

Temporospatial variation and health risk assessment of trihalomethanes (THMs) in drinking water (Northwest, IRAN)

Mohammad Mosaferi^{*1,2}, Mehrdad Asadi³, Hasan Aslani¹, Amir Mohammadi⁴, Sanaz Abedi⁵, Sepideh Nemati^{1,5}, Shahram Maleki⁶

¹Health and Environment Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

²Tabriz Health Services Management Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

³School of Engineering and the Built Environment, Anglia Ruskin University, UK

⁴Department of Public Health, Maragheh University of Medical Sciences, Maragheh, Iran

⁵Department of Environmental Health Engineering, School of Health, Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

⁶Medical Geography, Ministry of Health, Tehran, Iran

*Corresponding author: Mohammad Mosaferi

mmosaferi@yahoo.com, mosaferim@tbzmed.ac.ir

ORCID ID:orcid.org/0000-0001-6251-147X

Abstract

Trihalomethanes (THMs) are one of the most common classes of disinfection by-products. In this study, the temporo-spatial trends and health risks due to exposure to THMs in the Tabriz water distribution network were investigated. THMs series were analysed using gas chromatography equipped with electron capture detector. The non-carcinogenic and carcinogenic risks due to exposure to THMs were calculated using Monte Carlo simulations.

Mean concentrations of THMs in January (winter) and June (summer) were $10.2 \pm 9.3 \mu\text{g/l}$ and $252 \pm 185.9 \mu\text{g/l}$, respectively. More than 80% of THMs identified were bromodichloromethane. The mean values of lifetime cancer risks (LTCR) from THMs were calculated as $4.23\text{E-}06$ and $2.38\text{E-}04$ for winter and summer, respectively.

This study showed that there were noticeable levels of THMs in Tabriz's distribution network water, especially in the centre of the city. Although non-carcinogenic risks from THMs were below permissible recommended levels, carcinogenic risks likely remain due to high levels of THMs in some locations.

Keywords: Disinfection By-Products (DBPs), Water Quality, Cancer, Monte Carlo simulations, Tabriz

1. Introduction

Chlorination is used to treat surface water and groundwater in most conventional water treatment plants. Chlorination occurs both towards the beginning of the treatment process (prechlorination) and towards the end of the treatment process (postchlorination). Prechlorination reduces microbial contamination of raw water, prevents of algal growth throughout treatment facilities and enhances coagulation. Postchlorination provides a final disinfection and provides free residual chlorine in the distribution network (Hendricks 2016).

When water also contains natural organic matter (NOM, e.g. decaying vegetation) and bromide ions, disinfection by-products (DBPs) form as a result of the reaction between chlorine and precursor materials (Huang et al. 2019). Approximately 700 DBPs have been identified in drinking water (Rubirola et al. 2019). The main DBPs formed during chlorination are trihalomethanes (THMs), haloacetic acids (HAAs), haloketones (HKs) and halonitromethanes (HNMs). The majority of DBPs are THMs, which include chloroform (CF), bromodichloromethane (BDCM), dibromochloromethane (DBCM) and bromoform (BF) (Richardson et al. 2007; Tsitsifli and Kanakoudis 2018).

Temperature, pH and amounts of chlorine, NOM and bromide all affect the formation of DBPs. NOM is a main contributor to DBPs; both organic and inorganic agents (such as NO_2^- -N, Br^- and NH_4^+ -N), as well as pH, play important roles in the formation of HNMs (Zhou et al. 2019). Interestingly, Zhou's study (2019) also found that higher DBP levels were correlated with economic development (GDP), perhaps because the economic development caused more DBP precursors to be present in the source water.

Given temperature's influence on DBP formation, the concentration of DBP in drinking water, and therefore drinking water quality, may vary throughout the year. The United States Environmental

Protection Agency (EPA) set 80 µg/l as a maximum contaminant level (MCL) for THMs. The Maximum Contaminant Level (MCL) Goals for CF, BDCM, DBCM and BF are 70 µg/l, 0.0 µg/l, 60 µg/l and 0.0 µg/l, respectively (EPA 2018a). In the European Union (EU) (Union 2014) and Turkey (Alver et al. 2018), the MCL for THMs is 100 µg/l. In Iran, according to the national standard for drinking water (1053), the MCL for THMs is 80 µg/l (ISIRI 2012). The World Health Organization (2017) have also established drinking water guideline values for each THM species: CF, BDCM, DBCM, and BF levels should not exceed 300 µg/l, 60 µg/l, 100 µg/l and 100 µg/l, respectively, and the sum of the ratio of each compound to its MCL should not exceed 1 (see Eq 1 below), where C is concentration and GV is guideline value.

$$\frac{C(BF)}{GV(BF)} + \frac{C(DBCM)}{GV(DBCM)} + \frac{C(BDCM)}{GV(BDCM)} + \frac{C(CF)}{GV(CF)} \leq 1 \quad (1)$$

Measurements of DBPs levels in drinking water have been carried out regularly worldwide (Abbas et al. 2014; Furst et al. 2019; O'Driscoll et al. 2018; Yao et al. 2019). In Iran, a number of studies (Ahmadi and Ramavandi, 2014; Alipour and Ghanbarnejad, 2014; Babaei et al. 2015; Ghoochani et al. 2016; Kalankesh et al. 2019; Mohammadi et al. 2019; Mohammadi et al. 2016; Nadali et al. 2019; Ramavandi and Asgari, 2012) have investigated THMs formation potential, THMs concentrations in tap drinking water and related health risks in different parts of the country. These studies found THMs levels ranging from 10 ppb to more than 100 ppb.

Individuals can be exposed to THMs through ingestion, dermal contact, or inhalation of tap water. A 2001 study (Chowdhury et al.) in Canada reported that the relative risk (RR) of THMs- and HAAs-induced cancer was 2.1 (95% CI 0.67, 0.82). However, despite the high RR, DBPs are not presumed to be significantly associated with cancer. In the European Union, 5708 (95%CI 2,940-8,318) cases of bladder cancer are attributed to THMs exposure each year, varying from 0 cases in Denmark to 1,498 cases in Spain (Chowdhury et al., 2001). The underlying mechanism of how

BDPs may increase risk of cancer is not known; perhaps exposure to multiple THMs species may prompt additive effects, or there may be interaction (either synergistic or antagonistic) between the different THMs species (Hsu et al. 2001). The main influential factors appear to be duration and recurrence of washing, body surface area, and ingestion rate of drinking water.

The International Agency for Research on Cancer (IARC) has classified CF and BDCM as Group 2B, and DBCM and BF as Group 3 (Grosse et al. 2011). CF is usually found in the highest concentrations and much information is available about health issues arising from this compound. Based on the limited evidence of carcinogenicity in humans but sufficient evidence of carcinogenicity in experimental animals, the EPA considers CF “likely to be carcinogenic above a specified dose but not likely to be carcinogenic below that dose because a key event in tumor formation does not occur below that dose (L/N categories)”(USEPA 2018a).

The EPA considers BDCM “likely to be carcinogenic to humans” (L) (New Hampshire 2006). BDCM evaporates fairly easily so does not usually exist as a liquid in the environment. The most likely means of exposure to BDCM is through drinking chlorinated water. Animal studies show that almost all BDCM enters the body by moving from the stomach or intestines into the blood. The effects of BDCM is dependent on the dose applied. In animals, the main effects are injuries to the liver and kidney, where effects can occur within a short time. High concentrations of BDCM can also affect the brain, resulting in incoordination and sleepiness. Animal studies (Pardakhti et al. 2011; New Hampshire 2006; WHO 2005) found that BDCM ingestion (by food and water at levels of 190 parts per million and greater) for several years led to cancers of the liver, kidney, and intestines. It is not yet known what level of BDCM exposure is required to produce harmful health effects in humans. The EPA also considers BF “likely to be carcinogenic to humans” (New Hampshire 2006).

There is clearly a need to more deeply understand potential relationships between THMs levels and risks to human health (de Castro Medeiros et al. 2019). A major challenge, however, is for the risk assessor to effectively communicate the results of an analysis of variability and uncertainty. The Monte-Carlo Simulation (MCS) technique is widely used for probabilistic risk assessment (PRA) modeling due to its ability to quantify and evaluate uncertainty levels. Previous studies (Huang et al. 2010; Abbasnia et al. 2018) used MCS to obtain empirical distributions of health risks from probability distributions of input parameters: these distributions were calculated by repeated sampling and computing based on risk assessment models. The most recent study considering potential health and carcinogenic risks due to exposure to THMs through drinking water was carried out in Ardabil, located in North-Western Iran (Sadeghi et al. 2019). To the best of our knowledge, no study has considered seasonal variations in THMs concentrations and potential related health risks in Tabriz.

The present study, therefore, investigated temporal and spatial variations in concentrations of THMs in tap drinking water within Tabriz. The carcinogenic and non-carcinogenic risks to the population due to oral, dermal and/or inhalation exposure to THMs were evaluated using the Monte Carlo simulation technique.

2. Materials and Methods

2.1. Study area and sampling procedure

With a population of over 1.6 million people, Tabriz is the capital city of the East Azerbaijan Province located in northwest Iran (SCI 2016). Tabriz's drinking water supply comes from three major sources. The city requires an approximate flow rate of 4500 l/s (East Azerbaijan Regional Water Authority 2020).

123 The Nahand Water Reservoir and Treatment Plant Facilities are located in the northeastern part of
124 the Eynali Mountains. The facility has a capacity of 1200 l/sec (425-700 l/s, practical
125 performance), supplying almost 20% of Tabriz's water demand. This plant has a conventional
126 water treatment system including prechlorination, coagulation with ferric chloride (40%) using a
127 pulsator system, gravity filtration, and final disinfection by chlorine. Treated water is pumped to
128 reservoirs located in the city and distributed to central, northern and northeastern parts of the city.
129 Zarrinehrood (a river) Water Transfer Line, a second water source, provides approximately 60%
130 of Tabriz's public water. The line capacity is 5500 l/sec. Nearly half of the supply is designated
131 for drinking purposes in Tabriz; the rest is consumed by industrial users as well as small towns in
132 the suburb area. This water is treated at the Miyandoab Treatment Facilities. As with the Nahand
133 Treatment Facilities, the Miyandoab Treatment Facilities use a conventional water treatment
134 including prechlorination, coagulation, and flocculation with ferric chloride (40%) and poly
135 electrolyte (PE), gravity filtration and postchlorination. The treated water is then pumped 177 km
136 to Tabriz and is shared between different reservoirs located in the south of the city and distributed
137 by gravity. This water source predominantly supplies Tabriz's central, western and southwestern
138 regions.

139 A collection of 64 wells located in the east of the city's Saeidabad and Hervy regions are
140 considered a third source of drinking water. The wells provide 1200-1700 l/sec, accounting for
141 more than 20% of water demand. The only treatment applied to this water source is disinfection
142 by chlorine. After pumping, water is transferred to reservoirs, where it mixes with water from the
143 first two sources. The mixed water enters the distribution system in the east and southeast of
144 Tabriz.

Based on these three water sources, the city can be divided into four distinct zones. Zone I water is solely supplied from Nahand; Zone II water is solely supplied from Zarrinehrood; Zone III water is solely supplied from wells; Zone IV water is supplied by reservoirs fed by a mixture of sources. In this study, electric conductivity (EC) of water was considered a criterion for the zoning of the city; therefore, sampling points with similar EC values were located in the same zone. In most areas of the city, a mixture of surface and groundwater was collected, apart from certain areas in the north, northeast and south of the city.

Sample collection, preservation, transfer, preparation and analysis were carried out according to standard methods for water and wastewater examination (Clescerl et al. 1999). A total of 66 samples were collected from the Tabriz drinking water distribution network in January 2016 (winter) and June 2016 (summer). Figure 1 shows sampling points during this study. Each sample was collected in an amber glass bottle (135 ml). Tap water was allowed to flow over/into the bottle for 4-5 minutes until the bottle was full. Then 0.5 ml of 10% sodium thiosulfate solution was added to neutralize residual chlorine, and the sample was stored in a cold box at 4°C. Analysis was conducted within ten days of sample collection.

2.2. Analysis methods and Statistical analysis

Static headspace gas chromatography (GC) (Varian CP 3800, USA) using an electron capture detector (ECD) and a DB-1701 capillary column (30m × 0.25mm × 0.25mm, Optima, Germany) was used to measure the levels of THMs in each sample. The injector temperature and detector temperature of the GC were 250°C and 290°C, respectively. The oven was maintained at 35°C for 11.1 min, before being ramped (9°C/min) to 100°C and then further ramped (6°C/min) to 140°C. Calibration curves for each compound were prepared separately using standard solutions of THMs (CF, BF, BDCM, DBCM). Half of each 10 ml sample was transferred to a special vial capped with

PTFE. Prior to the injection, each vial was incubated at 70°C for 5 min. A volume of 300 µl from the headspace of each vial was injected into the GC, which used a gas mixture of 95% argon and 5% nitrogen at a flow rate of 25 ml/min. The detection limits of THMs for CF, BDCM, DBCM and BF were 3.2 µg/l, 2.5 µg/l, 0.9 µg/l and 0.3 µg/l, respectively. The linearity of this method was evaluated for soluble standards at concentrations of 0.1 - 300 µg/l.

During the study, temperature, EC, residual free chlorine, total chlorine, pH, alkalinity and hardness of calcium were also determined. A calibrated conductivity and TDS meter (Model AZ 8361) was used to determine temperature, EC and TDS. Residual free chlorine, total chlorine, pH, alkalinity and hardness of calcium were analyzed using a Pro-7 Color Q portable device (Chestertown, Maryland 21620 USA).

For quality control and to ensure the precision of the analysis, each assay was tested twice; relative standard errors (RSE) less than 10% were accepted. To control interferences and ensure the procedures' accuracies, calibration checks were performed and standard solutions and laboratory reagent blanks were analyzed after every 10 samples.

In addition to descriptive statistics and determination of mean, minimum, maximum and standard deviation of parameters, statistical tests were done using SPSS software (version 21). Shapiro-Wilk test (K-S) was used to check the normality of the data. Skewness and kurtosis were calculated for all parameters. One-way ANOVA and Tukey tests were used to compare mean concentrations of THMs between different sampling locations. One-sample t-tests were used to compare the results with standard values; independent samples t-tests were used to compare mean concentrations of THMs between seasons. Pearson's correlation coefficient was calculated to determine the correlation between determined parameters.

Spatial analysis of the THMs concentrations was done through ArcGIS 10.1 (supplier info here).
The Kriging interpolation method was used to generate independent raster layers for THMs.

2.3. Risk assessment methods

As indicated by EPA guidelines, the following steps must be taken to assess the risk of cancer: collection of data sets, assessment of exposure and toxicity, risk characterization and risk management (USEPA 1992).

The cancer risks from THMs were calculated using chronic daily intake (CDI) and the corresponding slope factor (SF) (USEPA 2018b; Wang et al. 2019). The CDI for each exposure route, i.e. oral, dermal, and inhalation, was calculated using Eqs. (2)-(4) as follows:

$$CDI_{ingest,i} = \frac{C_{w,i} \times IR \times EF \times ED \times CF}{BW \times AT} \quad (2)$$

$$CDI_{derm,i} = \frac{C_{w,i} \times SA \times F \times PC \times ET \times EF \times ED \times CF}{BW \times AT} \quad (3)$$

$$CDI_{inhal,i} = \frac{C_{a,i} \times VR \times AE \times ET \times EF \times ED \times CF}{BW \times AT} \quad (4)$$

$C_{a,i}$ values were taken from the resistance model recommended by Little (Little 1992)

$$C_{a,i} = (C_o + C_t)/2 \quad (5)$$

C_o is the initial value of THMs, taken to be zero in this case, and C_t is the concentration of THMs at any time (minute), assumed to be 10 min in this study. $C_{a,i}$ is determined from C_t according to previous studies (Amjad et al. 2013; Pardakhti et al. 2011).

A previous study (Chowdhury et al. 2001) assumed total water ingestion was 3.0 liters per capita per day. This study assumed ingestion was 1.8 liters per capita per day. Other input values used in exposure calculations and risk assessments are provided in Table S1.

Cancer risk characterization

The lifetime cancer risk (LTCR) for each species of THMs from different exposure pathways was estimated using Eq. (6):

$$Total\ LTCR = CDI_{inges,i} \times SF_{inges,i} + CDI_{derm,i} \times SF_{derm,i} + CDI_{inhal,i} \times SF_{inhal,i} \quad (6)$$

SF is the upper-bound assessment of LTCR. This coefficient was used to evaluate the possibility of developing cancer as a result of exposure to a chemical substance (Wang et al. 2019).

The values assigned to the SF coefficients were taken from the EPA (Cal/EPA) and Integrated Risk Information System (CEPA 2010; USEPA 2013). $SF_{inges,i}$ and $SF_{derm,i}$ values for chloroform, BDCM, DBCM and bromoform were 0.0079 mg/kg/day, 0.084 mg/kg/day, 0.062 mg/kg/day and 0.0061 mg/kg/day, respectively. $SF_{inhal,i}$ values for chloroform, BDCM, DBCM and bromoform were 0.0039 mg/kg/day, 0.094 mg/kg/day, 0.13 mg/kg/day and 0.081mg/kg/day, respectively (IRIS 2009).

Four classes of cancer risk were created: negligible risk ($LTCR < 10^{-6}$), acceptable low risk ($1 \times 10^{-6} \leq LTCR < 5.1 \times 10^{-5}$), acceptable high risk ($5.1 \times 10^{-5} \leq LTCR < 10^{-4}$), and unacceptable risk ($LTCR \geq 10^{-4}$) (Legay et al. 2011).

Non-cancer risk assessment

The hazard index (HI) was used to estimate the non-carcinogenic risks due to ingestion and dermal exposure to THMs (see Eqs 7 and 8):

$$HI_{inges,i} = CDI_{inge,i} / RfDi \quad (7)$$

$$HI_{derm,i} = CDI_{derm,i} / RfDi \quad (8)$$

The CDI value for risk due to inhalation is significantly less than the risk due to ingestion or dermal contact; therefore, inhalation risk was ignored and HI was calculated only for ingestion and dermal exposure (Wang et al. 2019).

This study used a Monte Carlo simulation (Crystal Ball Version 11.1.2.3, Decisioneering, Inc., Denver, CO, USA) to conduct a sensitivity analysis and incorporate an uncertainty risk assessment model. The simulation used 10,000 trials to produce a credible risk distribution, which was considered sufficient for certifying the stability of the results (Abbasnia et al. 2018).

3. Results and discussion

3.1. Summary of the Monitoring Data

The concentrations of THMs, EC, temperature, hardness, free and combined chlorine, and alkalinity for both winter and summer are shown in Table 1. All analyzed parameters were symmetrically distributed (Skewness number), with the exception of DBMC and BF. The distributions of residual chlorine, CF, DBCM and BF were not normal (Kurtosis number). According to the Shapiro-Wilk test, temperature, pH, alkalinity and hardness were all normal, whereas the remainder of the parameters were not.

Mean EC values for the Nahand Reservoir and Zarrinehrood River were 1000 $\mu\text{S}/\text{cm}$ and 500 $\mu\text{S}/\text{cm}$, respectively, while EC values from the well samples varied between 292 $\mu\text{S}/\text{cm}$ and 1370 $\mu\text{S}/\text{cm}$, indicating different TDS contents. TDS was calculated by multiplying the EC by a factor of 0.5 to 1.0; hence, the mean TDS value of Tabriz drinking water was about 400 mg/l, meaning the water was considered acceptable according to WHO guidelines (WHO 2017).

Samples varied between soft and very hard water (Table 1). As expected, THMs were generally present in Tabriz's drinking water (some samples had no THMs detected). THMs concentration was as high as 683 $\mu\text{g}/\text{l}$, with an average of $133.2 \pm 179.5 \mu\text{g}/\text{l}$ for both seasons, which was much higher than the concentrations recommended by the EPA (80 $\mu\text{g}/\text{L}$) (USEPA 2018a), WHO (WHO 2017) or Iranian national standard (100 $\mu\text{g}/\text{L}$) (ISIRI 2012).

Table 2 provides THMs concentrations which have been recorded in drinking water in other countries. Tabriz's mean THMs concentration was lower than the THMs concentration in Kallyanpur (Bangladesh), Ardabil (Iran), Barcelona (Spain), Rawalpindi (Pakistan) and Islamabad (Pakistan). The lowest mean THMs concentrations were recorded in the EU-28: $11.9 \pm 11.1 \mu\text{g/L}$, ranging from $0.0\mu\text{g/l}$ in Denmark to $66.2\mu\text{g/l}$ in Cyprus (Kogevinas et al. 2018). The highest mean THMs concentrations were recorded in Kallyanpur (Bangladesh).

3.2. Temporal and Spatial Assessment of THMs

Comparison of seasons

Discussions of Individual Results Parameters

Tabriz's mean THMs concentrations for winter and summer were $10.2 \pm 9.3\mu\text{g/l}$ and $252 \pm 185.9 \mu\text{g/l}$, respectively (Figure S1). Therefore, the mean concentration during the summer was 25 times that during the winter. In comparison, the mean THMs concentrations in Ardabil (northwest Iran), were $70.87 \pm 39.33 \mu\text{g/l}$ and $315.85 \pm 180.68 \mu\text{g/l}$, in the winter and spring, respectively (Sadeghi et al., 2019). Therefore, Ardabil had higher THMs concentrations than Tabriz, especially in the winter.

Given that the same water treatment method was used during the winter and summer, this seasonal difference in Tabriz's THMs concentrations may be attributed to variations in source water quality. These variations appeared to be particularly attributed to the NOM content and somewhat attributed to the chlorine dose in pre-chlorination (Pourmoghaddas and Stevens, 1995). In Tabriz, more NOM (e.g. allochthonous organic matter) and other contaminants (e.g. Br-) were transported from the water catchment areas to the water reservoirs due to more surface runoff (precipitation), algal growth and biomass production in the summer than in the winter. In addition to having more

THMs precursors in the summer, the water treatment facilities used more chlorine during pre-chlorination to control algal growth and reduce the microbial burden.

Temperature is another influential factor in the formation of THMs. The mean water temperature was 11.4 ± 0.5 °C (CI 95%: 10.2-12.6 °C) in the winter, and 20.7 ± 0.4 °C (CI 95%: 19.7-21.7 °C) in the summer. The reaction rate between chlorine and NOM to form THMs is slower at lower temperatures. A study conducted in Scotland (Valdivia-Garcia et al. 2016) concluded that ambient temperature was the primary predictor for THMs formation in potable water; every 1.8°C increase in temperature resulted in a 39% increase in THMs concentrations.

Despite the difference in reaction rate, there is debate about whether THMs proliferation is greater in winter or summer. Four studies (Williams et al. 1998; Rodriguez et al. 2004; Babaei et al. 2015; Sadeghi et al. 2019) suggested that THMs compounds were more prolific in the summer. A study (Deng et al., 2008) in China found that THMs and HAAs levels in drinking water were generally higher in the summer than in the winter, which is consistent with the present study. On the other hand, a study (Ates et al. 2007a; Ates et al. 2007b) conducted in Turkey found that 16 of the 29 surface water sources had the highest THMs formation potentials during winter. Similarly, a recent study (Zhou et al. 2019) in China reported higher levels of THMs in winter than in summer or spring, and higher concentrations of HAAs, HANs, HKs, and HNMs in the summer than in the winter or spring.

Discussions of Correlations between Individual Results Parameters

Temperature and pH were the only two parameters which showed significantly differences in the two seasons ($p = X, Y$, respectively).

300 No correlations were observed between THMs concentration and EC, alkalinity, hardness, and
301 residual chlorine of water. Moderate-to-good correlations were observed between total THMs, CF
302 and BDCM concentrations with temperature (CI=99%, $r = 0.72, 0.74, 0.69$, respectively).
303 Moderate correlations were found between DBCM and CF with alkalinity ($r = 0.55, 0.50$,
304 respectively). Moderate correlations were found for TTHMs, BDCM and DBCM with pH ($r = 0.6$,
305 $0.56, 0.62$, respectively).

306 Another study (Sadeghi et al. 2019) found correlations between pH and concentrations of THMs
307 and HAAs: THMs decreased and HAAs increased as pH decreased. Lee et al. (2019) found that
308 CF concentration decreased as TDS concentration increased; the reaction of the cation (Na^+)
309 preferentially with the functional groups of the organic material influenced the formation of
310 THMs.

311 The order of concentration of all types of THMs was $\text{CF} > \text{BF} > \text{BDCM}$ and DBCM during the
312 winter and $\text{BDCM} > \text{CF} > \text{DBCM} > \text{BF}$ during the summer (Figure S2). This finding was consistent
313 with the Ardabil study, which found CF comprised approximately half of the THMs in winter
314 whereas, in the spring, 82% of THMs were BDCM and only 10% were CF (Sadeghi et al. 2019).
315 Amjad et al. (2013) in Pakistan also found that >85% of THMs were CF. O'Driscoll et al. (2018)
316 in Ireland, Chang et al. (2010) in Taiwan, and Ahmed et al. (2019) in Bangladesh also found that
317 the majority of THMs in drinking water were CF.

318 Next, the WHO fraction calculation (Eq. 1) was conducted. During the winter season, the ratio of
319 measured-to-guideline concentrations were <1 in all drinking water samples (as WHO requires).
320 However, in the summer, approximately 75% of the water samples had ratios >1 , up to 10.29 times
321 higher. These high ratios were strongly influenced by high concentrations of BDCM, especially
322 since BDCM has a lower guideline concentration ($60 \mu\text{g/l}$) compared to the rest of the compounds.

Comparison of water source locations

The mean THMs concentration in Tabriz was $133.7 \pm 180.7 \mu\text{g/l}$ (Figure 2). THMs concentration was highest in Zone 1: $165 \pm 184 \mu\text{g/l}$, CI 95%= 73.6 - 256.6 $\mu\text{g/l}$. Concentrations in Zone II and Zone IV were similar: $131.4 \pm 187 \mu\text{g/l}$, CI 95%= 43.9 - 219 $\mu\text{g/l}$, and $129.8 \pm 188 \mu\text{g/l}$, CI 95%= 47.6 - 212 $\mu\text{g/l}$, respectively. However, in Zone III, where groundwater was the exclusive source of drinking water, the average THMs concentrations were much lower: $60.8 \pm 149 \mu\text{g/l}$, CI 95%= -95.5 - 217 $\mu\text{g/l}$.

In terms of THMs types, as with surface water, BDCM was also predominant in groundwater. ANOVA tests showed a significant difference between CF, DBCM and BF concentrations and EC level ($p < 0.05$) between the zones. However, for BDCM and TTHMs, the differences were not significant ($p > 0.05$). The highest THMs concentrations were observed in zones where water was supplied from surface water. Where pre-chlorination was performed as the first treatment stage, there were no other treatment options (e.g. granular activated carbon) for removal of formed DBPs. Total THMs concentrations during both seasons in all four zones are shown in Figure 3. In some small parts of the city, THMs concentrations were lower than the MCL (80 $\mu\text{g/l}$) set by the EPA and Iran. Most of Tabriz had twice as much THMs concentration as the EPA recommendation. THMs concentrations were highest in the central and western parts of Tabriz (160- 320 $\mu\text{g/l}$ and $> 320 \mu\text{g/l}$, respectively). THMs concentrations were relatively lower in the east, due to the dominant use of wells in this area.

Interestingly, there appeared to be a potential link between age of the water distribution system (i.e., pipelines) and high THMs concentrations. Zone 1 had the oldest pipelines and also the highest THMs concentration. Mohammadi et al. (2020) also reported significant differences between

THMs concentrations in the old and new water distribution systems of Yazd in central Iran. Perhaps the older pipelines result in more precipitation of chemical and biological compounds, more formation of biofilm layer in the water pipes and poorer water quality.

3.3. Multi-pathway evaluations of LTCRs for THMs

Ingestion route

The estimated cancer risk and CDI calculated for oral ingestion are shown in Table S2 and Figure 4. The LTCRs due to ingesting CF and total THMs were calculated to be $<10^{-6}$ and $<10^{-4}$, respectively, meaning they were in the negligible and acceptable risk categories. Of the four THM species, DBCM and BDCM made the highest contributions to LTCR, followed by CF.

These results were consistent with studies investigating the public water supply and reclaimed water in China (Niu et al. 2014; Wang et al. 2019).

The LTCR calculated in this study was several times lower than the LTCR reported in similar studies (Karim et al. 2011; Pardakhti et al. 2011; Wang et al. 2019). According to Krasner and Wright (2005), boiling water for two minutes causes more than 90% of THMs to evaporate, decreasing the LTCR. Therefore, boiling could be deemed a simple and appropriate means for purifying THMs from drinking water.

Dermal absorption

The second route for THM penetration into the body is skin contact during showering, bathing, swimming, and general washing activities. The cancer risks and CDI of THMs from contact with the dermal route are exhibited in Table S2 and Figure 4. The highest risk value between four THMs belonged to BDCM and DBCM with 10^{-5} to 10^{-7} respectively. This result is consistent with the results of study conducted in China (Wang et al. 2019). Nevertheless, in a research carried out in

India, chloroform was reported to be the highest compound for cancer risk from dermal route exposure (Kumari et al. 2015). The total risk of dermal exposure was determined to be in the negligible risk and acceptable high-risk category in the study periods. In Iran, females may run a higher risk from high dermal exposure as a result of investing more time washing. Boiling water is not effective for reducing risk from THMs in dermal and inhalation exposure. Machine washing clothes and dishes is the best recommendation for diminishing the risk of THMs by dermal content (Krasner and Wright, 2005).

Inhalation exposure

The inhalation exposure of THMs is related to air inhaled during various water usages like showering, pre and post-cooking activities and exposure during cooking processes. The cancer risks and CDI of THMs from contact with the inhalation route are given in Table S2 and Figure 4. The main risk value from among the four THMs were attributed to BDCM and DBCM in winter and spring seasons, respectively. This result is affirmed by other studies (Pardakhti et al. 2011; Wang et al. 2019). The reason is related to the cancer slope factor (CSF) since its value is extremely low for chloroform and higher for CHBrCl_2 and CHBr_2Cl . Furthermore, the inhalation route for THMs had the highest cancer risk from among the three THM exposure routes. This finding was reported in previous studies as well (Karim et al. 2011; Pardakhti et al. 2011; Wang et al. 2019). The best recommendation for diminishing (USEPA 2018b) the risk of THMs by inhalation content is the application of a suite fan in indoor places for air ventilation.

Non-cancer risk assessment

The HI levels through ingestion and dermal routes for January and June are demonstrated in Figure 5. According to the findings, the ingestion contact has more HI values than the dermal contact. Likewise, bromodichloromethan had the highest average of HI values from among the four THMs

compounds. Similar results were reported in previous studies (Karim et al. 2011; Kumari et al. 2015; Pardakhti et al. 2011; Wang et al. 2019). Accordingly, non-cancer risk of THMs exposure may lead to diseases including neurobehavioral effects, jaundice, enlarged liver, and subjective central nervous system effect (Amjad et al. 2013). As prescribed by the USEPA, for a hazard index greater than 1, there is concern over potential toxicity (USEPA 2000). HI value was less than 1 for TTHM in two seasons through oral and dermal routes, though it was in the allowed range of risk level for the contact route in this study.

Sensitivity analysis

Although THMs risk assessment appears to be an acceptable method, its results contain uncertainties which are caused by measurements, population exposure variables, and day-to-day or place-to-place changes in risk factors (Kim et al., 2002). Therefore, risk assessment studies usually need supplemental research. In order to determine the most important factor for cancer risk due to THMs' exposure, a sensitivity analysis was performed. As indicated by Figure S3, all factors for the calculation of CDI were surveyed for uncertainty analysis. The concentration of THMs for ingestion exposure, exposure frequency and ventilation rate for dermal and inhalation exposure, respectively had the the highest positive impact on CDI and cancer risk, as indicated by the results. Body weight had a reverse correlation with CDI value in oral, dermal and inhalation contact. However, the value of CDI in ingestion exposure was directly influenced by THM concentration.

4. Conclusions

Considering the health risk due to exposure to THMs in drinking water and lack of information about DBPs, further study is required for a better understanding of the problem and its management. The present study tried to determine the concentration of THMs in drinking water of NW city, Tabriz during cold and hot seasons for the first time. Average THMs concentration

was found to be $133.2 \pm 179.5 \mu\text{g/l}$, which is higher than the US ($80 \mu\text{g/L}$) and EU standards ($100 \mu\text{g/L}$). Also, the average levels are higher than in other part of Iran except Ardabil, another city located in the NW.

Insufficiencies of the present study comprise a lack of sampling and analysis during all seasons as well as lack of analysis of key parameters such as organic matter, bromine, nitrogen compounds, other DBPs e.g. HAA and other novel compounds. Acknowledging the results, there is a great need to investigate DBP formation along with all the parameters influencing its formation throughout the water treatment processes of the Tabriz drinking water supply. Furthermore, it seems necessary to study epidemiologically all health effects induced by exposure to DBPs, especially THMs.

Finally, based on the results from this study, there are perceptible levels of THMs in the distribution network water of Tabriz. Additionally, attributed health effects of THMs may lead to some health risks in consumers. In spite of the fact that the estimated non-cancer risk of THMs were under the permissible recommended level, a cancer risk still exists as a result of significant levels of THMs at some points. Drinking water supply companies need to adopt more inclusive responsibility for the monitoring of THMs and organic matter in the distributed water along with to warrant the accuracy and precision of their analysis.

5. Declarations

Compliance with ethical standards

This study was approved by the Research Ethics Committee of Tabriz University of Medical Sciences (Ethic code of IR.TBZMED.REC.1395.241).

Consent for publication

The manuscript does not contain data from any individual person so consent for publication is “not applicable”.

Availability of data and materials

All data generated or analysed in this study are included in this published article [and its supplementary information files].

Conflict of interest

The authors declare there is no conflict of interest.

Funding

This research was funded by the Vice Chancellor for Research at Tabriz University of Medical Sciences, Tabriz, Iran [grant number: 95-3-3/14001].

Authors' contributions

MM: Design of study, Data curation, Writing - original draft and correspondence, **MA:** Writing - review & editing, **HA:** THMs analysis, Review & editing, **AM:** Risk assessment, Review & editing, **SA:** Sampling, Data collection & analysis, **SNM:** Data curation, Revision of paper, **SHM:** Spatial analysis and Mapping of THMs concentration in Tabriz DWS. All authors read and approved the final manuscript.

Acknowledgments

We appreciate Mr. Masoud Javadpour's help with sample collection, and also Mr. Ali Rahimi's (Tabriz County, Environmental Health Department) support with onsite measurements of some parameters of water samples.

References

- Abbasnia, A., Ghoochani, M., Yousefi, N., Nazmara, S., Radfard, M., Soleimani, H., Yousefi, M., Barmar, S., Alimohammadi, M., 2018. Prediction of human exposure and health risk assessment to trihalomethanes in indoor swimming pools and risk reduction strategy. *Human and Ecological Risk Assessment: An International Journal*, 1-18.
- Ahmadi, M., Ramavandi, B., 2014. The formation potential of haloacetonitriles in the Dez River water, Iran. *Environmental technology* 35, 2347-2355.
- Ahmed, F., Khan, T.A., Fakhruddin, A.N.M., Rahman, M.M., Mazumdar, R.M., Ahmed, S., Imam, M.T., Kabir, M., Abdullah, A.T.M., 2019. Estimation and exposure concentration of trihalomethanes (THMs) and its human carcinogenic risk in supplied pipeline water of Dhaka City, Bangladesh. *Environmental Science and Pollution Research* 26, 16316-16330.
- Alipour, V., Ghanbarnejad, A., 2014. Trihalomethanes formation potential in water supply system of Bandar Abbas (Southern Iran): from source to distribution network. *Journal of Health Sciences & Surveillance System* 2, 36-41.
- Alver, A., Baştürk, E., Kılıç, A., 2018. Disinfection By-Products Formation Potential Along the Melendiz River, Turkey; Associated Water Quality Parameters and Non-Linear Prediction Model. *International Journal of Environmental Research* 12, 909-919.
- Amjad, H., Hashmi, I., Rehman, M.S.U., Awan, M.A., Ghaffar, S., Khan, Z., 2013. Cancer and non-cancer risk assessment of trihalomethanes in urban drinking water supplies of Pakistan. *Ecotoxicology and environmental safety* 91, 25-31.
- Ates, N., Kaplan, S.S., Sahinkaya, E., Kitis, M., Dilek, F.B., Yetis, U., 2007a. Occurrence of disinfection by-products in low DOC surface waters in Turkey. *Journal of hazardous materials* 142, 526-534.
- Ates, N., Kitis, M., Yetis, U., 2007b. Formation of chlorination by-products in waters with low SUVA—correlations with SUVA and differential UV spectroscopy. *Water research* 41, 4139-4148.
- Babaei, A.A., Alavi, N., Hassani, G., Yousefian, F., Shirmardi, M., Atari, L., 2015. Occurrence and related risk assessment of trihalomethanes in drinking water, Ahvaz, Iran. *Fresenius Environmental Bulletin* 24, 4807-4815.
- CEPA, 2010. Public Health Goal for Trihalomethanes in Drinking Water. (<http://www.calepa.ca.gov>).
- Chang, H.H., Tung, H.H., Chao, C.C., Wang, G.S., 2010. Occurrence of haloacetic acids (HAAs) and trihalomethanes (THMs) in drinking water of Taiwan. *Environmental Monitoring and Assessment* 162, 237-250.
- Chowdhury, U.K., Rahman, M.M., Mandal, B., Paul, K., Lodh, D., Biswas, B.K., Basu, G.K., Chanda, C.R., Saha, K.C., Mukherjee, S.C., 2001. Groundwater arsenic contamination and human suffering in West Bengal, India and Bangladesh. *Environ Sci* 8, 393-415.
- Clescerl, L., Greenberg, A., Eaton, A., 1999. Standard methods for the examination of water and wastewater. Amer Public Health Assn; 20th edition (January 1999).
- de Castro Medeiros, L., de Alencar, F.L.S., Navoni, J.A., de Araujo, A.L.C., do Amaral, V.S., 2019. Toxicological aspects of trihalomethanes: a systematic review. *Environmental Science and Pollution Research* 26, 5316-5332.
- Deng, Y., Wei, J., Wang, W., 2008. Study for distribution level of disinfection byproducts in drinking water from six cities in China. *Wei sheng yan jiu= Journal of hygiene research* 37, 207-210.
- East Azerbaijan Regional Water Authority, 2020. accessed August 2020, <https://azarwater.ir/>.
- Furst, K.E., Coyte, R.M., Wood, M., Vengosh, A., Mitch, W.A., 2019. Disinfection Byproducts in Rajasthan, India: Are Trihalomethanes a Sufficient Indicator of Disinfection Byproduct Exposure in Low-Income Countries? *Environmental science & technology* 53, 12007-12017.

516 Ghoochani, M., Rastkari, N., Heibati, B., Ghozikali, M.G., Jeddi, M.Z., Fawell, J., Nazmara, S., Mahvi,
 517 A.H., 2016. Risk assessment of haloacetic acids in the water supply of Tehran, Iran. *Water Science*
 518 *and Technology: Water Supply* 17, 958-965.
 519 Hendricks, D., 2016. *Fundamentals of water treatment unit processes: physical, chemical, and biological.*
 520 Crc Press.
 521 Hsu, C.-H., Jeng, W.-L., Chang, R.-M., Chien, L.-C., Han, B.-C., 2001. Estimation of potential lifetime
 522 cancer risks for trihalomethanes from consuming chlorinated drinking water in Taiwan.
 523 *Environmental Research* 85, 77-82.
 524 Huang, C.-H., Chen, C.-Y., Wang, G.-S., 2019. Temperature dependence of characteristics of organic
 525 precursors, bromide, and disinfection byproduct formation. *Science of The Total Environment* 662,
 526 746-754.
 527 Integrated Risk Information System (IRIS), 2009. USEPA (Electronic data base). Web link: [http://www.](http://www.epa.gov/iris/)
 528 [epa.gov/iris/](http://www.epa.gov/iris/).
 529 ISIRI, 2012. *Drinking water - Physical and chemical specifications*, in: Iran, I.o.S.a.I.R.o. (Ed.), 5th edition
 530 ed. Amendment no.1.
 531 Kalankesh, L.R., Zazouli, M.A., Susanto, H., Babanezhad, E., 2019. Variability of TOC and DBPs (THMs
 532 and HAA5) in drinking water sources and distribution system in drought season: the North Iran
 533 case study. *Environmental technology*, 1-28.
 534 Karim, Z., Mumtaz, M., Kamal, T., 2011. Health risk assessment of trihalomethanes from tap water in
 535 Karachi, Pakistan. *Journal of the chemical society of Pakistan* 33, 215-219.
 536 Kim, Y.M., Harrad, S., Harrison, R.M., 2002. Levels and sources of personal inhalation exposure to volatile
 537 organic compounds. *Environmental science & technology* 36, 5405-5410.
 538 Kogevinas, M., Evlampidou, I., Rojas-Rueda, D., Font-Ribera, L., Costet, N., Pearce, N., Vineis, P.,
 539 Villanueva, C., 2018. Bladder Cancer Burden from Exposure to Trihalomethanes in Drinking
 540 Water in the European Union, ISEE Conference Abstracts.
 541 Krasner, S.W., Wright, J.M., 2005. The effect of boiling water on disinfection by-product exposure. *Water*
 542 *research* 39, 855-864.
 543 Kumari, M., Gupta, S., Mishra, B., 2015. Multi-exposure cancer and non-cancer risk assessment of
 544 trihalomethanes in drinking water supplies—A case study of Eastern region of India. *Ecotoxicology*
 545 *and environmental safety* 113, 433-438.
 546 Lee, S., Kwak, Y., Hong, S., 2019. Effects of TDS on formation of THMs in drinking water treatment.
 547 *Journal of Korean Society of Water and Wastewater* 33, 225-234.
 548 Legay, C., Rodriguez, M.J., Sadiq, R., Sérodes, J.B., Levallois, P., Proulx, F., 2011. Spatial variations of
 549 human health risk associated with exposure to chlorination by-products occurring in drinking water.
 550 *Journal of environmental management* 92, 892-901.
 551 Little, J.C., 1992. Applying the two-resistance theory to contaminant volatilization in showers.
 552 *Environmental science & technology* 26, 1341-1349.
 553 Mohammadi, A., Ebrahimi, A.A., Ghanbari, R., Faraji, M., Nemati, S., Abdolahnejad, A., 2019. Data on
 554 THMs concentration and spatial trend in water distribution network (a preliminary study in center
 555 of Iran). *MethodsX* 6, 760-763.
 556 Mohammadi, A., Faraji, M., Ebrahimi, A. A., Nemati, S., Abdolahnejad, A., & Miri, M., 2020. Comparing
 557 THMs level in old and new water distribution systems; seasonal variation and probabilistic risk
 558 assessment. *Ecotoxicology and Environmental Safety*, 192, 110286.
 559 Mohammadi, A., Miri, M., Ebrahimi, A., Khorsandi, H., Nemati, S., 2016. Monitoring of THMs
 560 concentration in Isfahan water distribution system and zoning by GIS, a case study in the center of
 561 Iran. *Iranian journal of health, safety and environment* 3, 421-427.
 562 Nadali, A., Rahmani, A., Asgari, G., Leili, M., Norouzi, H.A., Naghibi, A., 2019. The Assessment of
 563 Trihalomethanes Concentrations in Drinking Water of Hamadan and Tuyserkan Cities, Western
 564 Iran and Its Health Risk on the Exposed Population. *Journal of research in health sciences* 19.
 565 New Hampshire, D.o.E.S., 2006. *Trihalomethanes: Health Information Summary*.

- Niu, Z.-G., Zang, X., Zhang, J.-G., 2014. Health risk assessment of exposure to organic matter from the use of reclaimed water in toilets. *Environmental Science and Pollution Research* 21, 6687-6695.
- O'Driscoll, C., Sheahan, J., Renou-Wilson, F., Croot, P., Pilla, F., Misstear, B., Xiao, L., 2018. National scale assessment of total trihalomethanes in Irish drinking water. *Journal of environmental management* 212, 131-141.
- Pardakhti, A.R., Bidhendi, G.R.N., Torabian, A., Karbassi, A., Yunesian, M., 2011. Comparative cancer risk assessment of THMs in drinking water from well water sources and surface water sources. *Environmental monitoring and assessment* 179, 499-507.
- Pourmoghaddas, H., Stevens, A.A., 1995. Relationship between trihalomethanes and haloacetic acids with total organic halogen during chlorination. *Water Research* 29, 2059-2062.
- Ramavandi, B., Asgari, G., 2012. Study of THMFP in Karun River Water, Iran. *International Proceedings of Chemical, Biological and Environmental Engineering (IPCBE)* 43, 114-118.
- Sadeghi, H., Nasseri, S., Yunesian, M., Mahvi, A.H., Nabizadeh, R., Alimohammadi, M., 2019. Trihalomethanes in urban drinking water: measuring exposures and assessing carcinogenic risk. *Journal of Environmental Health Science and Engineering*, 1-14.
- SCI, 2016. Statistical Center of Iran, accessed August 2020, <https://www.amar.org.ir>.
- Union, E., 2014. (Drinking Water) Regulations.
- USEPA, 1992. Guidelines for Exposure Assessment. Risk Assessment Forum, Washington, DC, EPA/600/Z-92/001.
- USEPA, 2000. Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures. United States Environmental Protection Agency. EPA/(630/R-00/002).
- USEPA, 2013. Integrated Risk Information System (IRIS). (<http://cfpub.epa.gov/ncea/iris/index.cfm>).
- USEPA, 2018a. 2018 Edition of the Drinking Water Standards and Health Advisories Tables, in: Agency, E.P. (Ed.). Environmental Protection Agency
- USEPA, 2018b. Integrated Risk Information System. [<https://www.epa.gov/iris>].
- Valdivia-Garcia, M., Weir, P., Frogbrook, Z., Graham, D., Werner, D., 2016. Climatic, Geographic and Operational Determinants of Trihalomethanes (THMs) in Drinking Water Systems. *Scientific Reports* 6.
- Wang, Y., Zhu, G., Engel, B., 2019. Health risk assessment of trihalomethanes in water treatment plants in Jiangsu Province, China. *Ecotoxicology and environmental safety* 170, 346-354.
- WHO, 2005. Trihalomethanes in Drinking-water, Background document for development of WHO Guidelines for Drinking-water Quality. World Health Organization.
- WHO, 2017. Guidelines for drinking-water quality, 4th edition, incorporating the 1st addendum, in: Organization, W.H. (Ed.), 4th edition ed. WHO.
- Yao, Z., Sun, S., Wang, M., Zhao, Q., Jia, R., 2019. The occurrence of THMs and AOX in drinking water of Shandong Province, China. *Environmental Science and Pollution Research*, 1-10.
- Zhou, X., Zheng, L., Chen, S., Du, H., Raphael, B.M.G., Song, Q., Wu, F., Chen, J., Lin, H., Hong, H., 2019. Factors influencing DBPs occurrence in tap water of Jinhua Region in Zhejiang Province, China. *Ecotoxicology and environmental safety* 171, 813-822

612
613
614

615
616
617
618
619
620
621
622
623
624
625
626
627
628
629

Table 1. Descriptive statistics of drinking water characteristics

	N	Min	Max	Mean	Std. Deviation	Variance	Skewness		Kurtosis	
							Statistic	Std. Error	Statistic	Std. Error
EC (µs/cm)	66	292	1370	617.7	271.7	73847.3	0.893	0.295	-0.072	0.582
pH	66	6.8	8.5	7.59	0.37	0.138	0.277	0.295	-0.329	0.582
Alkalinity (mg/L CaCO ₃)	66	110	241	158.1	27.9	783.156	0.838	0.295	.258	0.582
Ca Hardness (mg/L CaCO ₃)	66	58	325	158.4	50.4	2540.279	1.087	0.295	1.974	0.582
Temperature	66	4	25	16.1	5.5	31.326	-0.270	0.295	-0.911	0.582
Free Remained Chlorine (mg/L)	66	0.0	2.4	0.64	0.47	0.229	1.492	0.295	3.165	0.582
Total Remained Chlorine (mg/L)	66	0.0	3.3	0.97	0.58	0.338	1.263	0.295	3.058	0.582
CF-CHCl ₃	64	0.0	101	14.7	24.1	579.881	1.824	0.299	2.630	0.590
BDCM-CHCl ₂ Br	64	0.0	601	105.1	165.2	27277.983	1.484	0.299	1.212	0.590
DBCM-CHBr ₂ Cl	64	0.0	118	8.3	23.7	562.028	3.470	0.299	12.008	0.590
BF-CHBr ₃	64	0.0	79	4.1	13.9	193.123	4.210	0.299	18.150	0.590
TTHMs	64	0.0	683	133.2	179.5	32227.150	1.247	0.302	0.549	0.595

630 Table 2. Reported concentration of THMs in drinking water of some world countries during
631 recent decade

Researcher(s) (year)	Country (City/region)	Sample Number	Mean (µg/l)	SD
Wang et al (2019)	China (Jiangsu Province)	176	18.8 to 39.0 (range)	NM
			109 (Purana Paltan)	15 .96
			166.67 (Naya Paltan)	7.04
Ahmed et al. (2019)	Bangladesh (Dhaka, 6 region)	31	439.2 (Kallyanpur)	24.12
			87.5 (Shyamoli)	6.02
			99.2 (Malibagh-Rampura)	10.39
			20.2 (Panthapath)	8.40
			315.85 (Spring)	180.68
Sadeghi et al. (2019)	Iran (Ardabil)	104	353.96 (Summer)	201.33
			353.96 (Autumn)	201.33
			70.87 (Winter)	39.33
Mohammadi et al. (2019)	Iran (Yazd)	30	21.53 (Autumn)	3.34
			22.61 (Winter)	5.12
Kogevinas et al. (2018)	European Union (28 EU countries in 2010-2017)	NM	11.9	11.1
Font-Ribera et al. (2017)	Spain (Barcelona, 2003-2006)	109	144.2	NM
Mohammadi et al. (2016)	Iran (Isfahan)	30	37.98	2.56
Charisiadis et al. (2015)	Greece (Cyprus)	383	65	24
Siddique et al. (2015)	Saudi Arabia	NM	71.3 (Winter)	34.5
			72.3 (Summer)	34.5
Babaei et al. (2015)	Iran (Ahvaz)	90	32.1 to 60.57	NM
Zeng et al. (2014)	China (Wuhan)	54	21.39	NM
Abdullah A.M. (2014)	Egypt (Alexandria Governorate)	288	12 to 74 (range)	NM
Amjad et al. (2013)	Pakistan	NM	142.3 (Rawalpindi)	NM
			259 (Islamabad)	NM
Pardakhti et al. (2011)	Iran (Tehran)	63	0.81 and 9.0 (7 districts)	NM
Viana et al. (2009)	Brazil (Fortaleza)	900	105.3 to 141.1 (10 districts)	24.2 to 31.2
			10.2 (Winter)	9.3
Present study	Iran (Tabriz)	66	252 (Spring)	185.9
			133.2 (Total)	179.5

632 SD: Standard Deviation, NM: not mentioned

634 **Figure captions**

635

636 Figure 1. Water sampling locations

637 Figure 2. Mean concentrations (a) and boxplots (b) of THMs in each of the four zones in Tabriz

638 Figure 3. Mapping of mean concentrations of THMs in Tabriz drinking water during winter and
639 summer

640 Figure 4. Simulation histogram for CDI caused by THMs in the four zones

641 Figure 5. Oral and Dermal HI of THMs in water samples