release organic matter into the water [68]. A substantial correlation ($r = 0.7$, $p < 0.001$) was found between pH and TTHMs formation in water samples. Most studies confirm that pH has a positive correlation with THM formation, and as a result, the THM formation value increases with an increase in pH [7,59]. When the pH decreases, acid ionization during the chlorination process also decreases, likely increasing the interaction of chlorine with NOM in the water. However, decreasing the pH can also promote the non-ionization of humic acids, causing their accumulation and reducing their interaction with chlorine compared to what is observed at higher pH levels [7]. Another study conducted in Huzhou and Jinhua cities (China) showed no significant correlation between pH and most DBPs. This could be attributed to the similar geographical environment and economic conditions of these two cities [68].

No correlation ($r = 0.1$, $p = 0.364$) was observed between EC and TTHMs formation, which is consistent with the findings of Masafari et al., 2021 study, while in Urnine et al., 2024 study, a substantial correlation was found between EC and TTHMs formation [13,66]. A negative correlation ($r = -0.4$, $p = 0.014$) was observed between DO and TTHMs formation. This indicates that DO is not a significant factor in the formation of TTHMs in water. The consumption and production of DO are influenced by factors such as plant and algal biomass, sunlight, and water temperature, as well as seasonal variations [69]. Another study also reported a negative correlation between DO and TTHMs in water samples [69]. In the first step, chlorine reacts with the inorganic materials in the water, resulting in very low THM formation. In the second step, when chlorine reacts with fast-reacting organic materials, it causes the bulk of THM formation. Finally, in the third step, chlorine reacts with slow-reacting organic matter, forming THMs at a slower rate [70]. In many studies is reported that the formation of THE rise with enhancing consumption chlorine [70,71]. However, research indicates that free residual chlorine in excess of chlorine demand, have low influence on rising the THM formation rate. So that THM formation rising with rising chlorine dosage up to a point where the reaction is no longer chlorine confined. More this point the reaction is maybe to be TOC confined. It means if ratio of chlorine: TOC less than 1, chlorine had the highest effect on THM formation and above this ratio there was low change in THM formation rate [70]. In our study, FRC exhibited a negative correlation ($r = -0.8$, $p < 0.001$) with TTHMs formation. However, if the free residual chlorine is insufficient to drive further THM formation reactions, the rate of THM production will remain low. Additionally, due to THM decomposition, as free residual chlorine decreases, THM concentrations will also decrease [72]. This negative correlation between chlorine and THMs can be attributed to the fact that when chlorine is added to water, it forms hypochlorous acid (HOCl) and hypochlorite ion (OCl^-), with their relative concentrations dependent on pH. In acidic conditions, HOCl predominates, while in alkaline conditions, OCl^- is more prevalent. According to this study, the pH value of the WDN ranges from 6 to 7.6, indicating acidic conditions. Therefore, HOCl, which is responsible for THM formation, is the more prevalent chlorine species. This means that as THM concentration rises, the concentration of HOCl as free residual chlorine declines [73]. Radial diffusion and wall consumption of FRC contribute to an increase in THMs formation in the WDN. This indicates an inverse relationship between residual chlorine and THM formation [65]; as free residual chlorine levels decrease, TTHMs concentrations increase. These findings align with those of previous studies [59,72,74]. However, another study focusing on the drinking water distribution in Addis Ababa, Ethiopia and Saudi Arabia indicated that residual chlorine had a positive correlation with THMs formation which is not consistent with the results of our study [7,11]. Additionally, a study conducted in Iraq by Abdul Karim et al. observed that TTHM concentrations decreased as water traveled along the WDNs before consumption. This decrease may be due to the increased contact time of water with free chlorine [75]. Another study conducted in China in 2023 showed that high free residual chlorine and high temperatures could potentially increase the formation of THMs. This increase could be due to the rise in algal blooms during warm seasons, which leads to a higher demand for chlorine and enhances the formation of DBPs [68]. This could be due to differences in methodology and water characteristics. A moderate correlation ($r = 0.5$, $p = 0.003$) was found between TOC and THMs formation in drinking water. This may be attributed to the continuous reaction of disinfectants, such as chlorine, with organic compounds, leading to THM formation in the water distribution system. Similarly, a study by Tsitsifli et al. observed moderate correlations between THMs

and TOC in the water distribution system of Kayseri city (Turkey), with a correlation coefficient of 0.48 [76]. Additionally, many studies have demonstrated a positive correlation between TOC and THM formation [53,77,78]. In a study by Aleid et al. in Saudi Arabia, the concentration of halomethane compounds was found to be low due to the low levels of TOC. This indicates that microbial pollution was minimal [7]. Fig. 2 also presents the correlation coefficients between TTHMs and their species. TTHMs exhibit significant correlations with chloroform ($r = 0.955$, $p < 0.001$) and BDCM ($r = 0.689$, $p < 0.01$), but did not correlate with DBCM ($r = 0.205$, $p = 0.204$) and bromide ($r = -0.1$, $p = 0.523$). This can be attributed to the high contribution of chloroform and BDCM to the TTHMs, with more than 72 % and 12 % of the TTHMs compounds belonging to these two species, respectively. In contrast, the lowest proportions are attributed to DBCM and bromoform. Another reason for this could be the low concentration of bromide in the WDN. Previous literature confirms that chloroform is the main component of TTHMs [2,13,66]. A study by Tafesse et al. in Addis Ababa, Ethiopia, indicated that among the THM compounds, bromoform was the dominant compound formed during the chlorination of groundwater. This is likely because the groundwater contains natural bromide, which may originate from the soil's organic content [4]. In the present study, bromide was not significantly correlated with TTHM formation, likely due to the very low concentrations of bromide in the drinking water of our study area [19]. These findings are consistent with those of other similar studies [19,69,79]. Finally, Spearman's correlation coefficients show significant positive relationships between TTHM formation and the distance from the WTP ($r = 0.4$, $p = 0.026$). These results are consistent with previous studies [13,65,72].

Considering that the distance from WTP can serve as an indirect measure of contact time between organic matter and chlorine, it can be inferred that THM formation increases with greater distance from the WTP. This is likely due to the provision of sufficient reaction time between organic matter and chlorine, resulting in increased THM formation. Several studies have confirmed that increasing the contact time between TOC and chlorine leads to higher levels of THM formation [10,65,72]. However, another study conducted on the drinking water distribution in Martin County, Kentucky, USA showed a significant positive effect between distance from WTPs and HAA concentrations but did not find a significant correlation between THM formation and distance from WTPs. This could be attributed to the complexity of the WDN, which consists of many long service lines and multiple branches, each with varying and often low water demands [66].

3.3. Seasonal variation of TTHMs

Fig. 3 (a, b) shows the spatial distribution of TTHM concentrations during the summer and winter seasons at sampling points throughout Maragheh city. The distribution pattern of TTHM concentrations is similar in both seasons, with the highest concentrations observed primarily in the central and southern parts of the city. Given that Maragheh's WTP are located in the northwest, with mean, minimum, and maximum distances from the sampling points being 3.96 km, 2.23 km, and 7.76 km respectively, the observed pattern may be attributed to the distance from the WTP. This distance increases water residence time in the WDN, leading to reduced concentrations of free and total residual chlorine and an increase in TTHM concentrations [3,22,51,80]. In our study, significant positive and negative correlations were observed between TTHM formation and the distance from WTP and FRC concentrations, respectively ($p < 0.05$). Consequently, an increase in the distance from WTP may lead to a longer reaction time between organic matter and chlorine, thereby increasing THM formation. Seasonal variations in THM concentrations are presented in Table 4. The average concentrations of chloroform, DBCM, BDCM, bromoform, and TTHMs in summer were 53.33, 13.14, 3.11, 0.3, and 69.89 $\mu\text{g/L}$, respectively, while in winter they were 32.28, 12.17, 3.2, 0.3, and 50.97 $\mu\text{g/L}$, respectively. The average concentrations of chloroform, DBCM, BDCM, TTHMs, and TOC were significantly lower in winter than in summer ($p < 0.05$). These findings are consistent with other studies indicating higher THM concentrations in warmer seasons [47,68,81]. The primary reason can be explained as follows: high water temperatures accelerate the reactions between residual chlorine and organic compounds in drinking water, potentially enhancing THM formation [51,68,82].

3.4. Concentrations of THMs in old and new WDN

The statistical analysis comparing the concentrations of different THM species in the WDN revealed that the concentrations of chloroform, BDCM, DBCM, and total THMs in areas with an old WDN are significantly higher than those in areas with a new WDN ($p < 0.05$). This pattern is also evident in the spatial distribution of THM concentrations shown in Fig. 3(a and b), where the concentrations

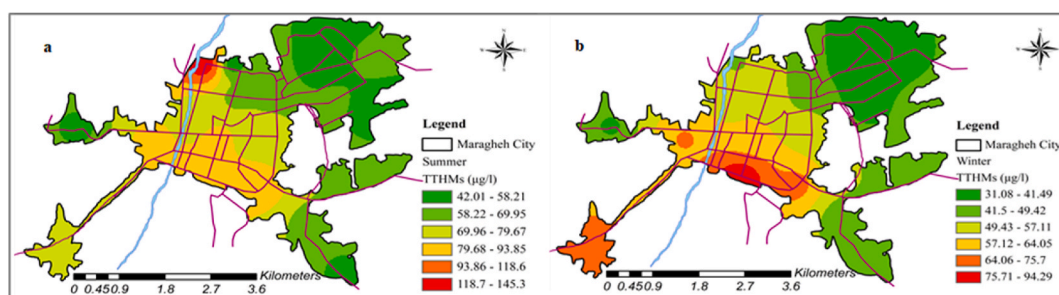


Fig. 3. The spatial distribution of TTHMs concentration in summer and winter seasons in the study area.

Table 4
Life time cancer risk via triple routes exposure with THMs species in the WDN.

| Season | Exposure route | Chloroform | BDCM | DBCM | Bromoform | TTHMs |
|---------------|-------------------|---------------------|---------------------|---------------------|---------------------|----------------------|
| Winter | Ingestion | 3.07E-06 ± 1.13E-06 | 2.85E-06 ± 8.95E-07 | 1.46E-05 ± 5.42E-06 | 3.44E-08 ± 2.77E-09 | 2.1E-05 ± 6.5E-06 |
| | Dermal | 2.62E-07 ± 8.36E-08 | 2.32E-07 ± 7.33E-08 | 1.66E-06 ± 6.18E-07 | 6.68E-09 ± 5.38E-10 | 2.134E-06 ± 6.98E-07 |
| | Inhalation | 2.9E-08 ± 1.1E-08 | 1.04E-10 ± 3.28E-10 | 5.85E-10 ± 2.19E-10 | 2.8E-12 ± 2.26E-13 | 3.05E-08 ± 1.08E-08 |
| | Total cancer risk | 8.02E-06 ± 1.03E-05 | 5.02E-06 ± 5.38E-06 | 1.58E-05 ± 1.77E-05 | 1.33E-08 ± 1.16E-08 | 2.89E-05 ± 3.34E-05 |
| Summer | Ingestion | 4.64E-06 ± 1.61E-06 | 2.8E-06 ± 7.01E-07 | 1.57E-05 ± 7.05E-06 | 6.01E-06 ± 2.08E-06 | 2.9E-05 ± 1.02E-06 |
| | Dermal | 3.42E-07 ± 1.49E-07 | 2.26E-07 ± 7.59E-08 | 1.79E-06 ± 5.78E-07 | 6.56E-09 ± 1.65E-24 | 2.37E-06 ± 8.79E-07 |
| | Inhalation | 4.3E-08 ± 1.6E-08 | 1.02E-09 ± 2.6E-10 | 6.25E-10 ± 2.84E-11 | 2.75E-12 ± 1.21E-27 | 4.46E-08 ± 1.59E-08 |
| | Total cancer risk | 4.26E-06 ± 2.11E-06 | 3.11E-06 ± 1.54E-06 | 1.65E-05 ± 8.46E-06 | 3.03E-06 ± 1.75E-06 | 2.71E-05 ± 1.37E-05 |

in the central regions of the city, which have older pipelines, are higher than in other regions. However, there was no substantial difference in the concentration of bromoform between the new and old WDN ($p > 0.05$). These results align with those from our earlier study [2]. The main reason can be explained in two ways: First, as the WDN ages, biological and chemical compounds accumulate on the inner walls of the pipes, leading to the formation of biofilms. This biofilm can react with water disinfectants like chlorine, resulting in increased THM formation [2,83,84]. The second explanation is that older WDNs are more likely to have fractures and damage in pipes and their joints. This can lead to the infiltration of trihalomethane precursors into the network, thereby increasing the formation of these compounds [2,83]. A study by Chen et al. in China showed that THMs concentrations and antibiotic resistance genes (ARGs) increased significantly in the old WDN. This increase was attributed to the enhanced strength and stability of biofilms, which triggered a stronger microbial antioxidant system response, leading to increased formation of THMs and ARGs [85].

3.5. Assessment of cancer risk of THMs

3.5.1. Ingestion pathway

For estimating cancer risk, the potency factors for the four types of THM compounds, related to the lifetime cancer risk (LTCR) for exposed individuals, were acquired from the Integrated Risk Information System (IRIS) [56,86]. The CDI associated with ingestion is depicted in Fig. 4. Table 3 presents the results of the LTCR for THM compounds via oral ingestion across two seasons. The mean LTCR values for chloroform, BDCM, and bromoform via oral ingestion in both winter and summer were below 10^{-6} , which the USEPA classifies as a negligible cancer risk. However, the mean LTCR values for DBCM and TTHMs via oral ingestion in both seasons exceeded 10^{-6} , classifying them as an acceptable low risk. Among the four THMs, DBCM exhibited the highest LTCR, with values of 1.46×10^{-5} and 1.57×10^{-5} in both seasons respectively, aligning with findings from a study of drinking water in Tabriz city, Iran [13]. The main reason might be due to the higher slope factor (SF) for DBCM compared to other THMs [76]. The average LTCR from the oral ingestion route for the contaminants in our investigation was ranked as follows: DBCM > TTHMs > BDCM > chloroform > bromoform. Our results are consistent with the findings from other studies on water distribution systems [2,87]. The LTCR values found in this study were lower than those reported in other studies [65,88]. This can be attributed to the low concentrations of THMs compounds found in our study.

3.5.2. Dermal absorption

Showering, bathing, swimming, and washing are the main routes of THMs absorption via dermal contact [59]. The results of CDI and LTCR for THMs compounds via dermal absorption are depicted in Fig. 4 and Table 4. The mean LTCR values for chloroform, BDCM, DBCM, bromoform and TTHMs from skin sorption in both seasons were lower than 10^{-6} , which, according to USEPA classification, is considered a negligible cancer risk. However, due to the higher SF of DBCM compared to other THMs, the highest and lowest LTCR levels from the dermal absorption route were associated with DBCM and bromoform, with values of 1.66×10^{-6} and 6.68×10^{-9} , respectively. This could be attributed to the higher SF and lower CF for DBCM [13]. These results are consistent with those from a study carried out in Yazd city, Iran [2]. Unlike the oral ingestion route, where boiling was found to be an effective method to reduce THMs exposure and associated cancer risk, boiling is not suitable for reducing cancer risk via inhalation and dermal exposures. Instead, employing washing machines for clothes and dishes is a more appropriate strategy [13].

3.5.3. Inhalation exposure

According to numerous studies, exposure to THMs through inhalation occurs when volatile compounds are released into the air during activities like showering, bathing, washing, and cooking. Additionally, the primary route of THM exposure is predominantly during bathing and swimming [2,64]. Fig. 4 shows the CDI associated with inhalation. Table 4 presents the results of cancer risk via the inhalation route of THMs compounds for both seasons. The mean LTCR values for chloroform, DBCM, BDCM, and bromoform from inhalation exposure in winter were 2.9×10^{-8} , 5.85×10^{-10} , 1.04×10^{-10} , and 2.8×10^{-12} , respectively, and in summer were 4.3×10^{-8} , 6.25×10^{-10} , 1.02×10^{-9} , and 2.75×10^{-12} , respectively. The mean LTCR for total THMs attributable to inhalation exposure was below 10^{-6} in both winter and summer, classified by the USEPA as a negligible cancer risk. The ranking of the mean LTCR values due to inhalation exposure of the four THMs species in this investigation was as follows: chloroform > BDCM > DBCM > bromoform. Unlike other exposure pathways for THMs, chloroform was the dominant contributor to total cancer risk via the inhalation route. This aligns with findings from other studies [62,64,89]. This could be attributed to the Henry's Law Constant and vapor pressures of THMs compounds. Chloroform, with its high vapor pressures, is the most volatile among other THMs species, potentially making it more

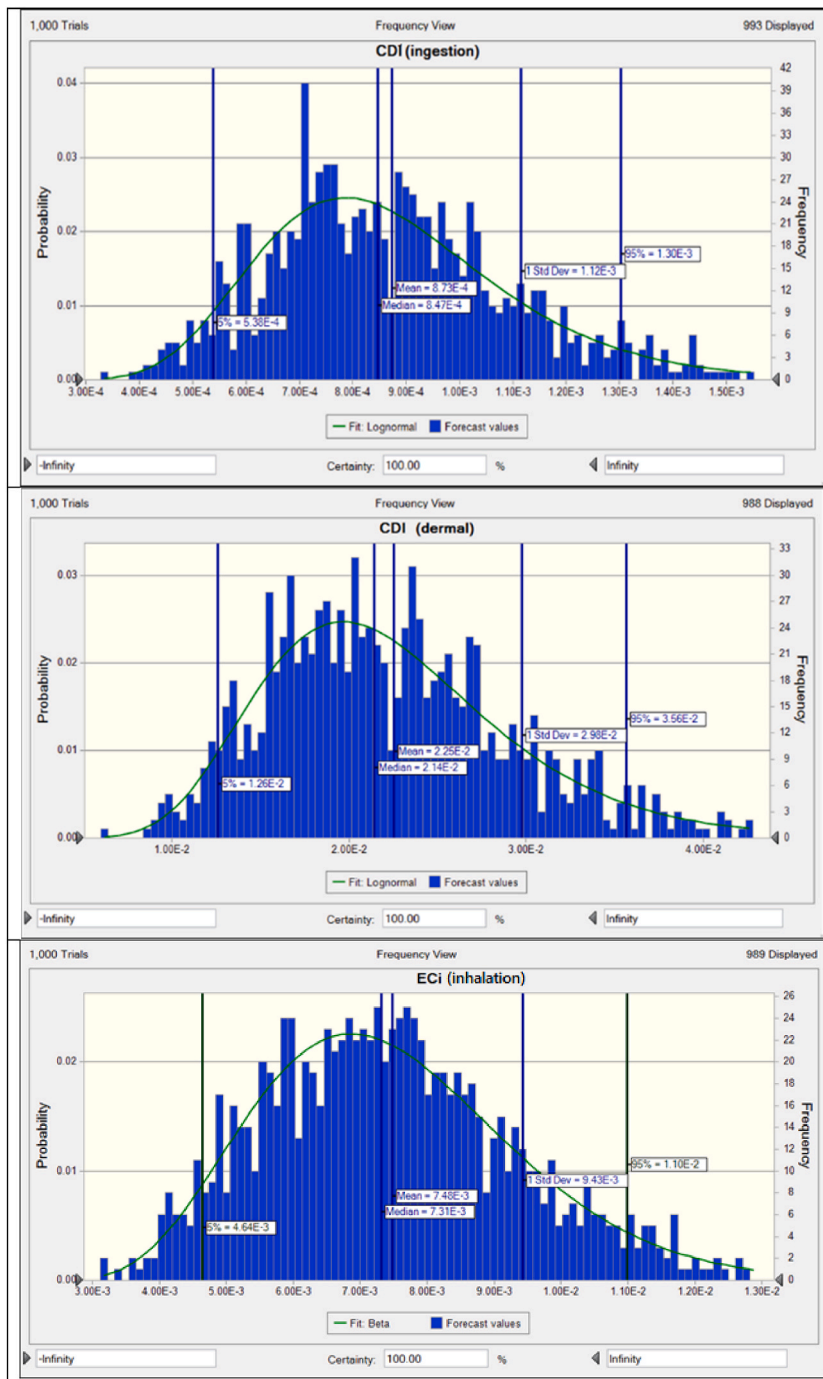


Fig. 4. Simulation histogram for CDI caused by multiple exposure routes.

carcinogenic and toxic [90]. Therefore, effective and intelligent air ventilation in homes, bathrooms, and swimming pools can be the best solution to mitigate the cancer risk associated with THMs through inhalation exposure.

3.6. Assessment of non-cancer risk of THMs

The Hazard Index (HI) was calculated to assess the non-cancer risk exposure of THMs in the drinking water samples. The HI values for THMs via oral ingestion and skin sorption routes are shown in Fig. 5. As illustrated, the calculated HI values for the oral ingestion route are higher than those for skin sorption. Chloroform, with HI values ranging from 3.2×10^{-2} to 4.5×10^{-2} for oral contact and

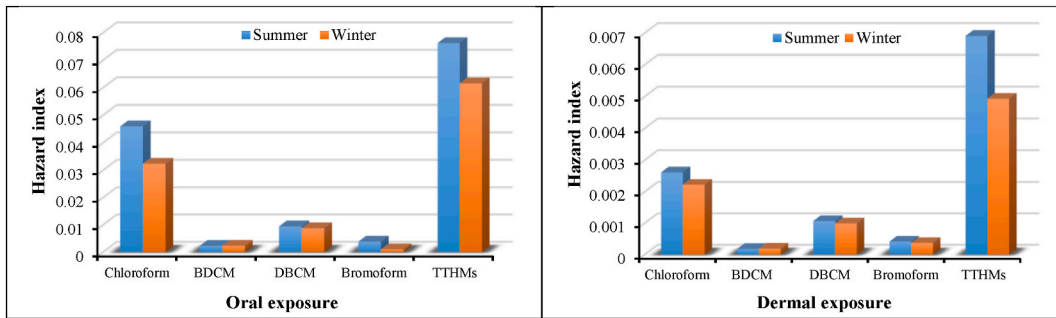


Fig. 5. Oral and dermal HI of THMs in drinking water samples.

from 2.23×10^{-3} to 2.62×10^{-3} for dermal contact, received the highest HI values among other THM compounds. Our results are consistent with the findings of other investigations [64,89]. HI values for both oral and dermal contact in both seasons were less than 1 (within the USEPA acceptable range) for THMs. Therefore, they do not have any notable effects on human health. However, exposure to THMs compounds may still lead to non-cancerous effects, including neurobehavioral changes, subjective effects on the central nervous system, jaundice, and enlarged liver.

3.7. Sensitivity analysis

Sensitivity analysis was performed to identify the primary parameters influencing LTCR due to THMs compound exposure via three routes (Fig. 6). According to Fig. 6 (a, b and c), the ingestion rate (IR) parameter has the greatest positive influence on CDI values and

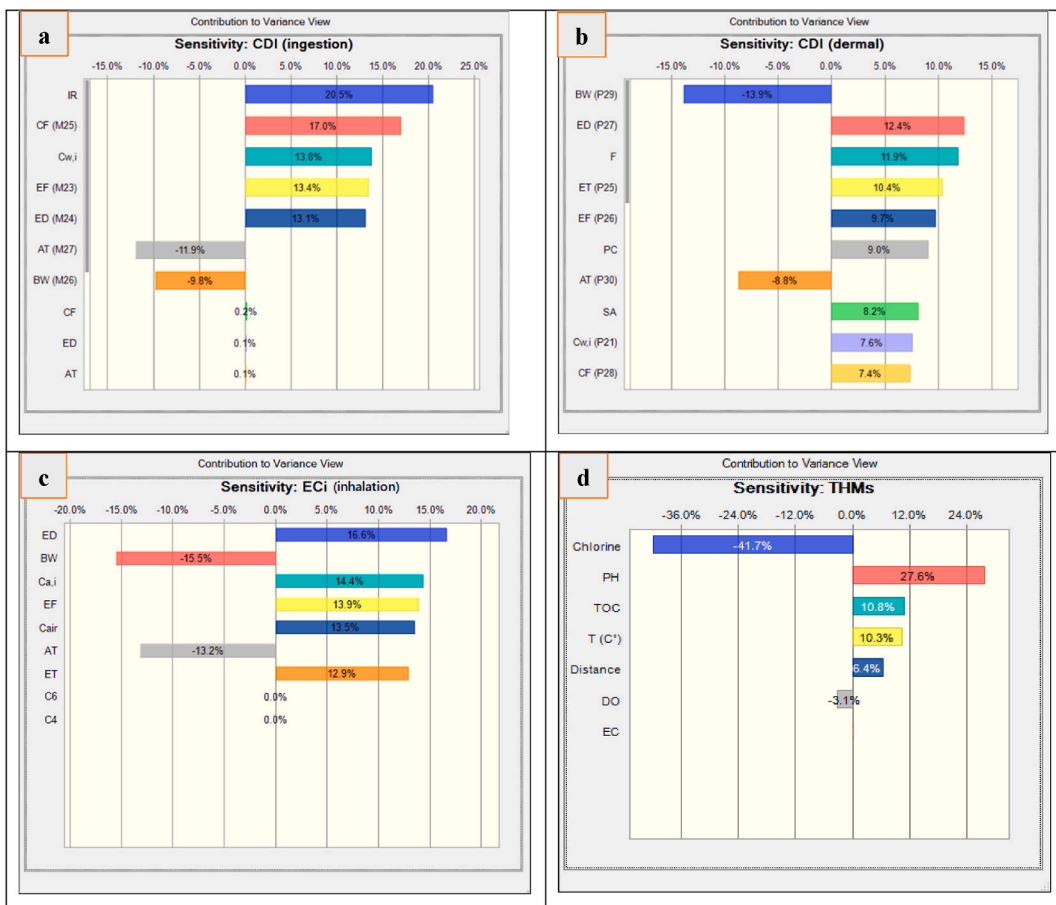


Fig. 6. Sensitivity analysis of the CDI model for THMs via multiple exposure routes (a–c) and sensitivity analysis of the studied variables on THMs formation (d).

cancer risk for oral contact, while exposure duration (ED) has the most significant impact on inhalation and dermal contact. According to the sensitivity analysis results, an increase in THM concentration and the duration of human exposure to THMs could elevate the cancer risk. Additionally, a negative correlation was found between bodyweight (BW) and CDI values in oral, dermal, and inhalation exposures. Sensitivity analysis was performed for the variables affecting THMs formation, and the results showed that the chlorine consumption rate had the most significant impact. Specifically, an increase in chlorine consumption in the WDN led to a rise in THMs formation, as shown in Fig. 6 (d). pH and TOC were the next most influential factors, with higher pH value and TOC concentrations in drinking water resulting in increased THMs formation.

4. Conclusion

The current study was performed to assess the concentration of THMs and estimate the potential cancer risk associated with exposure to these compounds in the WDN of Maragheh city. The results demonstrated that the mean concentration of TTHMs was below the guidelines set by the USEPA (80 µg/L), WHO, and the national standard of Iran (100 µg/L). Additionally, the study found significant positive correlations between TTHMs formation and factors like temperature, pH, TOC, and distance from WTPs, whereas DO and free residual chlorine showed negative correlations with TTHMs formation. A comparison of the concentration of various THMs compounds within the WDN revealed that areas with older networks exhibited significantly higher concentrations of THMs than newer areas ($p < 0.05$). The inhalation route was identified as having the highest cancer risk compared to other exposure routes. The HI values for oral and dermal contact were below 1, within the USEPA's acceptable range for THMs. Finally, sensitivity analysis indicated that the ingestion rate and exposure duration of THMs have the most substantial positive impact on CDI values and cancer risk.

Our recommendations for reducing the production of DBPs and mitigating their health effects are as follows.

- Minimize DBP production in WDN by removing organic matter before the initial chlorination point, which is the most effective method.
- Implement preventive maintenance and use alternative disinfectants such as ozone, monochloramines, hydrogen peroxide-ozone, UV-ozone, and UV-hydrogen peroxide. Regular flushing and controlling water residence time in the distribution network can also help reduce DBP concentrations.
- Conduct comprehensive investigations on all factors influencing the formation of DBPs.
- Perform further epidemiological studies to identify the health effects due to exposure to DBPs, particularly THMs.

5. Limitations of study

- Financial constraints and lack of access to pure standards for other disinfection by-products, such as haloacetic acids (HAAs) and halogenated acetonitrile (HAN), prevented us from investigating and analyzing these compounds.
- Given that the formation of DBPs, particularly trihalomethanes, depends on various factors, our study examined a limited number of these factors. Financial limitations prevented us from investigating additional influential factors.
- Insufficient information regarding the full details of the water distribution network (e.g., pipe types, diameters, and other characteristics) hindered our ability to investigate other factors affecting the formation of THMs.

CRedit authorship contribution statement

Negar Jafari: Writing – original draft, Methodology, Conceptualization. **Ali Behnami:** Writing – original draft, Methodology. **Farhad Ghayurdoost:** Methodology, Data curation. **Ali Solimani:** Validation, Software, Data curation. **Amir Mohammadi:** Writing – review & editing, Data curation. **Mojtaba Pourakbar:** Writing – review & editing, Conceptualization. **Ali Abdolajnejad:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare no conflicts of interest associated with this study.

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