Pollution, 6(3): 469-480, Summer 2020
DOI: 10.22059/poll.2019.290223.693
Print ISSN: 2383-451X Online ISSN: 2383-4501
Web Page: https://jpoll.ut.ac.ir, Email: jpoll@ut.ac.ir

Carcinogen Risk Assessment of Mutagen X in Chlorinated Drinking Water in West of Tehran, Using Probabilistic Approaches

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Received: 05.09.2019 Accepted: 27.05.2020

ABSTRACT: The present study aims at evaluating the risk of Mutagen X (MX) (3-chloro-4-(dichloromethyl)-5-hydroxy-2 (5H)-furanone) and adverse health effects, associated with direct ingestion of chlorinated drinking water in west of Tehran, supplied by chlorinated drinking water from surface and underground water sources. For one year, MX concentrations in tap water samples has been measured for consumers in four different zones in western Tehran. It has been found that average MX concentration in the whole study area is 24.16 ng/L, with the highest concentration being in Zone 1 with a value of 38 ng/L. Also, the role of water sources, seasonal changes, and effective factors such as Total Organic Carbon (TOC) have been evaluated on MX formation. The highest of excess lifetime cancer risk (ELCR), estimated as 0.0037E-05, belongs to Zone 1, which uses surface water to supply drinking water, while the lowest can be seen in Zone 4, being 0.0021E-05. This latter zone utilizes underground water as the water source. In all zones, the highest risk of excessive cancer is related to winter, ranging from 0.0045E-5 in Zone 1 to 0.0023E-5 in Zone 4. The estimated number of cancer cases for Zones 1 to 4 have been 0.012, 0.016, 0.016, and 0.004, respectively, based on their population. The estimated average risk and the number of ELCR, caused by exposure to MX, through direct ingestion of drinking water have been 0.0030E-5 and 0.047, respectively, in the entire studied area for the duration of one year.

Keywords: Drinking water, Chlorination, Mutagen X, Risk assessment, Uncertainties, Tehran, Iran.

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INTRODUCTION

In the past century, chlorination has been a key method to disinfect drinking water and due to reasonable cost and easy operation. Furthermore, chlorination is considered as the most effective disinfection method because of the presence of residual chlorine in water, which prevent the reactivation of the pathogens. However, the types of carcinogenic or mutagenic compounds that were identified in drinking water as disinfection-by-products (DBP), raised concerns over the safety of drinking water(Islam et al. 2016). These DBPs are formed due to the reaction of applied chlorine in the disinfection process with natural organic materials as well as synthetic organic materials created by human activities and discharging the industrial wastewater in raw water(Liu et al. 2018; Salam and Varma 2019; Anny et al. 2017).

Armelle Hebert et al. (Hebert et al. 2010) have identified the emerging disinfection by-products (EDBPs) which pose the greatest risk on the basis of their potential effects on public health. EDBPs are as follows: NDMA (N-nitrosodimethylamine) and other nitrosamines, Mutagen X and other halofuranones, acetaldehyde and formaldehyde, pentachlorophenol and 2, 4, 6-trichlorophenol, hydrazine and two unregulated halomethanes including tetrachloromethane and dichloromethane.

Mutagen X , one of the by-products produced during the chlorine disinfection process, is known as a strong mutagen(Smith et al. 2015). It is common to assume that humic substances in the water are precursors of several halogenated products(Zhuo et al. 2001).

It is structurally thought that the Cl and $CHCl_2$ substituents in a cis arrangement on a carbon-carbon double bond, which are located on a ring structure of hydroxyfuranone of Mutagen X, are responsible for its mutagenic activity(Wright et al. 2002). Mutagenicity of these substituents is due to combining into the 5-hydroxy-2-(5-hydrogen)-furanone ring system or an open structure that can easily be transformed into this ring system under mutagenic testing conditions(Onstad and Weinberg 2005).

A significant portion of the total mutagenicity of chlorinated water has been attributed to Mutagen X. In the studies of toxicity, contribution of Mutagen X to the Salmonella mutagenicity of drinking water has been estimated at 15 - 36 % in United States, 7 to 67% in Finland, 7 - 36 % in Japan, 30 to 60 % in the UK, 8.3 to 20 % in Spain, 15 to 57% in China, and 36 % in Russia(Ohe et al. 2004). The paths of entry of Mutagen X to the human body include drinking water, skin absorption, and inhalation (Geter et al. 2004; Ward et al. 2010).

Although the Mutagen X concentration in drinking water is typically 100 to 1000 times less than other common chlorinated by-products (e.g., trihalomethanes), some scientists believe that Mutagen X may play an important role in increasing the risk of developing cancer, which is associated with chlorinated drinking water(McDONALD and Komulainen 2005). This hypothesis is based on observations made in some clinical trials, which showed that Mutagen X is much stronger than THMs in causing DNA damage and changing paths involved in cell growth. In addition, some epidemiological studies associated with an increase in cancer rates with bacteria mutagenicity of disinfected water showed the considerable role of Mutagen X. It has been reported that Mutagen X is likely to be stronger mutagen than any other chlorination by-products in causing cancer in animals(Smith et al. 2015).

The workgroup for the drinking water guidance of World Health Organization (WHO) investigated the health effects of Mutagen X and concluded that because of inadequate data, is not possible to assess the recommended levels for Mutagen X toxicity(Organization 2003). Several studies have been published on Mutagen X

toxicity, and a two - year study of carcinogenicity and the results of two-stage tumor promotion tests were reported. Furthermore, according to the category of the international agency for research on cancer (IARC), Mutagen X was classified in Group 2B (possible human carcinogen)(Richardson et al. 2007). The paths of entry of Mutagen X to the human body include direct ingestion, skin absorption, and inhalation.

In recent Finnish ecological and cohort studies, a mutagenicity level of 3000 net revertants/L have been associated with kidney cancer (RR=1.32), bladder cancer (relative risk: RR= 1.21), stomach cancer (RR=1.11), Hodgkin's disease (RR=1.29), non-Hodgkin's lymphoma (RR=1.27), and pancreatic cancer (RR=1.13)(Ohe et al. 2004).

In this paper, we evaluate the risk of Mutagen X and adverse health effects associated with chlorinated drinking water. So far, the risk assessment of THMs has been performed for chlorinated water of Tehran, Iran(Pardakhti et al. 2011), but there is no related evaluation of Mutagen X, and in this study, the risk assessment of Mutagen X is investigated for western part of Tehran's drinking water.

MATERIAL AND METHODS

Tehran is the largest and most populous city in Iran, with a population of about 9 million(SCI 2016). The total volume of drinking water produced in Tehran is about 1,350 million m3/year, which accounts for 20% of the total drinking water produced in Iran. Supply and distribution of healthy drinking water for Tehran are carried out by Tehran Province Water and Wastewater Company (TPWWC). The water supply is performed by 6 regional companies, all under the supervision of TPWWC(TPWWC 2019).

The sources of drinking water in Tehran include surface resources (Amirkabir dam, Taleghan dam in the west of Tehran, and Latian Dam, Mamlu Dam, Lar dam in the east of Tehran) and underground resources (580 wells). The surface resources supply 60 to 75 percent of Tehran's drinking water and 25 to 40 percent is supplied by wells. The amount of harvesting from surface water resources and underground resources is dependent on rainfall. During droughts, harvesting from wells increases and during the rainy years, a larger share of surface water resources is harvested(Pardakhti et al. 2011).

About 70% of Tehran's drinking water comes from six water treatment plants. Also, the output water from the water treatment plants is mixed with water from the wells (27%) in the water reservoir containers and after the disinfection process reaches of consumers through the distribution network. Due to population growth and development of Tehran, about 3% of the population living in the western part of Tehran only benefit from groundwater resources(TPWWC 2019). Extracted water from wells enter the water reservoir containers and then disinfected with sodium hypochlorite. The areas that only have extracted water from wells are covered by the District 3 of TPWWC. Distributed drinking water in areas covered by District 3 of TPWWC includes:

1- Drinking water from the water treatment plant, 2- Drinking water comes from the mixing of water from the treatment plant and extracted water from wells and 3- Drinking water extracted from the wells.

Due to the wide range of drinking water distributed by the District 3 of TPWWC, this study evaluated the MX risk in drinking water comes from this company. The covered population is 1,557,797 people(TPWWC 2019).

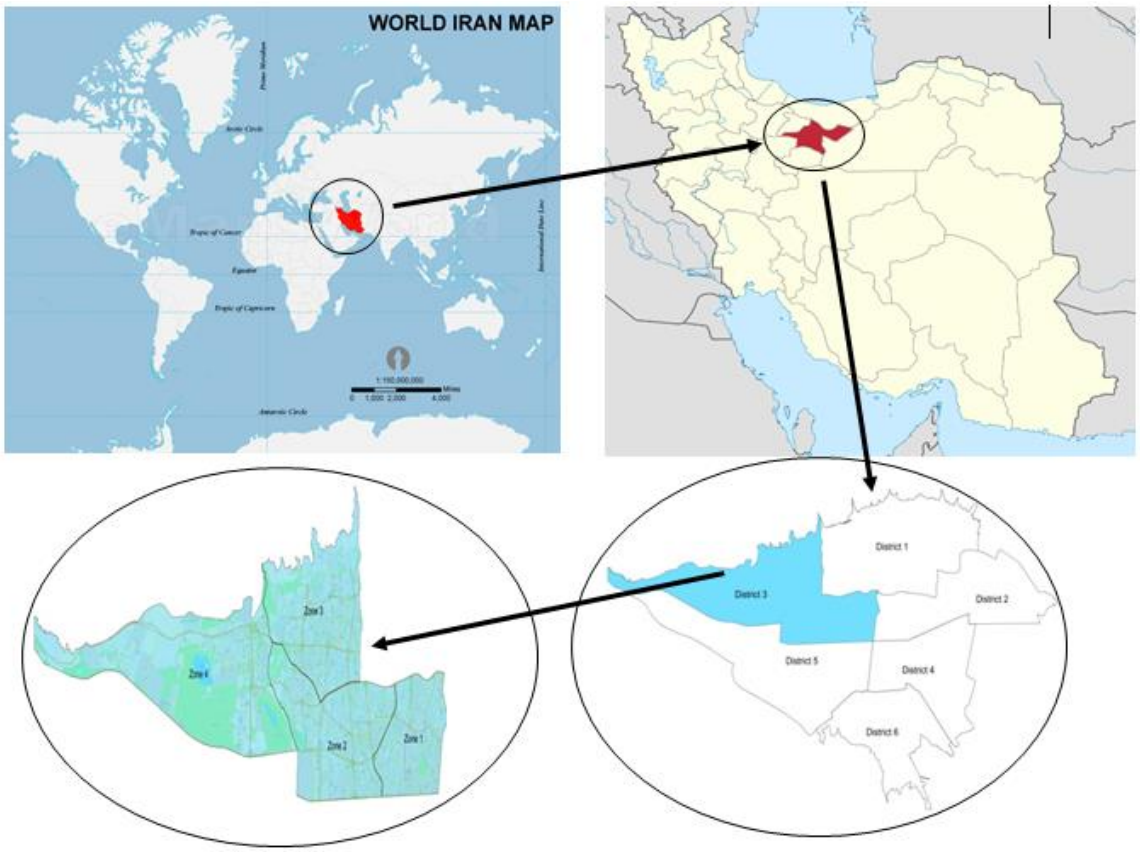

Fig. 1. Map of sample collection sites based on used resources

Firstly, based on the type of drinking water supplement (refined water from the water treatment plant, drinking water from wells mixed with refined water and extracted water from wells), the study district was divided into 4 zones. Also, based on the area extend and the population of consumers were selected 20 locations for sampling (5 locations in each of the 4 selected zones (Fig. 1). In the sampling district, 3 replicated samples were collected from every 20 locations. In each sampling, 60 samples were taken. Sampling was performed on a monthly basis and on the first Saturday of every month. The sampling procedure was continued for one year from September 2017 to September 2018. All samples were taken from consumers tap (residential and business). Sampling was performed according to EPA method(EPA.US 2000). The samples were stored in the dark glass containers previously washed with acid and distilled water and placed in a furnace at 300 °C for 2 hours. Samples transferring temperature was 4 °C and the samples were kept away from light and air. Ammonium sulfate (100 µL of 40 mg / mL $(NH_4)_2SO_4$) was used as an inhibitor, given that the collected samples had residual free chlorine that is capable of reacting with natural organic substances in water.

All samples were prepared and analyzed using a previously published method with the partially modification and validation (not published data) (Chinn et al., 2002). To measure the MX concentration, samples were firstly prepared. Using concentrated sulfuric acid (98% w/w) (Merck, Darmstadt, Germany), the pH of 250 ml of each sample reached about 2, and MX-analogues such as E-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid (EMX), Z-2-chloro-3-(dichloromethyl)-4-oxo-butenoic acid (ZMX) were transformed into MX form (Fig. 2).

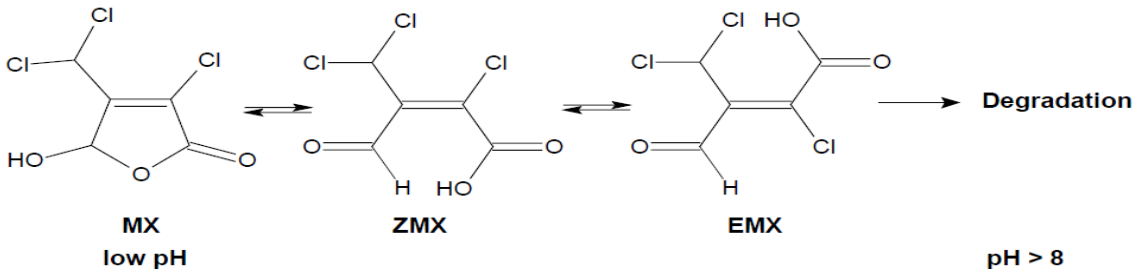

Fig. 2 Degradation and formation of MX(Kubwabo et al. 2009)

Samples extraction was performed 3 times with 50 ml of Methyl Tertiary Butyl Ether (MTBE) solvent (Merck, Darmstadt, Germany). Derivation of samples was done using (2% V / V) MeOH / H_2SO_4 solution at 70 °C for one hour. The esterified MX (MXR) analogs were extracted 2 times by Hexane (Sigma Aldrich, St. Louis, MO, USA). The hexachlorobenzene (HCB) (Sigma Aldrich) was utilized as the internal standard and the Mucobromic acid ($C_4H_2Br_2O_3$) MBA (Sigma Aldrich) was used as the surrogate. 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone (MX, 97%) was purchased from TRC (Toronto, Canada). The ultra-pure water was prepared using a Milli-Q® water purification system.

A BRUKER 450 gas chromatograph equipped with a Ni^{63} electron capture detector was used to identify and determine the amount of MX. Automatic injections in 1/5 split mode were performed with helium as carrier gas and nitrogen as the make-up gas. Chromatography was performed on a 30-m DB-5 capillary column with a 0.25-mm ID and 0.25 mm film thickness (Agilent Technologies, CA, USA).

Calibration curve was constructed using MX's standard solutions at the range of 5-500 ng/L at 5 points. The detection and quantification limits were 5 ng/L and 15 ng/L, respectively. Concentrations below the detection limit were declared as unidentified. In order to check the decomposition recovery rate, 10 ultra-pure water samples, which were spiked with 250 and 500 ng/L MX, were extracted. Average recycling rate was 88%. In each series of samples, a control sample of ultra-pure water was also analyzed. Measurable amounts of MX were not observed in solvents, internal standard, surrogate, and ultra-pure water.

TOC analysis was carried out by a TOC-L analyzer (Shimadzu, Japan) equipped with a scrubber tube to remove interferences such as water vapor and chlorine gas. High-temperature combustion was performed at 680°C in an oxygen-rich atmosphere in the presence of a platinum catalyst. A high-purity air supply with a pressure of 200±10 kPa was used as the carrier gas. Non-dispersive infrared (NDIR) method was used to quantify the produced carbon dioxide. Calibration was performed using a potassium hydrogen phthalate (KHP) standard solution.

In this study, the carcinogenic risk of MX was estimated for the population under study which was contacted with MX by direct ingestion of drinking water. The assessment of MX effects on human health can be achieved from various ways, including direct ingestion, skin and respiratory contact, which in this study merely "the carcinogenic risk of MX through direct ingestion" had been assessed. In the exposure assessment phase, the findings of the Karyab et.al.(Karyab et al. 2016) were used to determine the factors of exposure. He studied the exposure factors of chemicals through direct ingestion of drinking water in Tehran for one year.

In the scientific literature, a limited number of cancer slope factors (CSFs) were

found for MX. In the reference provided by USEPA in 2000, the CSF level is 0.18 (mg/kg-day) $^{-1}$ (EPA.US 2000). In a study conducted by McDonald and Komulainen(McDONALD and Komulainen 2005), the average carcinogenic potency of MX is 2.3 (mg/kg-day) $^{-1}$ and an upper 95% percentile estimate of 4.5 (mg/kg-day) $^{-1}$. In another study, Hirose et al.(Hirose et al. 1999) used the magnitude of the CSF of MX equal to 0.181 (mg/kg-day) $^{-1}$ for estimating this compound in drinking water. Melnick et al.(Melnick et al. 1997) evaluated the liver cancer risk for MX equal to 1 (mg/kg-day) $^{-1}$. This amount was more than 5 times than the carcinogenic potential estimated by Hirose et al. A cancer oral slope factor of 3.7 (mg/kg/day) $^{-1}$ was calculated by Komulainen et al. (Komulainen et al. 1997). According to the presence of further documentation in the study of Hirose et al.(Hirose et al. 1999) and its close finding with the USEPA report in 2000, in this study, the CSF of MX was selected equal to 0.181 (mg/kg-day) $^{-1}$ as the reference value.

The literature review shows that there was no evidence of the possibility of using age-dependent adjustment factor (ADAF) in risk estimation of MX. In order to evaluate whether children are more sensitive to the toxic effects of MX than adults, there are insufficient data available(EPA.US 2003). Therefore, in this study, the estimated carcinogenic risk of MX was considered to be equal for different age groups (this is included in the study limitations).

According to the USEPA report in 2003, the absorption of MX through the digestive system is about 35%(EPA.US 2003). Also, in the IPCS documentation, approximately 20-35% of MX is absorbed by the digestive system that enters the human body directly through ingestion(Albertini et al. 2000).In this study, the absorption of MX by direct ingestion is considered equal to 35%.

Subsequently, the lifetime average daily dose (LADD) was estimated. The equation used to estimate the LADD was based on the USEPA(EPA.US 2004), which is given in the below equation.

$$\mathrm{LADD} = \frac{\mathrm{C_i} \times \mathrm{IR} \times \mathrm{EF} \times \mathrm{ED} \times \mathrm{AF}}{\mathrm{BW} \times \mathrm{AT}} \quad (1)$$

The amount of LADD was calculated in mg/kg/day, C_i, *IR*, *EF*, *ED*, and *AF* were the mean concentration of MX in water (mg/L), the water intake rate (L/day), the exposure frequency (350 days in a year), the exposure duration (years), and the absorption factor (35%) (Amy et al. 2000), respectively. Also, *BW*, and *AT* were the body weight (kg) and the averaging time (70 yr×365day/yr), respectively(Karyab et al. 2016). The exposure parameters of direct water ingestion exposure to MX in the different age groups are shown in Table 1. The associated risk with MX ingestion from drinking water was estimated using Eq. 2, which was based on USEPA(EPA.US 2004) . In this equation, the oral CSF is the MX's CSF for direct ingestion, which indicates the relationship between MX dose and the corresponding response.

$$\text{Ingestion ELCR} = \text{LADD} \times \text{oral CSF} \quad (2)$$

Table 1. Exposure parameters for exposure to MX through tap water direct ingestion for different age groups (mean ± SD) (Karyab et al. 2016; Organization)

		Age groups (yr)			
		< 2	**2-< 6**	**6-<16**	**> 16**
water intake rate (IR) (L/capita/day)	Tap	0.45±0.12	0.51±0.14	1.12±0.27	1.23±0.27
Exposure duration (ED) (years)		2	4	10	55
Average body weight (BW) (kg)		12.5	16.5	40.7	65

RESULTS AND DISCUSSION

MX concentrations were detected in all samples from 15 to 38 ng/L. The maximum concentration of MX (38.00 ng/L) was observed in Zone 1, which receives surface water and the minimum concentration (15.00 ng/L) was determined in Zone 4, which only receives groundwater resources. A mixture of surface water and groundwater was used for Zones 2 and 3 which the average concentration of MX were 24.35 and 25.03 ng/L, respectively.

The measured MX concentrations for each zone were shown in Table 2. The reason for the increased concentration of MX in Zone 1 may be related to the higher levels of organic matter in surfaced water rather than ground water. The measured TOC concentrations for each zone were shown in Table 3.

Table 1 shows the highest direct intake of water by direct ingestion for groups older than 16 years and the lowest amount of mutagen ingestion for children under 2 years old. Based on the selected scenario, using the mean value of MX and accepting the exposure parameter by direct ingestion for different age groups, according to Table 1, the lifetime average daily dose (LADD) was calculated.

As shown in Table 4, the total LADD for zone 1, zone 2, zone 3, and zone 4 were 2.06E-7, 1.66E-7, 1.71E-7, and 1.17E-7, respectively.

Table 2. MX concentration in different zones (ng/L)

Parameter	Z1	Z2	Z3	Z4	Total
Average	30.15	24.35	25.03	17.20	24.18
Median	30.00	24.00	25.00	17.00	24.00
Max	38.00	33.00	33.00	22.00	38.00
Min	21.00	16.00	20.00	15.00	15.00
STD	4.40	4.40	3.05	1.94	5.88

Table 3. TOC Concentration in different zones (mg/L)

Parameter	Z1	Z2	Z3	Z4
Average	0.55	0.44	0.40	0.20
Median	0.69	0.52	0.50	0.23
Max	1.00	0.80	0.70	0.30
Min	<0.2	<0.2	<0.2	<0.2

Table 4. The lifetime average daily dose (LADD) of MX through direct ingestion of drinking water (mg/kg/d) for different zones.

Zone		Age group				
	Seasons	<2	2-<6	6-<16	>16	Sum
Z_1	Autumn	0.10×10^{-7}	0.19×10^{-7}	0.36×10^{-7}	1.36×10^{-7}	2.01×10^{-7}
	Winter	0.13×10^{-7}	0.24×10^{-7}	0.46×10^{-7}	1.66×10^{-7}	2.49×10^{-7}
	Spring	0.09×10^{-7}	0.17×10^{-7}	0.33×10^{-7}	1.18×10^{-7}	1.77×10^{-7}
	Summer	0.11×10^{-7}	0.19×10^{-7}	0.38×10^{-7}	1.35×10^{-7}	2.03×10^{-7}
	Average	0.11×10^{-7}	0.20×10^{-7}	0.39×10^{-7}	1.37×10^{-7}	2.07×10^{-7}
Z_2	Autumn	0.09×10^{-7}	0.16×10^{-7}	0.32×10^{-7}	1.16×10^{-7}	1.73×10^{-7}
	Winter	0.11×10^{-7}	0.19×10^{-7}	0.38×10^{-7}	1.34×10^{-7}	2.02×10^{-7}
	Spring	0.07×10^{-7}	0.12×10^{-7}	0.24×10^{-7}	0.86×10^{-7}	1.29×10^{-7}
	Summer	0.08×10^{-7}	0.15×10^{-7}	0.30×10^{-7}	1.08×10^{-7}	1.61×10^{-7}
	Average	0.09×10^{-7}	0.16×10^{-7}	0.31×10^{-7}	1.11×10^{-7}	1.67×10^{-7}
Z_3	Autumn	0.09×10^{-7}	0.16×10^{-7}	0.30×10^{-7}	1.09×10^{-7}	1.64×10^{-7}
	Winter	0.10×10^{-7}	0.19×10^{-7}	0.37×10^{-7}	1.30×10^{-7}	1.96×10^{-7}
	Spring	0.08×10^{-7}	0.15×10^{-7}	0.29×10^{-7}	1.05×10^{-7}	1.57×10^{-7}
	Summer	0.09×10^{-7}	0.16×10^{-7}	0.31×10^{-7}	1.12×10^{-7}	1.69×10^{-7}
	Average	0.09×10^{-7}	0.16×10^{-7}	0.32×10^{-7}	1.14×10^{-7}	1.71×10^{-7}
Z_4	Autumn	0.06×10^{-7}	0.11×10^{-7}	0.22×10^{-7}	0.77×10^{-7}	1.16×10^{-7}
	Winter	0.07×10^{-7}	0.12×10^{-7}	0.24×10^{-7}	0.86×10^{-7}	1.29×10^{-7}
	Spring	0.06×10^{-7}	0.10×10^{-7}	0.21×10^{-7}	0.74×10^{-7}	1.11×10^{-7}
	Summer	0.06×10^{-7}	0.11×10^{-7}	0.21×10^{-7}	0.75×10^{-7}	1.13×10^{-7}
	Average	0.06×10^{-7}	0.11×10^{-7}	0.22×10^{-7}	0.78×10^{-7}	1.17×10^{-7}

Therefore, the excess lifetime cancer risk (ELCR) due to intake of tap water in z1, z2, z3 and z4 was estimated to be 0.0037E-05, 0.0030E-05, 0.0031E-05, and 0.0021E-05, respectively. Table 5 showed the results of risk assessment for the oral direct ingestion of tap drinking water.

According table 5, the ELCR for the age group of under 2 years old varies from 0.0001E-5 to 0.0002E-5. Also, the cancer risk through direct ingestion for the age group of 2-<6 was in the range of 0.0002E-5 to 0.0004E-5. In addition, the risk of cancer for the age group of 6-<16 varies from 0.0004E-5 to 0.0008E-5 and for the adult group from 0.0013E-5 to 0.0029E-5. Also Fig.3 showed the average annual of ELCR in different age groups.

The highest risk of exposure to MX was related to zone 1 with an average annual of $0.0037*10^{-5}$ and the lowest risk of exposure was observed in zone 4 with an average annual of $0.0021*10^{-5}$.

Table 5. Excess lifetime cancer risk caused by exposure to MX through direct ingestion of drinking water

Zone		Age group				
	Seasons	<2	2-<6	6-<16	>16	Sum
Z_1	Autumn	0.0002×10^{-5}	0.0003×10^{-5}	0.0007×10^{-5}	0.0024×10^{-5}	0.0036×10^{-5}
	Winter	0.0002×10^{-5}	0.0004×10^{-5}	0.0008×10^{-5}	0.0029×10^{-5}	0.0043×10^{-5}
	Spring	0.0002×10^{-5}	0.0003×10^{-5}	0.0006×10^{-5}	0.0021×10^{-5}	0.0032×10^{-5}
	Summer	0.0002×10^{-5}	0.0003×10^{-5}	0.0007×10^{-5}	0.0024×10^{-5}	0.0036×10^{-5}
	Average	0.0002×10^{-5}	0.0003×10^{-5}	0.0007×10^{-5}	0.0024×10^{-5}	0.0036×10^{-5}
Z_2	Autumn	0.0002×10^{-5}	0.0003×10^{-5}	0.0006×10^{-5}	0.0021×10^{-5}	0.0032×10^{-5}
	Winter	0.0002×10^{-5}	0.0003×10^{-5}	0.0007×10^{-5}	0.0024×10^{-5}	0.0036×10^{-5}
	Spring	0.0001×10^{-5}	0.0002×10^{-5}	0.0004×10^{-5}	0.0015×10^{-5}	0.0022×10^{-5}
	Summer	0.0002×10^{-5}	0.0003×10^{-5}	0.0005×10^{-5}	0.0019×10^{-5}	0.0029×10^{-5}
	Average	0.0002×10^{-5}	0.0003×10^{-5}	0.0006×10^{-5}	0.0020×10^{-5}	0.0031×10^{-5}
Z_3	Autumn	0.0002×10^{-5}	0.0003×10^{-5}	0.0006×10^{-5}	0.0019×10^{-5}	0.0030×10^{-5}
	Winter	0.0002×10^{-5}	0.0003×10^{-5}	0.0007×10^{-5}	0.0024×10^{-5}	0.0036×10^{-5}
	Spring	0.0001×10^{-5}	0.0003×10^{-5}	0.0005×10^{-5}	0.0019×10^{-5}	0.0028×10^{-5}
	Summer	0.0002×10^{-5}	0.0003×10^{-5}	0.0006×10^{-5}	0.0020×10^{-5}	0.0031×10^{-5}
	Average	0.0002×10^{-5}	0.0003×10^{-5}	0.0006×10^{-5}	0.0020×10^{-5}	0.0031×10^{-5}
Z_4	Autumn	0.0001×10^{-5}	0.0002×10^{-5}	0.0004×10^{-5}	0.0014×10^{-5}	0.0021×10^{-5}
	Winter	0.0001×10^{-5}	0.0002×10^{-5}	0.0004×10^{-5}	0.0016×10^{-5}	0.0023×10^{-5}
	Spring	0.0001×10^{-5}	0.0002×10^{-5}	0.0004×10^{-5}	0.0013×10^{-5}	0.0020×10^{-5}
	Summer	0.0001×10^{-5}	0.0002×10^{-5}	0.0004×10^{-5}	0.0014×10^{-5}	0.0021×10^{-5}
	Average	0.0001×10^{-5}	0.0002×10^{-5}	0.0004×10^{-5}	0.0014×10^{-5}	0.0021×10^{-5}

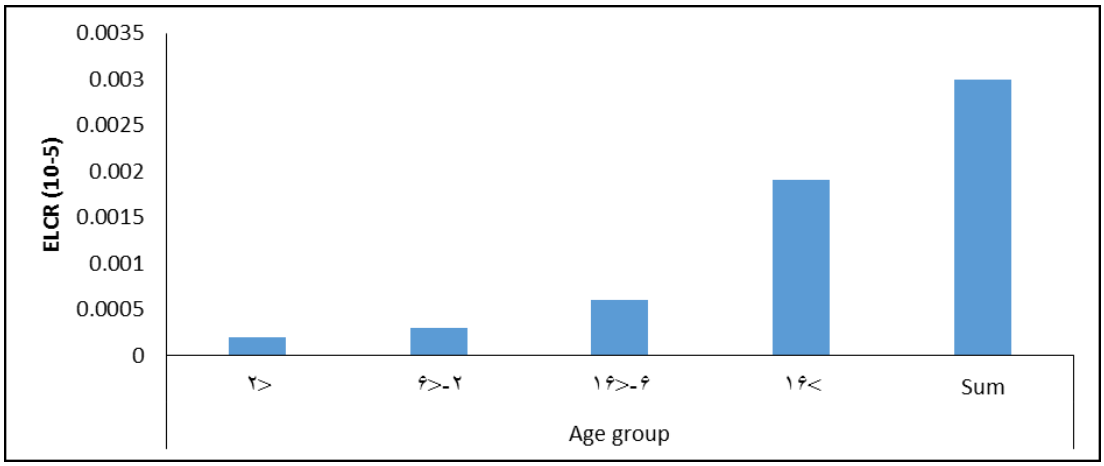

Fig. 3. Comparison of annual average ELCR in different age groups.

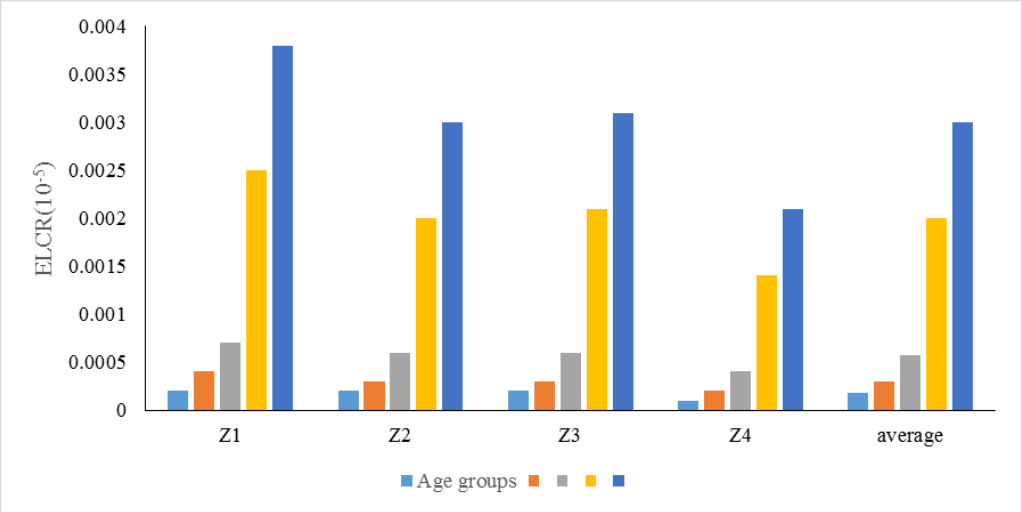

Fig. 4. Comparison of ELCR in all zones for different age groups

As shown in Fig. 4 ELCR from MX through drinking water in Zone 1 is higher than other zones, as the main source for supplying drinking water in zone 1 was surface waters that contained more natural organic substances. Also, zone 4, due to its full use of well water that had less natural organic matter, therefore, was less likely to be exposed to MX.

As shown in Figure 5, in all zones, the highest LADD through direct exposure of MX ingestion from drinking water and, consequently, according to Figure 6, the highest risk of exposure to MX was in winter which varies from 0.0045E-5 in Zone 1 to 0.0023E-5 in Zone 4. This could be due to the increasing of contact time (C_t) of chlorine in cold water which was more than warm water. Where C_t was the contact time needed to disable or eliminate the pathogens by chlorine. As a result, for specified C_t , the required dose of chlorine in winter, when the water temperature is lower, will be higher than in summer(Sadiq and Rodriguez 2004).

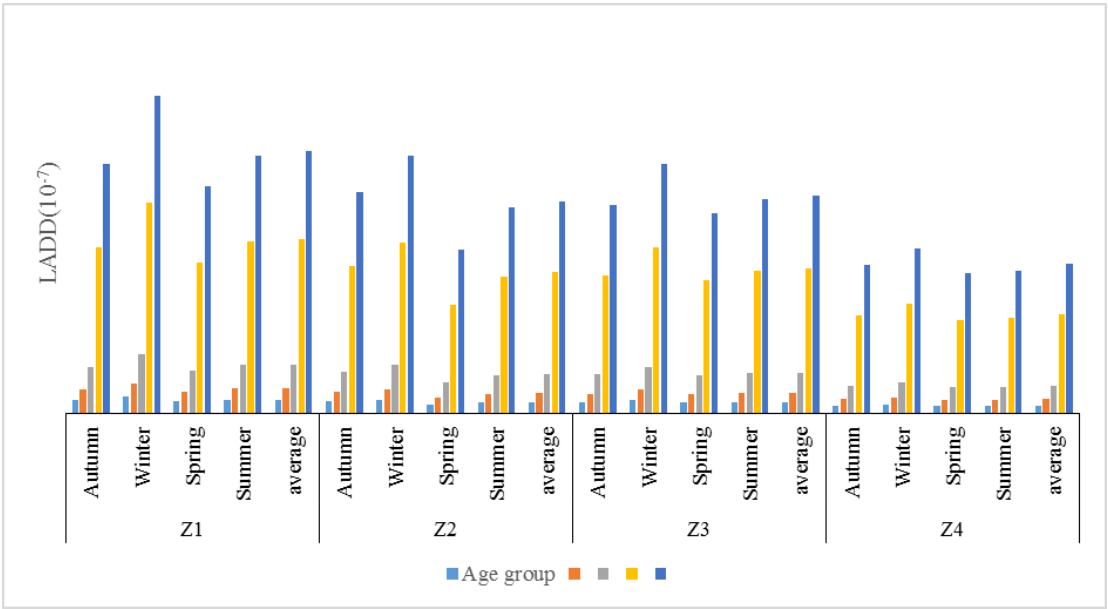

Fig. 5. Comparison of LADD for different zones in all seasons

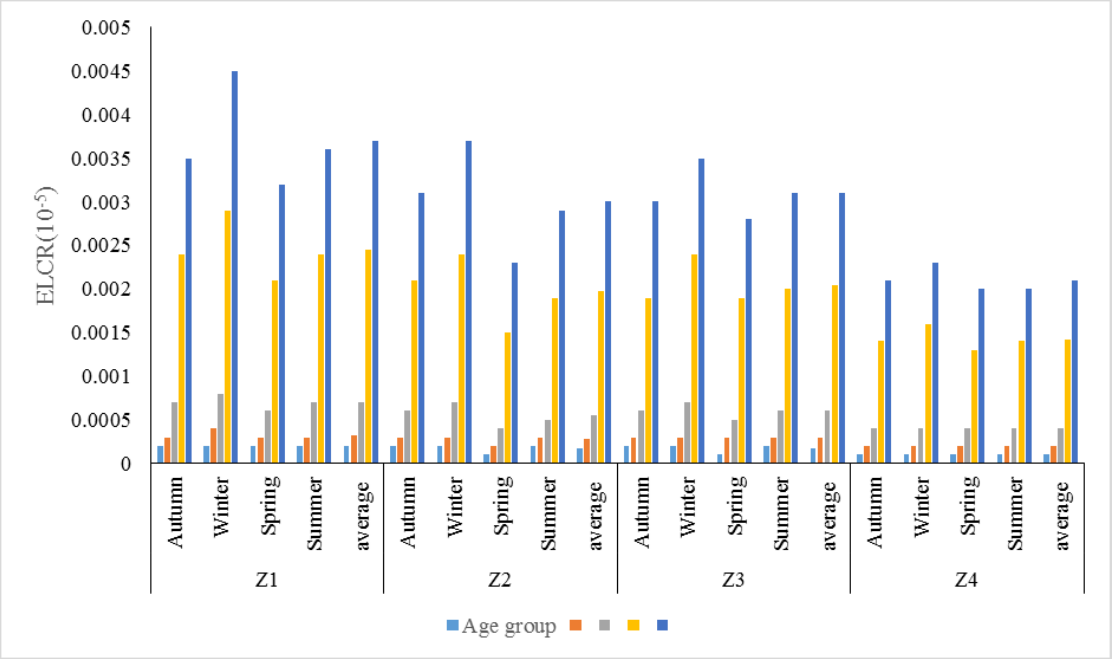

Fig. 6. Comparison of ELCR for different zones in all seasons

The population of z_1, z_2, z_3, and z_4 approximately were 3.31E5, 5.47E5, 5.11E5, and 1.68E5, respectively. Therefore, the expected cancer cases for zones z_1 to z_4 were 0.012, 0.016, 0.016, and 0.004, respectively, using the risk values of MX from Table 5.

The average risk in all studied zones for MX exposure was 0.0030E-5. Based on the population of the entire studied area and using the mean concentration of MX for the whole region, the number of ELCR caused by exposure to MX through drinking water was 0.047 in one year.

CONCLUSION

The obtained values for the cancer risk of MX exposure from direct ingestion for z_1, z_2, z_3, and z_4 were estimated to be 0.0037E-05, 0.0030E-05, 0.0031E-05, and 0.0021E-05, respectively, which all were lower than the accepted value by the World Health Organization.

The maximum amount of ELCR was in winter which was due to the higher chlorine dose in winter than in the summer for special C_t.

Comparing the values of ELCR in all studied age groups showed that in all seasons the highest values were related in the age group of over 16 years old. The age groups of 2-<6 and 6-<16 years old were placed in lower levels. Also, the lowest values of ELCR were related to the age group of under 2 years old.

The water zone which completely utilizes surface water sources had the highest concentration of MX, such as zone 1, so drinking water in those areas had the highest risk of exposure to MX. Also, Zone 4, which received underground water from wells, had the lowest concentration of MX, resulting in minimal exposure to MX through drinking water and the least risk of cancer. Zone 2 and Zone 3, which were using a mixture of surface water and groundwater, had a close average concentration and therefore no significant difference was observed in the risk of cancer arising from exposure to distributed drinking water in those areas.

Finally, the estimated average risk was about 0.047 cancer cases per year due to exposure of MX through daily ingestion of tap drinking water in the whole studied area.

GRANT SUPPORT DETAILS

The present research has been financially supported by Tehran University of medical science (grant No. 132-1113) and the Arian Fanazma Center for providing the GC / ECD device.

CONFLICT OF INTEREST

The authors declare that there is not any conflict of interests regarding the publication of this manuscript. In addition, the ethical issues, including plagiarism, informed consent, misconduct, data fabrication and/ or falsification, double publication and/or submission, and redundancy has been completely observed by the authors.

LIFE SCIENCE REPORTING

No life science threat was practiced in this research.

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