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Concentration of cadmium, arsenic, and lead in rice (*Oryza sativa*) and probabilistic health risk assessment: A case study in Hormozgan province, Iran

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Abstract

Background: The presence of toxic heavy metals in cereal grains like rice is one of the main human and environmental health concerns. Their importance is because of their non-biodegradability nature, high half-time, and bioaccumulation ability in the human body. Among heavy metals, cadmium (Cd), lead (Pb), and arsenic (As) are most critical, so their concentrations in rice were evaluated in this study.

Methods: In this study, the concentration of Cd and Pb was determined by graphite-furnace atomic absorption spectrometer (GF-AAS), while the concentration of As was measured by atomic spectrum poll after acid digestion of the milled rice samples. The probabilistic health risk assessment of Cd, As, and Pb through consumption of different types of rice including local rice and two types imported from India (IND) and Pakistan (PAK), was estimated for the adults in Hormozgan province using Monte Carlo simulation (MCS) technique.

Results: It was revealed that the concentrations of all Cd, As, and Pb in the local rice samples were lower than those in the PAK and IND samples. The average concentration of As, Pb, and Cd in the rice samples were 0.045, 0.057, and 0.022 mg/kg, respectively. The estimated total target hazard quotient (TTHQ) for this population was lower than 1, representing negligible non-carcinogenic risk through rice consumption. However, total carcinogenic risk (TCR) via As intake showed a considerable carcinogenic risk (TCR > 1E-4) for this population.

Conclusion: According to the results, it is necessary to perform continuous monitoring for concentration of Cd, As, and Pb especially in the imported rice samples.

Keywords: Heavy metal poisoning, *Oryza*, Environmental pollution, Monte Carlo method

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Introduction

Rice (*Oryza sativa*) along with wheat and corn are the main food crops in the world. Rice is considered as a staple food in several Asian countries, including Iran, from ancient times (1-4). In other words, rice is the main source of carbohydrates in the diet of people in Asia (2,5). Although rice consumption is declining, due to the diversity of dietary habits, and thus, industrialization, but 4.2 billion people in the world consume rice as their staple food (5-7). In Iran, per capita rice consumption (the second most widely consumed food in the country) is estimated to be 40 kg. Due to high demand for rice and high cost of local rice, Iran is considered as one of the most significant importers of this product (8,9).

Heavy metals are environmental pollutants that human exposure to these contaminants through water and food can cause chronic and sometimes acute toxicity (10,11). Of these, metals such as lead (Pb), cadmium (Cd) and arsenic (As), are xenobiotic; not only are not needed for the body's metabolism but even their small amounts are also harmful to humans (12). In addition to the natural contamination sources of crops with heavy metals, these products are infected through human activities, such as agriculture, mining, construction, fertilizers, irrigation with wastewater, sewage sludge on agricultural land, application of manure and pesticides, and industrial processes (13,14). Rice is a special product among the crops, because it has high uptake and accumulation of Cd, Pb, and As (15).

Cd is an environmental pollutant heavy metal that enter the environment by both natural and synthetic sources (16-18). The most important sources of artificial soil contamination include discharge of sludge and industrial wastewater, the use of fertilizers and superphosphate, buried non-ferrous scrap in the ground and agricultural lands around mines of Pb and zinc or refineries (18-21). Cd has a long biological half-life with the ability to accumulate in the liver and kidneys and damage them (22). Also, by entering the food chain, it can cause damage to the lungs and bones, leading to anemia and sometimes, high blood pressure (23).

Although Pb is available in the environment naturally; but it is mainly enter the environment through human activities. Pb is one of the four metals that have the greatest effects on humans (24). Naturally, its concentration in the soil is approximately 70 mg/kg, but industrial activities, such as mining, steel processing, and combustion increase its concentration (25). Acute Pb poisoning in humans lead to severe damages to the body organs, such as the kidneys, liver, brain, reproductive system, nervous system, cardiovascular system, red blood cells, anaemia, and sometimes, death (26).

One of the environmental sources of As is As compounds which are used as pesticides. As has similar properties to phosphorus, therefore, As compounds and phosphorus compounds coexist in the nature (27). As can lead to damages to the cardiovascular system, skin, nervous system, kidneys, and the hematopoietic system (28). Moreover, long-term exposure to As even at low levels (0.05 mg/L), increases the risk of skin, lung, urinary tract, bladder, and kidney cancers (29). The adverse effects of As include chronic poisoning, general weakness in the muscles, loss of appetite, nausea, diarrhoea, vomiting, inflammation of the mucous membranes of the eyes, skin lesions, anaemia, and reducing white blood cells and malignant tumours (30).

Given that the existence of Cd, Pb, and As in food has a particular importance in terms of health, research on the absorption of these metals in food products, as well as the toxicity and adverse effects of them on humans is very important (31,32). Hence, determination of their concentrations in different foods especially rice has always been of interest to researchers.

Most of the studies conducted, especially in Iran, only evaluated the concentration of these metals in food products, and there are few studies on health risk of consumer due to the concentrations of Cd, Pb, and As in food, therefore, the present study was conducted to fill the gap. Since rice is the main part of the Iranian society diet, the present study was conducted to determine the concentration of these potentially toxic elements (PTEs) in different types of rice including local Iran (IRN), Pakistan (PAK), and India (IND) available in Bandar Abbas market and estimate the non-carcinogenic and carcinogenic risk due to the exposure to As, Pb, and Cd through rice consumption in the adults using Monte Carlo simulation (MCS) technique.

Materials and Methods

Study area

The study area was Bandar Abbas, the capital of Hormozgan province and the economic capital of Iran. Bandar Abbas with a population more than half a million people in the south of Iran, is considered as the main gateway for Iran's exports and imports.

All chemicals (nitric acid and hydrochloric acid) and standard stock solutions of As, Pb, and Cd (HPLC grade with purity > 99%) were purchased from Merck company (Darmstadt, Germany).

Sample collection and preparation

To determine the concentrations of As, Cd, and Pb in different types of rice, 75 samples of rice including 25 samples of each studying rice were collected from Bandar Abbas market in 2019. Then, the collected samples were transported to the laboratory and coded based on their types before the analysis. After grinding the rice samples thoroughly, 10 g of each milled rice samples was weighted and placed on the flame. In order to make ash, the burned samples were held in the furnace at a temperature of 200-250°C for about 8 hours. Then, about 3 mL of double distilled water was added to the obtained ash and was held on the hot water bath to evaporate the extra water.

Measurement of Cd and Pb

To prepare the samples for determination of the Cd and Pb concentration, 50 mL of HCl (6 M) and about 10-30 mL of nitric acid (1 M) were added to the material obtained from the previous section. Finally, this solution was filtered by Whatman filter (No. 41) in a volumetric flask, then, its volume was adjusted to 50 mL with double distilled water. Finally, the concentration of Cd and Pb was determined by graphite-furnace atomic absorption spectrometer (GFAAS), according to the AOAC standards.

Measurement of As

To prepare the samples for determination of the As concentration, 2 mL of the concentrated nitric acid was added to the material obtained from section 2.2 and placed on the hot water bath to evaporate extra acid. After the addition of about 10-15 mL of HCl (2 M) in order to solve the residual contents, the solution was stirred about 2 hours for solving all contents in the solution. Subsequently, the obtained solution was filtered and 50 mL of HNO_3 (0.1

N) was added to the flask. Finally, the concentration of As was determined by hydride generation, according to the AOAC standards.

Probabilistic risk assessment

Daily intake estimation (EDI)

In the residents, EDI of rice ingestion was calculated by the following equation (33,34):

$$EDI = \frac{C \times IR \times EF \times ED}{BW \times AT} \quad (1)$$

Where *C* is the concentration of PTEs (mg/kg), *IR* is the ingestion rate of rice (g/n-day), *ED* (year) is the exposure duration (30 years), *EF* (days/year) is the exposure frequency (350 days/year), *BW* (kg) is body weight (77.45 ± 13.6 kg), and *AT* (days) is the average lifespan (for non-carcinogenic risk: 10 950 days; and for carcinogenic risk: 25 550 days).

Per capita rice consumption as well as its patterns were determined using a questionnaire in a 400-person statistical population in Hormozgan providence. The overall consumption of rice was obtained to be 19.71 kg/n-year and daily per capita consumption of the IRN, IND, PAK, and other types of rice (Thailand, Argentina, etc.) were equal to 12.25 (22.68%), 21.06 (39.03%), 16.74 (31.00%), and 3.94 (7.29%) g/n-day, respectively.

Non-carcinogenic risk

The non-carcinogenic risk was calculated by the following equation (33,35):

$$THQ_i = \frac{EDI}{RfD\ or\ TDI} \quad (2)$$

Where *THQ* is the target hazard quotient, *EDI* is estimated daily intake (mg/kg-d), *RfD* is oral reference dose (mg/kg-d), and *TDI* is the tolerable dietary intake (mg/kg-d). Oral RfD for As (inorganic) and Cd is 0.0003 and 0.001 mg/kg-d, respectively (36). According to the World Health Organization (WHO) health risk assessment protocol, TDI for Pb is equal to 0.0036 mg/kg-d (37).
The total target hazard quotient (TTHQ) was calculated using the following equation (38,39):

$$TTHQ = (THQ_{As} + THQ_{Cd} + THQ_{Pb})_{IND} + (THQ_{As} + THQ_{Cd} + THQ_{Pb})_{IRN} + (THQ_{As} + THQ_{Cd} + THQ_{Pb})_{PAK} \quad (3)$$

Carcinogenic risk

The carcinogenic risk (CR) was calculated using the following equation (40, 41):

$$CR = EDI \times CSF \quad (4)$$

Where *CSF* is cancer slope factor (mg/kg-d)$^{-1}$ (42). Based on the Environmental Protection Agency (EPA) health risk assessment protocols, CSF for inorganic As is equal to 1.5 (mg/kg-d)$^{-1}$ (43).

The total carcinogenic risk (TCR) due to the presence of As in rice was calculated using the following equation:

$$TCR = CR_{IND} + CR_{IRN} + CR_{PAK} \quad (5)$$

Monte Carlo simulation technique

MCS is a probabilistic approximation technique for considering uncertainty and variability in the health risk assessment (44). The probabilistic risk assessment of PTEs concentration in rice for adult residents were estimated using MCS technique by Crystal Ball software (Version 11.1. USA, Inc.). In this study, 10 000 repetitions were used to estimate the variances of THQ and CR using the study variables (C, IR, and BW). These variables have a lognormal distribution. Percentile 95% of THQ and CR were considered as the benchmark health risk.

Results

Table 1 shows the concentration of Cd, Pb, and As in the IRN, PAK, and IND rice samples. As shown in this table, the concentration of Cd, Pb, and As in the imported rice (PAK, IND) were higher than that in domestic rice samples (IRN). The average amount of Pb, As, and Cd was 0.057, 0.045, and 0.022 mg/kg, respectively (Table 2). The rank order of rice types based on their THQ due to As was IND (0.062) > PAK (0.051) > IRN (0.028); Cd, IND (0.0089) > PAK (0.0085) > IRN (0.0029); and Pb, IND (0.0069) > PAK (0.0067) > IRN (0.0031) (Figure 1). The rank order of PTEs based on their THQ in the IND rice was As (0.062) > Cd (0.0089) > Pb (0.0069); IRN rice, As (0.0280) > Pb (0.0031) > Cd (0.0029); and PAK rice, As (0.051) > Cd (0.0085) > Pb (0.0067) (Figure 1). The rank order of rice types based on their TTHQ was IND (0.077) > PAK (0.066) > IRN (0.034), and overall TTHQ due to PTEs in the rice samples was equal to 0.177 (Figure 2). The rank order of rice types based on the CR of As was IND (8.28E-05) > PAK (8.21E-05) > IRN (7.919E-05) (Figure 3). The TCR was equal to 2.44E-04, which shows that residents are at a considerable carcinogenic risk due to the ingestion of rice containing As (Figure 4).

Discussion

Concentration of As, Cd, and Pb in rice samples

Heavy metals including As, Cd, and Pb are one of the most important environmental pollutants, which could enter the plants like rice through contaminated air, water,

Table 1. The concentration of PTEs in the IND, PAK, and IRN rice samples (Mean ± SD, mg/kg)

PTEs	Type of Rice		
	IND	PAK	IRN
As	0.047 ± 0.035	0.048 ± 0.009	0.035 ± 0.007
Cd	0.021 ± 0.009	0.028 ± 0.018	0.009 ± 0.002
Pb	0.055 ± 0.040	0.066 ± 0.080	0.040 ± 0.008

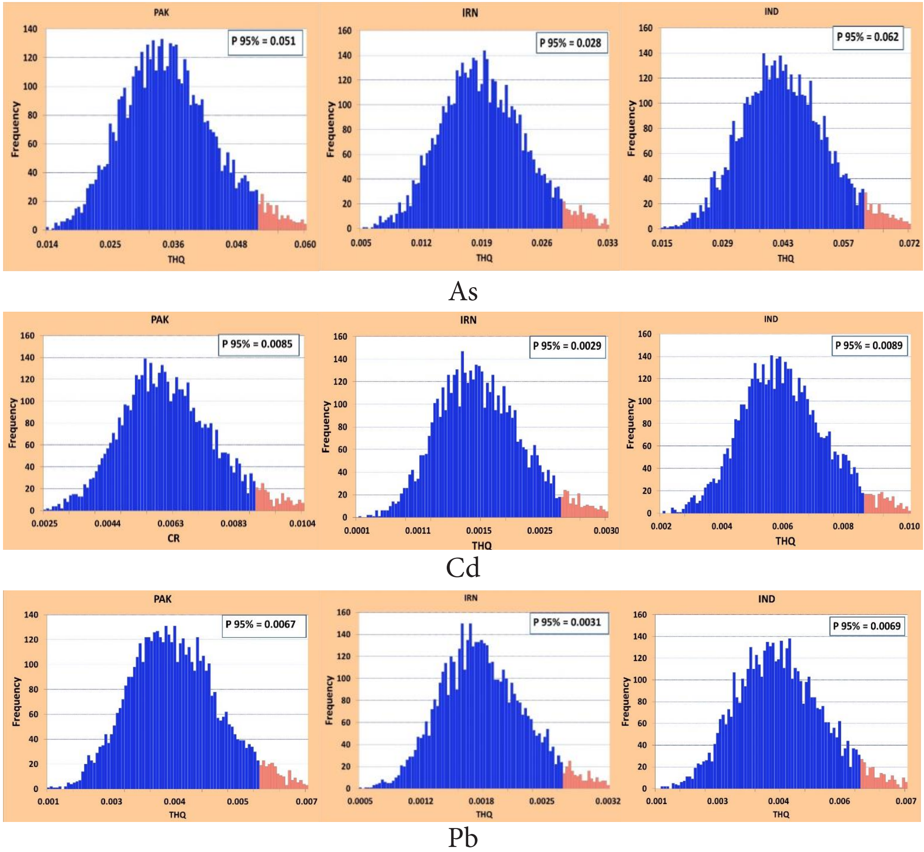

Figure 1. The non-carcinogenic risk in the consumers of the PAK, IRN, and IND rice containing PTEs.

and soil mainly due to the industrial emissions, burning of fossil fuels, traffics, mining, and agricultural practices (55). Thus, they can accumulate in the human body via dietary exposure and result in several disorders in many organs and their functions like cancer, hypertension, and bone problems (63). For instance, International Agency for Research on Cancer (IARC) has classified As and Cd as carcinogenic compounds (class 1) and Pb as a possible carcinogenic substance to humans (class 2A) (64).

As shown in Table 1 , the concentration of Cd, As, and Pb in the imported rice (PAK, IND) were higher than that in domestic rice samples (IRN) ($P < 0.05$). This difference could be possibly due to the cultivation of the former types in the extremely contaminated soil, which could result in the transfer of As, Cd, and Pb from the soil to the rice grain. Furthermore, the use of polluted groundwater for rice plant irrigation and the application of pesticides and fertilizers containing heavy metals (especially As and Pb) have been reported as other possible reasons for the accumulation of PTEs in rice cultivars (53,55).

Moreover, in all the studied rice types, Pb and Cd represented the highest and lowest concentrations, respectively, which is consistent with the results of previous studies (59,65). These differences are possibly due to the existence of higher amounts of Pb and As in the soil and water used for rice cultivation, using pesticides rich in Pb and As, and higher ability of plant to transfer them from soil (66). Regarding the recommended safe limits of Iran national standards and WHO/FAO for As, Cd, and Pb (0.15, 0.06, and 0.15 mg/kg and 0.15, 0.1, and 0.2 mg/kg, respectively) in rice and comparing them with the calculated concentrations represent that these samples met the safe limits for the presence of PTEs in the rice grains (30,67). Table 2 shows the concentration of As, Cd, and Pb reported by several studies. There are some differences between the calculated concentration of PTEs in the present study and that in the previous studies done all over the world, which can be due to the differences

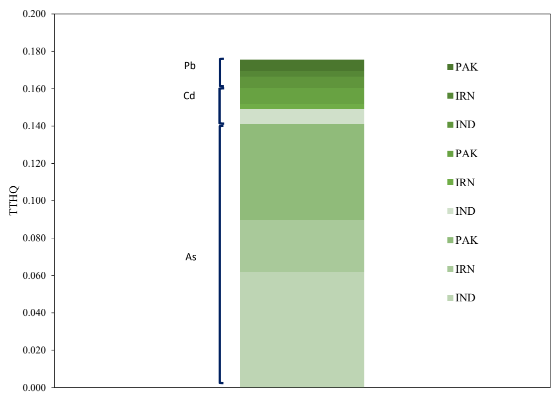

Figure 2. TTHQ in the consumers of the PAK, IRN, and IND rice containing PTEs.

Table 2. Concentrations of As, Cd, and Pb in rice reported by different studies (mg/kg)

Country	As	Cd	Pb	Reference
Korea	0.1	0.08	0.05	(45)
Korea	-	0.026	0.029	(46)
Brazil	0.051	1.6	0.44	(47)
Italy	-	0.025	0.02	(48)
Pakistan	0.41	0.09	0.26	(49)
India	-	0.05	0.62	(50)
India	0.36	0.26	0.15	(51)
Saudi Arabia	0.02	6.16	0.92	(52)
Bangladesh	0.47	0.045	0.71	(53)
Bangladesh	0.17	0.19	0.057	(54)
Argentina	0.237	0.025	0.006	(55)
China	0.39	0.23	2.01	(56)
China	-	0.015	0.57	(57)
China	0.119	0.05	0.062	(58)
China	0.089	0.087	0.036	(59)
Iran	0.16	0.19	0.93	(60)
Iran	-	0.082	0.077	(61)
Iran	0.37	0.034	0.12	(62)
Iran	0.045	0.057	0.022	Present study

in the rice variety, geographic locations, the chemical composition of soil, water, and air used in the cultivation of rice crops (30).

Non-carcinogenic risk

The THQ in residents due to the ingestion of the imported rice was higher than the local rice due to higher concentration of PTEs, and also, the higher ingestion rate of the imported rice. The THQ of As in three types of rice (local and two imported type from India and Pakistan) consumed in Hormozgan, was higher than that of Pb and Cd (Figure 1). The main reason is that As had higher concentrations in rice (Table 1), and also, As has lower RfD than Pb and Cd (36,37). The TTHQ of the imported (IND and PAK) rice was higher than that of the local rice due to higher ingestion rate of IRN rice and also higher concentrations of PTEs (68).

If THQ and/or TTHQ is lower and equal to 1, the non-carcinogenic risk is acceptable, but when THQ and/or TTHQ is higher than 1, the exposed population are at a significant non-carcinogenic risk (69). Therefore, residents of Hormozgan province are not at a considerable non-carcinogenic risk due to the consumption of rice containing As, Cd, and Pb.

Inconsistent findings have been reported in terms of non-carcinogenic risk. In a study by Wang et al in Tianjin, China, the THQ of Pb and Cd in rice were obtained to be 0.02 and 0.03, respectively (70). In another study by Li et al, THQ of Cd in six types of Chinese rice ranged from 0.6 to 2 (71). In the other study by Sharafi et al in Iran, the TTHQ due to the ingestion of PTEs (As, Cd, and Pb) in the IRN, IND, and PAK rice was obtained to be 0.62, 1.28, and 0.61, respectively (72). The TTHQ obtained in the conducted studies was different because of different concentrations of PTEs in raw rice, type of PTEs, ingestion rate, exposure duration, and exposure frequency (73-75).

Carcinogenic risk

When CR and/or TCR is higher than 1.00E-04 value, the exposed population are at a significant carcinogenic risk, but if CR and/or TCR is lower than 1.00E-06 value, the exposed population are not at a considerable carcinogenic risk (38). Also, if CR and/or TCR is between 1.00E-04 to 1.00E-06 value, the exposed population are at threshold cancer risk (38).

Since the As concentration in the imported rice (IND and PAK) was higher than that in the IRN rice samples (Table 1), hence, CR due to the ingestion of imported rice was higher than that due to the IRN rice ingestion.

In a study by Sharafi et al, the carcinogenic risk due to the consumption of rice containing As in the IRN, PAK, and IND rice was 2.2E-4, 2.1E-4, and 3.7E-4, respectively

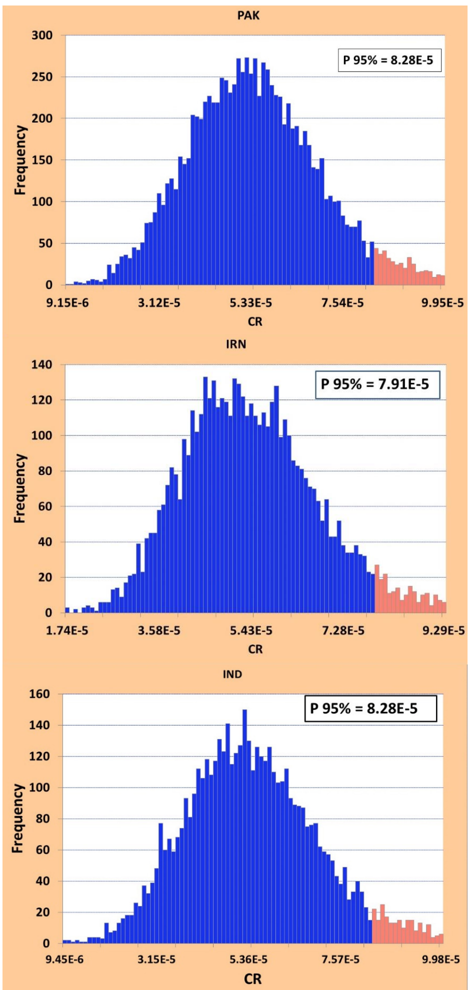

Figure 3. Carcinogenic risk in the consumers of the PAK, IRN, and IND rice containing As.

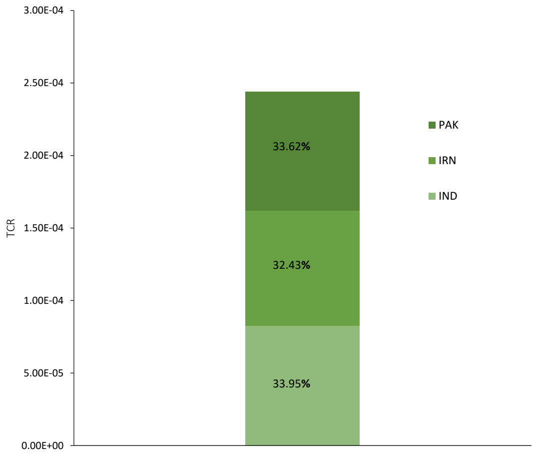

Figure 4. TCR in the consumers of the PAK, IRN, and IND rice containing As.

(72).

Although the TCR in the exposed population was significant, but the application of processes, such as washing and cooking can reduce the concentration of PTEs in rice before consumption (76-78). Also, after ingestion of cooked rice, some of the PTEs in the rice may be unabsorbed in the digestive gastrointestinal processes (79), hence, the cancer risks calculated in the present study can be lower than the actual cancer risk.

Conclusion

In the present study, the concentrations of Cd, As, and Pb in the imported rice (PAK, IND) was higher than those in local rice samples (IRN). Furthermore, the average concentrations of Pb, As, and Cd in the studied rice samples were 0.057, 0.045, and 0.022 mg/kg, respectively, which are lower than the permitted levels stated by the regulation references. The results revealed that the non-carcinogenic risk is negligible, while the rice consumers are at a considerable carcinogenic risk. Concerning the high consumption rate of rice in the studied population and health risks of dietary exposure to Pb, As, and Cd, there is a need to modify the diet habits and monitor imported rice rigorously to reduce the exposure to PTEs through rice ingestion.

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Ethical Issues

The study protocols were approved by the Ethics Committee of Hormozgan University of Medical Sciences, Hormozgan, Iran (Ethical code: IR.HUMS.REC.14572).

Conflict of interests

The authors declare that they have no conflict of interests.

Authors' contributions

All authors contributed and were involved in the problem suggestion, experiments design, data collection, and manuscript approval.

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