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Assessment of emerging endocrine-disrupting compounds, namely estrone, 17-beta-estradiol, estriol, and 17-alpha-ethinyl estradiol, in the drinking water piping network of Tehran

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ABSTRACT

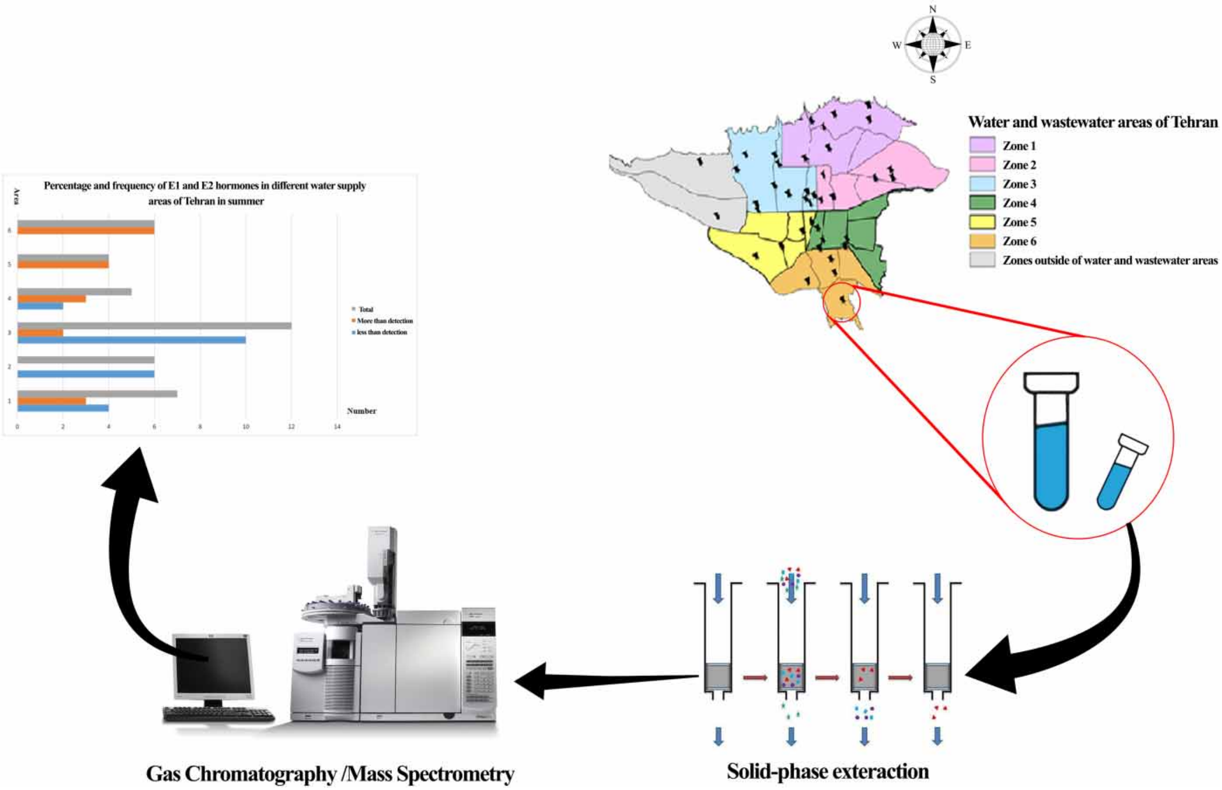
In recent decades, micro-pollutants like estrogen hormones have been considered due to adverse health effects on humans and the environment despite very low concentrations of 0.1–20 ng/L. In the present study, drinking water was sampled from the six areas of Tehran in summer (August 2020), autumn (November 2020), winter (February 2021), and spring (May 2021) to evaluate natural and synthetic estrogen hormones (estrone (E1), 17-beta-estradiol (E2), estriol (E3), and 17-alpha-ethinyl estradiol (EE2)). The samples were transferred to the laboratory and the solid-phase extraction (SPE) method was used to extract the hormones, and the type and amount of hormones were examined by gas chromatography–mass spectrometry. According to the results, the highest concentrations were related to E1 and E2 compounds at 1.96 and 2.13 ng/L, respectively, in summer and autumn (device detection limit = 0.5 ng/L). In addition, concentrations of compounds E1 and E2 were lower than the detection limit in spring and winter in all samples, and compounds E3 and EE2 were not identified in any samples or seasons. Commonly, the concentration of steroid hormones increased in the dry seasons (summer and autumn), while in the spring and winter concentrations were less than the device detection limit because of rainfall.

Key words: drinking water, gas chromatography–mass spectrometry, solid-phase extraction, steroid hormones

HIGHLIGHTS

- Endocrine-disrupting hormones were evaluated in the drinking water of Tehran city
- E1 and E2 were detected only in summer and autumn.
- E1 and E2 were not detected in spring and winter.
- E3 and EE2 were not detected in any region or any season.

GRAPHICAL ABSTRACT



INTRODUCTION

Nowadays, the development of societies and human activities leads to the introduction of many contaminants of emerging concern (CECs) into the environment. These compounds include different types of organic and inorganic chemical compounds such as disinfection byproducts, endocrine disruptors, natural toxins, persistent organic pollutants, brominated flame-retardants, pesticides, pharmaceuticals, and personal care products (PPCPs), which have the potential to harm biota and humans (Motta *et al.* 2008; Fiorentino *et al.* 2017; Bilal & Iqbal 2019). Among the mentioned compounds, endocrine-disrupting compounds (EDCs) are xenobiotic compounds that, according to the World Health Organization (WHO), alter the functions of the endocrine system and adversely affect the organism or offspring even at low environmental concentrations (ng/L and μg/L) (Damstra *et al.* 2002).

EDCs include steroid estrogens derived from cholesterol synthesis, which are characterized by a cyclopentanoperhydrophenanthrene ring. Among EDCs, steroid estrogens that act as hormones secreted by the adrenal cortex, testes, ovaries, and placenta can be mentioned (Snyder *et al.* 1999). Some hormones cause more alarm for adverse health effects than other EDCs, such as natural and artificial human steroid hormones, namely estrone (E1), 17-beta-estradiol (E2), estriol (E3), and 17-alpha-ethinyl estradiol (EE2) (Snyder *et al.* 1999). They stand out in the literature for their high estrogenicity that, even at low concentrations, can cause adverse effects on biota (de França *et al.* 2020).

This can be explained by the presence of a phenol ring (known as one of the essential functional groups to react with the estrogen receptor) in the molecule (Jürgens *et al.* 2002). Synthetic steroid estrogens are produced in the pharmaceutical industry and are applied to contraceptive pills, such as hormone replacement therapy, and in livestock farms to promote hormonal growth in cattle. Oral contraceptives contain 30–50 μg of EE2 per pill (Haynes *et al.* 2016). Over the past 50 years, using these pills has increased in developed countries until one-third of women prefer to use contraceptive pills (25–50 μg/day) (Jobling *et al.* 2002; Nejedly & Klimes 2017). Estradiol E2 and estriol E3 are the most important EDCs in natural estrogen hormone groups by disrupting the ability of endocrine glands thousands of times more than other synthetic chemicals such as nonylphenol (Baronti *et al.* 2000; Wee *et al.* 2021). The main difference between EE2 and previous compounds is stability in the environment (about 20–40 days in river water) (Servos 1999).

Epidemiological studies have illustrated the significant effects of endocrine-disrupting chemicals on wildlife and human health (Myers *et al.* 2004). Preliminary studies have also shown that they play a role in breast and prostate cancer and metabolic diseases such as obesity and affect human reproductive, thyroid, cardiovascular, and neuroendocrinology systems. There are also some studies that have noted immunological and neurological disorders in humans at relatively low concentrations of 0.20–1 ng/L (Simpson 2003; Haynes *et al.* 2016). Therefore, it has become a global public health concern (Kortenkamp 2017), and the US Environmental Protection Agency (US EPA) has considered EDCs as one of the top six research priorities since 1996 (Gültekin & Ince 2007); furthermore, the International Agency for Research on Cancer (IARC) ranked steroid estrogens in the group of carcinogenic compounds (group 1) in 1987 (Rousseau *et al.* 2005).

The occurrence of emerging contaminants (ECs), also called micropollutants, is derived from various sources that could be anthropogenic as well as natural substances (Galindo-Miranda *et al.* 2019). There are several sources of steroidal estrogens entering the environment, and mainly the pathways are domestic and pharmaceutical wastewater, agricultural runoff, and livestock industries. Wastewater effluent containing estrogenic compounds is discharged into rivers while the sludge is used as a fertilizer (Aris *et al.* 2014). Mainly excreted in urine are natural steroid estrogens and synthetic residues from contraceptive pills and other drugs (Johnson *et al.* 2000). Therefore, increasing world population, urbanization, and consequently the increase in the use of synthetic steroid estrogens has led to an increase in the number of steroid estrogens in domestic wastewater, and domestic wastewater stands as the most important source of steroidal estrogens in the environment (Ying *et al.* 2004). Waste waste containing estrogens is taken together with wastewater into wastewater treatment plants (WWTPs) and then distributed into the aquatic environment, including drinking water (Pratush *et al.* 2020). The concentration of these compounds can increase from a few nanograms per litre (ng/L) to 15 μg/L, which is high enough to generate acute and chronic toxicity (Li *et al.* 2014; Verlicchi *et al.* 2015).

Hormones, when released by humans and released into the wastewater, are in a conjugated form but less active. The process of conversion to the active form can occur in the wastewater course between the residence and the WWTP, or inside the WWTP during treatment (de França *et al.* 2020).

The discharge of wastewater (e.g., brine) degrades water quality and thus the water cannot be directly used for potable water (via desalination) and industrial applications (Panagopoulos & Giannika 2022a, 2022b, 2023).

In recent years, WWTPs have been considered the hot spots of chemical pollutants such as endocrine-disruptive chemicals (EDCs), PPCPs, and active pharmaceutical ingredients or pharmaceutically active compounds (Kibambe *et al.* 2020). Conventional wastewater treatment systems are not able to remove these emerging pollutants, so they will enter the surface water, groundwater, and eventually drinking water directly and indirectly. Therefore, the failure of conventional wastewater treatment technologies to completely remove a wide range of these compounds poses human, animal, and environmental health concerns, and it is necessary to investigate the existence of steroid estrogens in water, especially drinking water, and remove them if the concentration is higher than the standard (Filali-Meknassi *et al.* 2004). Also, the lack of a wastewater collection system to dispose of wastewater, especially domestic wastewater and the use of absorption wells, causes the leakage of wastewater and polluting compounds and hormones into underground water and surface water. The pollution of the water leads to the entry of polluting compounds into the bodies of humans and other living organisms and poses a risk to their health. Hence, it is necessary to monitor these compounds in drinking water (Ismail *et al.* 2022; Nguyen *et al.* 2022; Nworie *et al.* 2022).

A drinking water supply system usually consists of a drinking raw water source, a drinking water treatment plant, and a drinking water supply (the distributed treated water). Surface river water is the main source of raw water intake used by drinking water treatment plants for treatment and following the supply of drinking water in most countries. Point sources (e.g., treated and untreated discharges) and nonpoint sources (e.g., runoff and leachate) discharge EDCs into the body of raw water (Aris *et al.* 2014; Barber *et al.* 2015; Wee *et al.* 2020). The last point of protection against chemical exposure between the environment (i.e., drinking water source) and the users is the drinking water treatment plant. Unfortunately, the removal of EDCs by conventional treatments is not effective since the treatment process has not been designed for EDC removal, contributing to EDC loading in the global drinking water supply, i.e., potable water (Leung *et al.* 2013; Gabarrón *et al.* 2016; Wee *et al.* 2020).

In a study conducted in 45 areas of Chicago, the highest concentrations of E1, E2, and EE2 were reported as 1.5, 1.4, and 1.4 ng/L, respectively (Bradley *et al.* 2020). In another study, the highest concentrations of E1, E2, E3, and EE2 were reported as 5.3, 3.71, 5.6, and 4.47 ng/L, respectively, in drinking water (Sodré & Sampaio 2020). However, there was no detected concentration of estrone, 17-beta-estradiol, and 17-alpha-ethinylestradiol in the drinking water of Latin America (Reichert *et al.* 2019), which was the same as Piracicaba City in São Paulo for hormones E1, E2, E3, and EE2 by the detection limit of 0.7 ng/L (Torres *et al.* 2015). Also, the range of 1.7 ng/L–n.d was reported for estrone, 17-beta-estradiol, estriol, and 17-alpha-ethinylestradiol in Asia, North and South America, and Oceania (Zhang *et al.* 2016). The concentration of estrogenic hormones in two types of water purified by conventional and advanced purification was investigated in China, and estrogenic hormones were not detected in any of the samples; therefore, the overall concentration of hormones was less than 1 ng/L (Zhang *et al.* 2013). According to Fan *et al.* (2013), the average concentrations of E1 and E2 were 0.4 and 0.05 ng/L, respectively, and they were 1.2, 5.2, 0.1, and 0.5 ng/L for estradiol, estriol, estrone, and ethynylestradiol, respectively, in Wang *et al.* (2011).

Therefore, the aim of this study was environmental monitoring of estrogen hormones such as estrone (E1), 17 beta-estradiol (E2), estriol (E3), and 17-alpha-ethinyl estradiol (EE2) and investigating the quantity and quality of the hormones in potable water in different areas of Tehran in different seasons during one year.

METHODS

Iran (the Islamic Republic of Iran) is a country in Western Asia, which is considered to be the second most populous nation in the Middle East region. The main environmental issues in Iran are air pollution, water quality and quantity crisis, municipal and industrial wastes, and climate change. Tehran (35°41′21″N, 51°23′20″E), the capital of Iran with a population of nearly nine million, as a megacity, suffers from various environmental and social problems, such as severe air pollution and water crisis (Ardalan *et al.* 2019). The characteristics of Tehran are described in Table 1 (Khoshnoodmotlagh *et al.* 2021).

Tehran drinking water sources and plants

Drinking water in Tehran is sourced from both surface and underground reservoirs. Surface water is collected from the Lar and Latian dams in the northern region, as well as the Amir Kabir and Taleghan dams in the northwest of Tehran, and Mamlu Dam in the east of Tehran. This water is then transported through pipelines to water treatment plants after passing through intake structures. Once at the treatment plants, the water undergoes physical and chemical treatments (conventional treatment) before being stored in reservoirs and distributed throughout the city's water distribution system.

Tehran is equipped with seven surface water treatment plants. Treatment Plant No. 1 (Jalaliyeh) is historically significant as one of Iran's oldest treatment facilities, boasting a capacity of 7.2 m^3/s. Its water supply is derived from the Amir Kabir and Taleghan dams via the Bilqan intake station. Treatment Plant No. 2 (Kan) stands as Iran's largest treatment plant, which is located in western Tehran, with a capacity of 8 m^3/s. Similar to Treatment Plant No. 1, it receives its water supply from the Amir Kabir and Taleghan dams, which are treated at this facility following passage through the Bilqan intake location. The Tehranpars treatment plants (Nos 3 and 4) each have a capacity of 4 m^3/s. These plants draw their raw water input from the Latian Dam, which is situated in eastern Tehran, providing water to eastern areas as well as parts of northern, central, and southern Tehran. Treatment Plant No. 5 operates in northeastern Tehran with a capacity of 5.7 m^3/s, sourcing its water supply from the Lar Dam. Lastly, Water Treatment Plant No. 7, which is situated in southeast Tehran, has a capacity of 2.5 m^3/s and receives its water supply from the Mamlu Dam reservoir. Overall, these treatment plants play a vital role in ensuring that Tehran's residents have access to clean drinking water by effectively treating both surface and underground sources before distribution throughout the city's extensive network. Additionally, a portion of Tehran's drinking water is sourced from underground wells. The amount of groundwater utilized varies depending on factors such as the condition of the supplying sources, consumption levels, and different seasons. This range can be anywhere from 20% to 40% of Tehran's total water requirements. Presently, there are a total of 441 operational deep wells within the city with an approximate production capacity of 14.5 m^3/s. The distribution and dispersion of these wells across Tehran are determined by various factors

Table 1 | The characteristics of Tehran city

Area (km^2)	730
Population	9,382,000
Population density (people per km^2 of the land area)	11,877
Average rainfall (mm)	62.7

including the quantity and quality of the aquifer, water demand in each area, accessibility to purification plants, reservoirs, pipelines, and other considerations that influence the design of water supply networks. It is worth noting that well water does not require purification and is stored in water reservoirs after chlorination before being distributed into the drinking water network alongside the treated surface water from treatment plants. Consequently, within each of the six areas covered by the Tehran Water and Wastewater Company, drinking water for the population is supplied through a combination of treated surface water from water treatment plants (60%–80%) and groundwater (20%–40%) (Tehran Water and Wastewater Company 2023).

Sampling

In this study, the concentration of hormones such as estrone (E1), 17-beta-estradiol (E2), estriol (E3), and 17-alpha-ethinyl estradiol (EE2) in the drinking water of Tehran is investigated. The water has passed through the conventional treatment process in Tehran's water treatment plants, mixed with the disinfected underground water in storage tanks, and entered the drinking water distribution network of Tehran, where the people can use tap water for drinking. It was necessary to take samples from the tap water in the entire city. In order to better manage water resources and water distribution, Tehran Water and Wastewater Company has divided the city of Tehran into six areas, and the drinking water of the whole city is provided from surface water that is stored behind dams (80%–60%) and underground water (20%–40%). In order to determine the type and concentration of hormones in the drinking water of Tehran, sampling stations were placed in each area according to the size of the area, the population covered, and the population density, and 40 sampling stations were placed in the whole city. Then one sample was prepared from each station in the middle of the seasons of summer (August 2020), autumn (November 2020), winter (December 2020), and spring (May 2021). Hence, four samples were collected from each station during one year. Figure 1 illustrates the geographical location of sample points in the Tehran drinking water pipeline network. In order to take samples, a 1 litre amber glass bottle was washed with hot water and acetone solvent was used, which was filled with tap water and transferred to the chemistry and environmental laboratory of the Faculty of Health, Tehran University of Medical Sciences, in a cool box at ± 4 °C. The samples were analyzed after passing fiberglass filters of 0.45 μm GF/F and then 0.2 μm.

Chemicals and reagents

Methanol and EDCs (EE2, E2, and E1) were purchased from Merck (Darmstadt, Germany) and Sigma (UK), respectively. N,O-bis(trimethylsilyl) trifluoroacetamide (BSTFA) containing 1% of trimethylchlorosilane (TMCS) was supplied by Aldrich (Dorset, UK). Ultrapure water was supplied from a Millipore Ultrapure water system (Zhang *et al.* 2006; Mohagheghian *et al.* 2014).

Solid-phase extraction and gas chromatography

After transferring the samples to the laboratory, they were passed through a GF/F fiberglass filter of 0.45 μm and then 0.2 μm in order to remove possible suspended solids, and then the hormones were taken out of the water sample using the extraction method and a C18 cartridge. To prepare the C18 cartridge, 12 ml of methanol was passed over the adsorbent under very low suction pressure so that the adsorbent was immersed in methanol for about 15 min (to ensure the complete removal of the compounds adhered to the absorbent). Next, the adsorbent was washed using ultrapure water with a flow rate of 1–2 ml/min. Finally, it was prepared for the passage of drinking water and the absorption of steroid hormones. The water sample was passed through the adsorbent with a flow rate of less than 5 ml/min. Then, the steroid hormones were separated using methanol and entered the liquid phase (Mohagheghian *et al.* 2014), and the stage was reached for the gas chromatography–mass spectrometry (GC–MS) analysis to determine the concentration of hormones.

GC–MS analysis

The instrument used in order to identify the quantity and quality of the estrogenic hormones was GC–MS. Helium (99.999% purity) with 1 ml/min flow rate was used as carrier gas. At first, 1 μl sample was injected, and the temperature of the inlet was set at 280 °C. The column temperature was kept at 80 °C for 0.5 min. Then, the temperature was increased to 300 °C with a gradient of 20 °C/min to 250 °C and with a gradient of 5 °C/min, and it was kept at this isothermal temperature for 4 min. In addition, the temperature of the auxiliary section was set to 300 °C. Concentrations of 0.5, 1, 10, 50, and 100 ng/L of E1, E2, E3, and EE2 mixture were used in order to draw the calibration curve; 19/03–15/76 min were the time variations to identify the components.

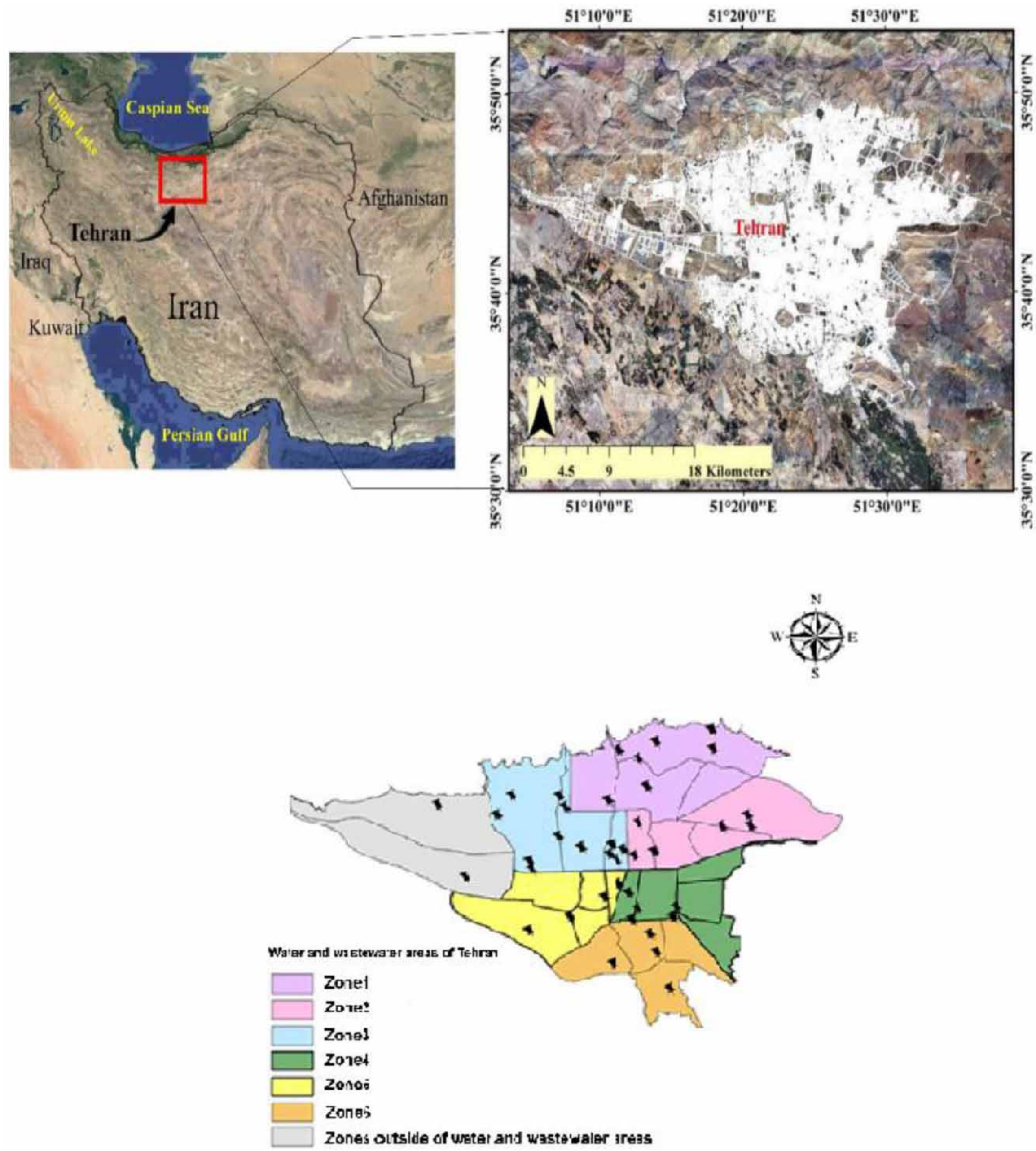


Figure 1 | The geographical location of drinking water sampling points in Tehran.

Statistical analysis

In this study, χ^2 and Fisher's exact test were used to analyze the results obtained from the examination of the concentration of hormones in potable water.

RESULTS AND DISCUSSION

The calibration curve of steroid hormones

In this study, the concentration of E1, E2, E3, and EE2 was investigated in different areas during one year. In order to determine the concentration of hormones in the samples, first, the standard solution was prepared using methanol, and then the calibration curve was drawn. At the end, the amount of extracted hormones was determined by the solid-phase extraction (SPE) method. The results are illustrated in Table 2.

The concentration of steroid hormones during a year

The concentration of E1, E2, E3, and EE2 was investigated during different seasons of the year and the average concentrations are given in Table 3. In total, out of 160 drinking water samples examined, the concentration of only 72 samples was higher than the detection limit of the device. Based on the results, E1 and E2 were detected in all samples of summer and autumn with the annual average concentration of 0.792 and 1.071 ng/L for E1 and 0.934 and 1.230 ng/L for E2 in summer and autumn, respectively; that they were not detected in spring and winter can be attributed to heavy rainfall in these seasons followed by the dilution of hormones (Esteban *et al.* 2014). However, E3 and EE2 concentrations were lower than the device detection limit (0.5 ng/L) and were not detected in any seasons, which can be attributed to heavy rainfall in these seasons followed by the dilution of hormones, and also the decreased use of underground water and increased use of surface water sources for drinking. Groundwater is one of the main sources of water supply in Tehran (Ardalan *et al.* 2019). In addition, the concentration of hormonal compounds is reduced by important factors including high temperature and high water flow. This is similar to the results reported by Esteban *et al.* (2014) regarding hormonal compounds in drinking water in Madrid, Spain. The main sources of natural and artificial estrogen hormones are effluent from municipal WWTPs, but some compounds such as EE2 are not detected in drinking water and there are many reasons. The effective factor in the absence of EE2 in drinking water can be the very low solubility (4.8 mg/L in 20 °C) of this synthetic estrogen compound compared with other natural estrogen compounds E1 and E2 (13 mg/L in 20 °C) (Pojana *et al.* 2007; Aris *et al.* 2014). Also, EE2 is a non-polar and hydrophobic compound with a low vapor pressure (4.5×10^{-11} mmHg), which makes it resistant to its biological degradation (Li *et al.* 2013). Although the concentration of EE2 was halved within 25 km from the source of the sewage effluent, it was still detectable up to 100 km along the river. Due to the hydrophobic and lipophilic properties of EE2, the concentration of this compound in water was very low or below the detection limit of the device, but it had a high concentration in sediments and sludge (Aris *et al.* 2014). Several studies showed that E3 and EE2 in water had very low concentrations or even undetectable concentrations in some cases (Stachel *et al.* 2003; Viganò *et al.* 2006; Ying *et al.* 2009; Zhang *et al.* 2009; Kinani *et al.* 2010; Sodré *et al.* 2010; Gong *et al.* 2011; Zhang *et al.* 2011; Liu *et al.* 2012). As mentioned, the hormonal compounds that enter the wastewater are not decomposed by conventional wastewater treatment methods, and some of them enter the sludge due to their hydrophobic properties, and the sludge resulting from wastewater treatment due to the presence of nutrients after the processing is used as a fertilizer in agriculture, so the management of the nutrients and pollutant is not advanced either. Nutrients of the soil are consumed in agriculture and discharged with

Table 2 | Pearson's coefficient and the average amount of extracted hormones in the SPE method

Composition	R^2	Average of extraction (%)	Composition	R^2	Average of extraction (%)
E1	0.998	87.12	E3	0.995	81.32
E2	0.993	90.58	EE2	0.997	79.23

Table 3 | Mean concentration of steroid hormones and standard deviations during a year ($n = 72$)

Hormones \ Seasons	Mean spring (ng/L) ± SD	Mean summer (ng/L) ± SD	Mean autumn (ng/L) ± SD	Mean winter (ng/L) ± SD
Estrone (E1)	ND	0.792 ± 0.24	1.071 ± 0.41	ND
17-beta-Estradiol (E2)	ND	0.934 ± 0.32	1.230 ± 0.47	ND
Estriol (E3)	ND	ND	ND	ND
17-alpha-ethinyl estradiol (EE2)	ND	ND	ND	ND

ND, not detected.

wastewater into the aquatic ecosystems, where they can trigger some environmental problems such as water pollution (Ardalan *et al.* 2019).

The concentration of steroid hormones in different areas

Table 4 shows the highest concentrations of E1, E2, E3, and EE2 in six areas of Tehran. The results illustrate the highest concentrations of E1 and E2 in area numbers 5 and 6 (southern areas of Tehran) and the lowest concentrations of E1 and E2 in area numbers 1, 3, and 4, but E3 and EE2 were not detected in any of the areas (concentration lower than the device detection limit (0.5 ng/L)).

The results of this study showed that area 6 of the Tehran Water and Wastewater Treatment Company was the most polluted area, and this area is located in the southern and southeastern areas of Tehran, and the drinking water needed in this area is supplied from the Mamlu Dam, which is located on the Jajrud and Damavand rivers. Considering that the new city of Pardis is located in the northwest region of Tehran, only about 50% of the wastewater produced by its population of 600,000 people is treated and the rest enters the Jajrud River catchment area without treatment. Also, agricultural lands, livestock farms, and industrial areas are located along the Jajrud River and discharge their produced wastewater into the catchment area of this river. The results of this study showed that all the samples obtained from this area in the summer and autumn seasons are contaminated with E1 and E2 hormones and clearly demonstrated the contamination of Mamlu Dam water with human, agricultural, animal husbandry, and industrial wastewater. But in the spring and winter seasons, due to the increase in rainfall and the increase in the water flow of rivers and the dilution of pollution, the desired hormones were not detected (Salam Nu News 2020). Also, according to the Tehran Water and Wastewater Treatment Company, some parts of area 5 are supplied by Mamlu Dam, and in some of the samples obtained from this area, contamination of hormones E1 and E2 was observed.

The relationship between seasons and regions in the concentration of steroid hormones

The concentrations of E1, E2, E3, and EE2 were measured in different areas and different seasons to investigate the existing relationship. According to Table 5, the concentrations of E1 and E2 were the highest in area numbers 5 and 6 and the season autumn. In addition, in the spring and winter, none of the hormones was observed in any of the areas, and their concentration was lower than the device detection limit. Moreover, E3 and EE2 compounds were not detected in any season or any area.

Table 4 | The highest concentration of steroid hormones in different areas

Hormones \ Area	1 (ng/L)	2 (ng/L)	3 (ng/L)	4 (ng/L)	5 (ng/L)	6 (ng/L)
Estrone (E1)	0.790	ND	0.710	0.670	1.390	1.960
17-beta-Estradiol (E2)	0.850	ND	0.770	0.760	1.610	2.130
Estriol (E3)	ND	ND	ND	ND	ND	ND
17-alpha-ethinyl estradiol (EE2)	ND	ND	ND	ND	ND	ND

Table 5 | E1, E2, E3, and EE2 concentration ranges (ng/L) in summer and autumn seasons and all areas ($n = 72$)

		Area number					
Season	Compound	1	2	3	4	5	6
Summer	E1	ND–0.66	ND	ND–0.56	ND–0.54	0.79–0.98	0.86–1.15
	E2	ND–0.73	ND	ND–0.59	ND–0.63	0.92–1.15	1.09–1.54
	E3	ND	ND	ND	ND	ND	ND
	EE2	ND	ND	ND	ND	ND	ND
Autumn	E1	ND–0.79	ND	ND–0.71	ND–0.67	0.97–1.39	1.29–1.96
	E2	ND–0.85	ND	ND–0.77	ND–0.76	1.23–1.61	1.42–2.13
	E3	ND	ND	ND	ND	ND	ND
	EE2	ND	ND	ND	ND	ND	ND

According to the results, E1 and E2 (1.96 and 2.13 ng/L, respectively) had the highest concentrations in the network drinking water in the autumn and in area number 6; however, it was lower than the detection limit in spring and winter. In addition, E3 and EE2 were not detected in any season or any area. The results of this study illustrated the various concentrations of steroid hormones based on seasons and areas. Since the concentrations of the studied compounds were less than the device detection limit in more than 50% of the samples, because of the decreased ability to compare means and averages, two groups were established consisting of (1) variables higher than the device detection limit and (2) variables less than the device detection limit. Fisher's exact test was used (the conditions were not suitable for performing the χ^2 test). The comparisons were done only in summer and autumn. Outlier data (higher and lower concentrations than the device detection limit) were investigated in different areas, and the *p*-value was obtained by performing the Fisher test (Table 6).

Considering that E1 and E2 were detected in summer and autumn in most areas, the results were investigated in these two seasons. According to Table 7, in summer, hormone concentrations were higher than the device detection limit in 100% of the samples in area numbers 5 and 6 (south and southeast of Tehran), and in autumn, the highest hormone concentration was observed in area numbers 5 and 6; however, in number 2 region, no compounds were found in any of the samples.

As shown in Figures 2 and 3, the isothermal maps of E1 and E2 were drawn in summer and autumn according to the steroid hormone threshold concentration (≥1 ng/L; the detection limit of the present study is 0.5 ng/L) for the EU (European Union) dimension (De Jong *et al.* 2021). Based on the maps, concentrations were higher than the threshold limit in area numbers 5 and 6.

The sources of drinking water in Tehran include surface water (60%–80%) (Lar, Latian, Amirkabir, Taleghan, and Mamlu Dams) mostly in the northern, northeastern, and eastern areas of Tehran and underground water sources (20%–40%) scattered in Tehran. The absence of any steroid hormones in the samples taken from area number 2 proved the point that the surface water source for drinking supplies from Tehranpars Water Treatment Plant, which is the Latian Dam, is located in

Table 6 | Frequency and percentage of E1 and E2 in different areas

Area number	Number (%) of samples with a concentration lower than the detection limit	Number (%) of samples with a concentration higher than the detection limit	Total number of samples
1	22 (78.6)	6 (21.4)	28 (100)
2	24 (100)	0 (0)	24 (100)
3	44 (91.6)	4 (8.4)	48 (100)
4	14 (70)	6 (30)	20 (100)
5	8 (50)	8 (50)	16 (100)
6	12 (50)	12 (50)	24 (100)
All the regions	124 (77.5)	36 (22.5)	160 (100)

Fisher's exact test value: 30/461, and *p*-value: 000.

Table 7 | The percentage of E1 and E2 in different areas in summer and autumn

Area number	Percentage of the samples with a concentration higher than the device detection limit (0.5 ng/L) in autumn	Percentage of the samples with a concentration higher than the device detection limit (0.5 ng/L) in summer
1	14.29	42.9
2	0	0
3	5.56	16.6
4	20	60
5	33.33	100
6	50	100

Fisher's exact test value: 21/052, *p*-value: 000.

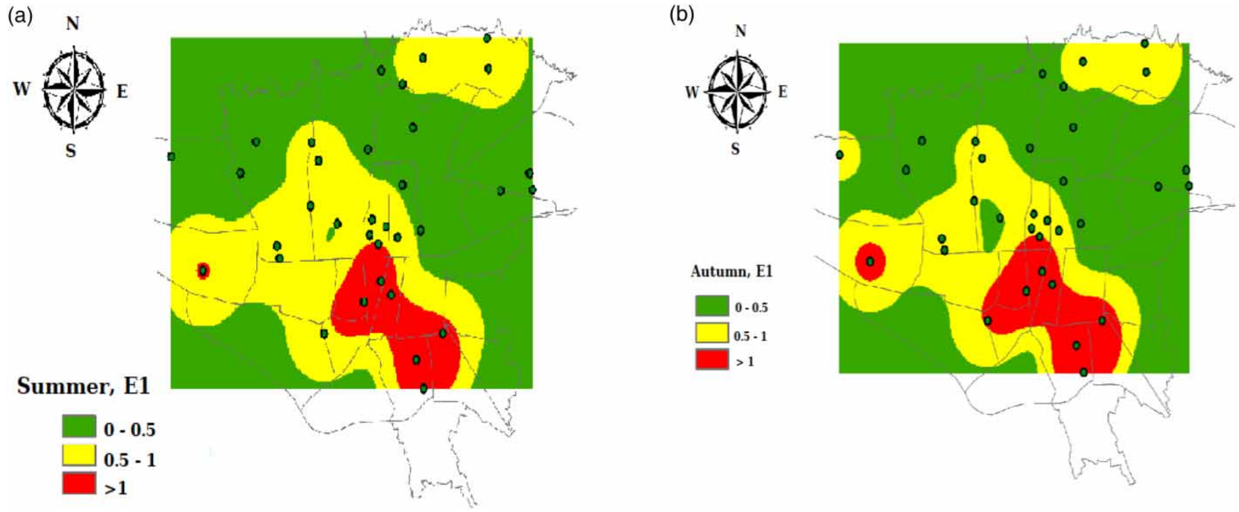


Figure 2 | Concentration of E1 in different areas of Tehran in (a) summer and (b) autumn.

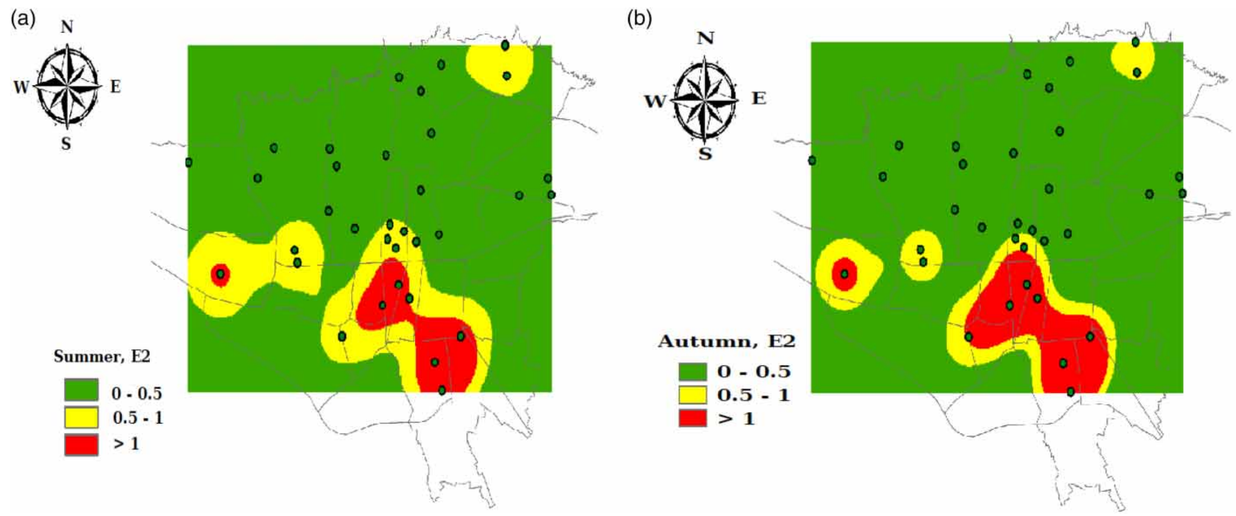


Figure 3 | Concentration of E2 in different areas of Tehran in (a) summer and (b) autumn.

the mountainous areas northeast of Tehran and not much sewage is discharged into it, so that as the results show, this water is almost clean and without hormonal pollutants. According to the programs of Tehran Water and Wastewater Company, the drinking water needed in the southern and eastern areas of Tehran is supplied by the Mamlu Dam. Due to the contamination of the water of this dam with human, agricultural, livestock, and industrial wastewater, there is a high probability of emerging pollutants and hormones in it, and because these compounds are not removed from the water by conventional treatment methods, hormones E1 and E2 in the tap water of areas 5 and 6 of Tehran were identified. Also, by moving toward the southern and eastern areas of Tehran, the possibility of the presence of pollutants in surface and underground water increases. The reason for this can be various factors such as the existence of absorption wells especially for municipal sewage disposal in Tehran, the geographical slope of the city toward the south and the east and the leakage of pollutants from the absorption wells into the underground water, the use of animal and human fertilizers and sludge from WWTPs in the agricultural areas of southern Tehran, and the presence of industrial, animal husbandry, and agricultural centers in these areas, whose activities and lack of proper management of wastewater and waste production will lead to the pollution of underground water. The studies carried out on the quality of underground water confirm this content (Helperin *et al.* 2001;

Tran 2001; Garduño *et al.* 2011; Shirani *et al.* 2013). The use of wastewater and effluent to irrigate agricultural lands and livestock waste as a fertilizer in the southern areas leads to an increase in the presence of steroid hormones and other pollutants not only in groundwater but also in surface water (Yazdan *et al.* 2022).

The other factors that have caused the high concentration of steroid hormones in the drinking water of area number 6 of Tehran could be the high population density, irrigation of green spaces with sewage, use of animal and chemical fertilizers in green spaces, and the presence of numerous runoffs in this area (Shirani *et al.* 2013). According to the results, it was found that E1 and E2 have the maximum concentration in summer (1.15 and 1.54 ng/L) and autumn (1.96 and 2.13 ng/L) in the samples of the area number 6. Other research results show that the concentration of estrogen hormones is less than ng/L and sometimes pg/L in the potable water that reaches people's drinking consumption; however, this can also threaten human health (Bradley *et al.* 2020; Du *et al.* 2020). The studies found E1 and E2 concentrations of ND–1.7 ng/L in drinking water sources (Wang *et al.* 2011; Jardim *et al.* 2012; Dévier *et al.* 2013; Fan *et al.* 2013; Zhang *et al.* 2013; Esteban *et al.* 2014; Torres *et al.* 2015; Zhang *et al.* 2016; Reichert *et al.* 2019; Bradley *et al.* 2020) and reported the data 5.3 and 3.71 ng/L, respectively, as the highest concentrations of E1 and E2 in drinking water (Sodré & Sampaio 2020). In Europe, the concentration of steroid hormones 17-beta-estradiol and 17-alpha-ethinylestradiol was reported as ND–17 ng/L in drinking water (Tiedeken *et al.* 2017). Generally, in most studies, the concentration of estrogen hormones in drinking water was lower than the device detection limit and it was not identified in the samples (Jardim *et al.* 2012). Comparing the results of previous studies and the present study shows that the steroid hormone concentration in Europe is higher than in Tehran (Tiedeken *et al.* 2017); nevertheless, other studies in Latin America, North and South America, Asia, and the Pacific show a lower concentration of steroid hormones than the present results (Fan *et al.* 2013; Zhang *et al.* 2013; Torres *et al.* 2015; Zhang *et al.* 2016; Reichert *et al.* 2019). In addition, according to the zoning, it was found that the E1 concentration in the summer and autumn in number 5 and 6 regions is higher than the E1 concentration in the Philippine drinking water source of Laguna Lake (0.3–0.03 ng/L) (Ana & Espino 2020), and it is very similar to the E1 concentration reported in the main drinking water source of Lake Titicaca (1.56 ng/L); however, the E2 (2.27 ng/L) concentration is higher than the result of the present study (Zamalloa Cuba *et al.* 2021). On the other hand, based on the results of the present study, the concentration of E3 and EE2 in all regions and seasons was reported to be below the device detection limit (0.5 ng/L), which is in accordance with the environmental quality standards of the EU (the annual average concentrations of E2 and EE2 are 0.4 and 0.035 ng/L, respectively). E2 and EE2 concentrations in surface waters are 0.08 and 0.007 ng/L, respectively (European Commission 2003). Additionally, in the Zamalloa Cuba *et al.* (2021) study, EE2 concentration was detected as 13.88 ng/L, while this hormone was not detected in any region and season in the current study. Zamalloa Cuba *et al.* (2021) suggested that the reason for the existence of the hormones was the non-proper treatment and discharge of wastewater into the lake in their study. Given that the concentration of EE2 was in accordance with the environmental quality standards and was not detected in any season and region, it can be concluded that this hormone had a very low concentration or was not present at all, which can be attributed to the hydrophobic and lipophilic properties of EE2, and the concentration of this compound in water was very low or below the detection limit of the device, but it had a high concentration in sediments and sludge (Aris *et al.* 2014). Therefore, it can be concluded that wastewater is one of the ways by which estrogenic compounds enter into water sources.

Studies have also shown that the removal efficiency of EE2 is 25.90%–66.3% in the Tehran WWTP (Mohagheghian *et al.* 2014), in contrast to the high efficiencies (71%–78%) reported in other studies (Auriol *et al.* 2006). In addition, decomposition, biological transfer, and absorption lead to a reduction in the EE2 concentration (Aris *et al.* 2014). In Tehran, the main method of wastewater disposal has been the use of absorption wells in homes, and in recent years, a WWTP has been established in the south of Tehran for the collection of municipal wastewater, but still all the wastewater produced in the city is not completely collected. For this reason, there is a possibility of sewage discharge to both underground and surface waters in Tehran. Studies also confirm the pollution of surface and underground waters (Shirani *et al.* 2013; Javid *et al.* 2016; Ghahremanzadeh *et al.* 2018). In another study, the concentration of E3 was lower than the device detection limit (0.5 ng/L) (Mohagheghian *et al.* 2014). Several studies showed that E3 and EE2 in water had very low concentrations or even undetectable in some cases (Stachel *et al.* 2003; Viganò *et al.* 2006; Ying *et al.* 2009; Zhang *et al.* 2009, 2011; Kinani *et al.* 2010; Sodré *et al.* 2010; Gong *et al.* 2011; Liu *et al.* 2012). Area number 2 is one of the clean areas due to the high percentage of surface water for drinking water. Generally, E1, E2, and E3 are of human and animal origin (Praveena *et al.* 2016; Yazdan *et al.* 2022). Unfortunately, these pollutants enter into water sources and the environment without any treatment (Kassotis *et al.* 2020; Vieira *et al.* 2021). In addition, women's use of contraceptives containing ethinylestradiol compounds leads to an increase in the concentration of estrogenic hormones in rivers (Torres *et al.* 2015). Results of the study in Tehran showed that women preferred hormonal methods (66%) to other methods for preventing pregnancy (Amiri 2014). In another study, the results showed that the trend of using modern contraceptive methods has been decreasing, and traditional methods have been increasing; and the desire to get pregnant is increasing very slowly among women younger than 35. The use of male methods, especially condoms, is regularly increasing, and modern female methods including the intrauterine device (IUD), birth control pills, tubectomy, and injection had a decreasing trend, so the percentage using male methods is increasing. It was more female than modern methods, which had no significant relationship with the level of education and the number of children (($p = 0.15$) and ($p = 0.08$)). The change in the population policies of the country in order to increase fertility has led to a gradual decrease in the use of modern methods of pregnancy prevention (Behboudi-Gandevani *et al.* 2016). On the other hand, it was observed that the concentration of hormones in Tehran's drinking water is higher than in other parts of the world in most cases. It can be related to the period of the present study (August 2020–May 2021), in which water consumption generally increased as well as drug consumption (Balacco *et al.* 2020; Feizizadeh *et al.* 2021; Hu *et al.* 2022). Many studies have confirmed the presence of steroidal estrogens in both groundwater and surface water due to livestock wastewater and human urine (E2, EE2, and E3 at about 58%, 96%, and 69%, respectively) (Kassotis *et al.* 2020; Vieira *et al.* 2021; Yazdan *et al.* 2022). Generally, an E1 concentration of more than 10 mg/L can effectively reduce the production of extracellular polymer substances and metabolic activities (Zhang *et al.* 2021). Some studies have also shown the reverse effect on fish life due to the presence of hormonal residues, such as feminized phenotypes, effects on the reproductive system, and ovulation (Torres *et al.* 2021). Therefore, considering the bioaccumulation of lipophilic hormones followed by toxicity to fish is important (Zamalloa Cuba *et al.* 2021). In studies that were conducted to investigate hormones E1, E2, E3, and EE2 in water, the results showed that hormones E1 and E2 have a similar concentration range in almost all studies, and all studies believe that the use of birth control pills and municipal and livestock wastewater, due to the presence of hormones in the urine, are responsible for the presence of these hormones in surface and underground water. Also, failure to remove these hormonal pollutants with conventional treatment methods in water treatment plants and resistance to biological degradation are another factor for the presence of this pollutant in tap water (Viganò *et al.* 2006; Zuo *et al.* 2006; Jafari *et al.* 2009; Ying *et al.* 2009; Singh *et al.* 2010; Sodré *et al.* 2010; Zhang *et al.* 2011; Liu *et al.* 2012; Aydin & Talinli 2013). The results of another study that was conducted in Turkey showed that hormones have a much higher concentration. The authors stated that the reason for this is the direct discharge of high-flow wastewater into the rivers and surface waters under investigation (Aydin & Talinli 2013).

CONCLUSION

The results obtained from the investigation of steroid hormones E1, E2, E3, and EE2 in the drinking water of Tehran showed that hormones E1 and E2 in area numbers 5 and 6, which are located in the south and southeast of Tehran, in the summer seasons (0.792 and 0.934 ng/L for E1 and E2) and autumn (1.071 and 1.230 ng/L for E1 and E2), respectively, have the highest concentrations. The high concentration of these hormones in these regions and in these seasons could be due to the decrease in the flow of rivers and the increase in the concentration of hormones and other pollutants due to the discharge of urban, agricultural, livestock, and industrial wastewater into surface and underground waters. The results of this study confirm the discharge of wastewater into surface and underground waters of eastern and southern areas of Tehran. It also confirms the contamination of the Mamlu Dam, which is located on the Jajrud River, with man-made pollution. However, these hormones were not detected in the drinking water samples of any of Tehran's regions in the winter and spring seasons, which could be due to the increase in pollution due to rainfall in these seasons. Also, E3 and EE2 hormones were not detected in any of the drinking water samples collected from different regions in any season throughout the year, which is due to the tendency of these hormones to settle in sediments and mud, in addition to increasing rainfall and their hydrophobic properties and resistance to biological degradation. Also, based on the results of this study, it can be concluded that the water of Taleghan, Amirkabir, and Lar and Latian dams, which are located in the northern and northeastern areas of Tehran and in the mountainous areas, is almost free from man-made pollution and sewage, and in terms of hormones, it is not a threat to the population consuming their water.

The results obtained from this study can tell the drinking water supply officials of Tehran that the water in the eastern and southern areas of Tehran is polluted and the water source in these areas needs more monitoring and treatment. The amount of sewage and pollution entering the Jajrud River and its catchment area should be investigated, so that the level of pollution does not exceed the self-purification capacity of the river; and by using the self-purification capacity of the river and the water treatment plant, healthy and pollution-free water can be provided to the people of this region. It should be remembered that emerging pollutants and hormones can have harmful health effects in the long term even though in low concentration. Furthermore, intake of these pollutants can show adverse effects more strongly in adulthood than in the early years of life and may be transmitted to the next generations. Therefore, it is necessary and obligatory to identify and remove them from the environment.

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DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

CONFLICT OF INTEREST

The authors declare there is no conflict.

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