Original Article

Zamzam water is pathogen-free, uricosuric, hypolipidemic and exerts tissue-protective effects: relieving BBC concerns

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Abstract: Zamzam water is the most frequently used drinking water by millions of people in Saudi Arabia. It is carried all the time by millions of pilgrims to their home countries as gifts to close and near relatives and friends. Safety of constituents of Zamzam water is a vital health topic. British Broadcasting Corporation (BBC) raised many health concerns regarding the high serum arsenic and nitrate contents in Zamzam water that may cause cancer. It is role of scientific research to present scientific facts to relieve such concerns. Arsenic is a carcinogen while nitrate causes methemogloinemia that affect oxygen carriage by haemoglobin. An ethical committee approval was obtained. Eighteen white albino mice (40-45 g) were used in this study. Three experimental groups were allocated (six mice per group): tap water group, distilled water group and Zamzam water group. Our data revealed that Zamzam water exerts tissue-protective effects that contradict malignancy. Our data proved that Zamzam water is pathogen-free causing no bacterial growth on CLED agar colonies. Zamzam water consumption for three consecutive months in mice was quite safe for the general health and significantly decreased serum uric acid (p < 0.05) (possibly due to Zamzam-induced urine alkalinisation facilitating uric acid excretion). Regular Zamzam water consumption significantly decreased serum cholesterol (p < 0.05) and serum triglycerides (p < 0.05). Hypolipidemic effects of Zamzam water may be due to its high mineral content facilitating increased lipids metabolism. Our data confirmed safety of prolonged use of Zamzam water comparable to other drinking water types regarding the metabolic and synthetic functions of the liver. Nitrates in Zamzam water are thought to be an original constituent that may be useful (exerting vasodilation, antithrombotic, and immunoregulatory effects) and not harmless. This may occur due to high Zamzam content of calcium, magnesium and selenium. Histologically, our data confirmed that Zamzam water was quite safe to renal parenchyma and comparable to other types of drinking water. In conclusion, health concerns raised by BBC regarding Zamzam water safety were a good chance for fruitful scientific research investigations that confirmed safety and beneficial effects of Zamzam water for human health.

Keywords: Zamzam water, kidney functions, liver functions, uric acid, histology, BBC concerns

Introduction

Zamzam water (Zam Zam water) is the most preferred potable water and is considered superior to other drinking water sources in all Arabic and Islamic countries. Zamzam water well is sterile and is devoid of bacteria and fungi. It is located in the east of Al-ka'ba (Muslims' prayer destination) at Makkah city, Saudi Arabia. Zamzam water is the most frequently used drinking water by millions of citizens in Saudi Arabia and millions of international residents living in Saudi Arabia. It is always consumed for 1-3 successive months by millions pilgrims who come yearly to Saudi Arabia and carry it also to their home countries as gifts to near relatives and friends. Understanding the effects of constituents of Zamzam water on human health is a vital health topic. Interestingly, Shomar reported that constituents of Zamzam water are stable over a relatively long time period [1]. Zamzam water and Zamzam well are not contaminated by biological growths (bacteria or fungi). Moreover, Zamzam water was reported to be free from any contaminants and is not chemically treated in any way [2]. More interestingly, Zamzam water was reported to exert weak antifungal effects to same break-point as some antifungals [3]. Zamzam water is rich in minerals. Based on that, health properties of Zamzam water (taste, odour and smell) are stable and not changed with time. Four essential metal ions are present enormously in Zamzam water. Those include sodium, potassium, magnesium and calcium. In addition, seven trace metal ions are also available in Zamzam water. They include vanadium, manganese, iron, cobalt, copper, zinc and molybdenum. Trace metals are well-known to be required for the normal biological functions in humans [4]. The characteristic mineral content of Zamzam water did not change the mineral and electrolyte levels in people whom their daily maximum intake is Zamzam water. Moreover, kidney function tests of people dependent on Zamzam water are within the normal range [1, 5].

Zamzam water was reported to exert a wide range of therapeutic and pharmacological properties e.g. antioxidant, antitumor, anxiolytic and antidepressant agents. Co-treatment using methadone and Zamzam water significantly attenuated the spontaneous withdrawal symptoms (body weight loss, rare standing and sniffing) of morphine-dependent rats [6].

It is the role of science and research to alleviate peoples' concerns, to settle health facts and to remove the public fears and misunderstanding regarding any health topics. British Broadcasting Corporation (BBC) had raised many health concerns regarding the high serum arsenic and nitrate in Zamzam water. Arsenic is a carcinogen and nitrate causes methemogloinemia that affect oxygen carriage by haemoglobin. Health concerns were raised by BBC over many years regarding safety of Zamzam water. In order to settle scientific research facts and avoid misunderstanding, we conducted this study.

The health concerns raised by BBC regarding safety of Zamzam water for human consumption deserve a lot of light to be shed on them and consequently a lot of research interest and efforts. Zamzam water is not only a mere potable water source but it is also a prophetic medicine remedy that is described in the prophetic hadith as having a food benefit and a natural healer for ailments. Our data confirmed that in a recent report [7]. There is no single case report of arsenic or nitrate toxicity to support BBC concerns. Cancer incidence is not increased among citizens and inhabitants in Makkah and Al-Madinah or Saudi people. Arsenic and nitrate-related cancers did not score any reported increase in Makkah and Al-Madinah or other cities in Saudi Arabia.

In our recent report, mice administering Zamzam water exclusively for 90 days had no abnormality or tissue dysfunction compared to those exclusively using other water sources for the same period. There was no malignancy or tissue damage [7]. Unfortunately, debate is still

present as BBC concerns were published from time to time and turned to be public misconceptions. Zamzam water is still not allowed to be consumed in UK.

In this study, we investigated the health effects of consumption of Zamzam water for three consecutive months on mice. Serum uric acid (a kidney function test), renal histology, and serum total proteins (a synthetic liver function test) were evaluated. Effects of exclusive Zamzam water consumption on blood lipids (serum cholesterol and triglycerides) were also evaluated.

Methodology

Animal preparation

All animal handling maintenance, methodology, experimentation and manipulation were performed in agreement with the ethical research guidelines of Sohag University, Egypt. An ethical committee was approved by the Center of Scientific Foundation for Experimental Studies and Research, Ismailia, Egypt (in March 30th, 2019). Eighteen white albino mice (40-45 g) were used in this study. Three experimental groups were allocated (six mice per group): tap water group, distilled water group and Zamzam water group. Mice ages were within 9-12 months. They were randomly grouped. Negative control administered tap water exclusively. Animals were kept in an aseptic environment in pathogen-free conditions at 25°C. Animals were maintained using a standard laboratory diet with open access to water sources during the whole period of the study (90 days).

Investigation of potential contamination of Zamzam drinking with bacteria using CLED agar plate

Three different samples of Zamzam drinking water were collected from public drinking tanks in the prophetic masjid (mosque) in Al-Madinah, Saudi Arabia. Each water sample was centrifuged. No sediment was seen. As reported by Banginwar and Dawande [8] and other reports [9], a drop of each water sample was immediately placed on CLED agar plate and allowed to be incubated for 48 hours at 37°C. The presence of any growth or colour of colonies on the plate was observed for 48 hours.

Laboratory parameters assessment

Serum uric acid assay kits (BioSystems, Barcelona, Spain), and serum total proteins assay

kits (BioSystems, Barcelona, Spain) were used. Serum triglyceride assay kits (Crescent, Jeddah, Saudi Arabia) and serum cholesterol assay kits (Crescent, Jeddah, Saudi Arabia) were used. This study also aimed at assessing a possible tissue-protective effect of chronic administration of Zamzam water.

Histological examination of the kidneys

As previously reported, the kidney specimens were collected then measured by the liquid displacement method of Scherle [10] where the kidney was separated into several minor fragments. Such fragments were maintained at room temperature for two days in a fixative (freshly prepared 4% w/v formaldehyde in 0.1 M phosphate buffer, pH 7.2). Later, it was embedded in Paraffin (Sigma Co., St. Louis, MO, USA), sectioned at 3 μ m thickness, and the sections were stained with hematoxylineosin (H&E) as previously reported [11]. A number of photomicrographs were taken at (100 ×) magnification.

Statistical analysis

Data was collected, analyzed using SPSS software version 16 and presented as mean \pm standard error of mean. Paired samples t test was used to compare results between experimental groups. * indicated p < 0.05.

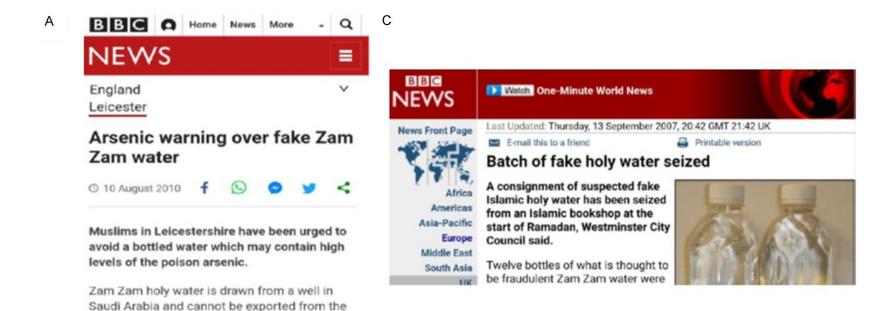
Results

Zamzam water is pathogen-free with no growth on CLED agar

Incubating the three different Zamzam water samples for 48 hours on CLED agar failed to show any bacterial growth or any colonies (Figure 2).

Effects of chronic exclusive administration of Zamzam water on serum uric acid

Serum uric acid was estimated for all the experimental groups. Our data revealed also that all the three experimental groups kept a normal level of serum urate (3-7 mg/dl). Mice receiving exclusive Zamzam water drinking had the lowest serum levels of uric acid that was significantly lower than the two other experimental groups (p < 0.05). However, drinking Zamzam water exclusively produced a further decrease in serum uric acid (**Figure 3A**).





country for commercial sale.



Figure 1. BBC reports exhibited big health concerns regarding Zamzam water originality and safety. A. BBC was concerned regarding a non-genuine Zamzam water consumed in UK. B. BBC was concerned regarding a cancer risk posed by a non-genuine Zamzam water. C. BBC was concerned regarding a high arsenic content in a non-genuine Zamzam water. D. BBC was concerned regarding a cancer risk posed by high arsenic content in Zamzam water samples.

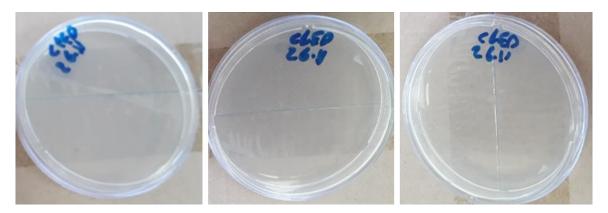


Figure 2. There is no bacterial contamination in Zamzam water. Three different samples of Zamzam drinking water were collected from public drinking tanks in the prophetic masjid in Al-Madinah, Saudi Arabia. All water samples were centrifuged. No sediment was seen. A drop of each water sample was immediately placed on CLED agar plate and allowed to be incubated for 48 hours at 37 °C. No bacterial growth was there.

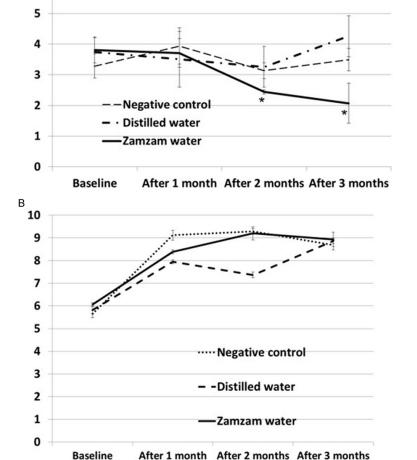


Figure 3. Zamzam water is nephroprotective and hepatoprotective. A. Zamzam water is uricosuric. B. Zamzam water enhances protein synthesis in the liver. * indicates p < 0.05, a significant difference compared with the negative con-

Zamzam watewr is quite safe to synthetic liver functions

Regarding serum total proteins, all mice in the three experimental conditions (drinking Zamzam water, tap water and distilled water) had normal serum total proteins levels with no significant values (p >0.05) among them (Figure 3B).

Effects of prolonged exclusive Zamzam water drinking on serum cholesterol and triglycerides

Serum cholesterol was monthly estimated in all mice in the three experimental groups. There were no significant differences in serum cholesterol lev-

Baseline

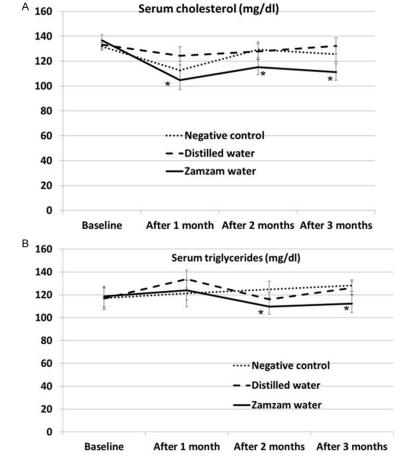


Figure 4. Zamzam water exerts hypolipidemic effects. A. Zamzam water exerts hypocholesterolemic effects. B. Zamzam water decreases serum triglycerides. * indicates p < 0.05, a significant difference compared with the negative control.

els among mice drinking either tap water or distilled water and there were no significant differences (p > 0.05) between animals in both experimental conditions in the monthly readings. However, mice drinking Zamzam water exclusively exhibited a significant decrease (p < 0.05) in serum cholesterol in the three readings taken during the three months of the study (**Figure 4A**). Moreover, mice drinking Zamzam water exclusively exhibited a significant decrease (p < 0.05) in serum triglycerid than mice drinking tap water and distilled water (**Figure 4B**).

Histopathological evaluation

The kidney of the control group revealed a preserved tissue architecture of renal medulla. The tubules in renal medulla were normal and intact. The distilled water & Zamzam water

groups had normal histological picture of the renal medulla. Glomeruli were normal in all mice of the three treatment groups. Histological examination revealed a normal renal interstitium with unremarkable blood vessels (no pathological abnormality).

Discussion

For BBC, many sequential health concerns regarding Zamzam water were reported [7] and Figure 1A-D. BBC reported that any water on sale that is labelled as Zam Zam water is of unknown origin and poses a health risk (Figure 1A). Then, BBC reported that water on sale under the name "Zam zam water" is a fake water. Zamzam water cannot legally be exported (Figure 1B). Fake Zam Zam water contains high levels of arsenic, a potential carcinogen (Figure 1C) almost three times the legal limit (Figure 1A, 1D). People have been told not to buy Zam Zam water after tests showed three times the permitted level of arsenic (Figure 1B). This leads

to prohibiting Zamzam water sale and consumption in UK. The penalty for selling false Zam Zam water is an unlimited fine or two years imprisonment (**Figure 1A**). BBC concerns were also directed to nitrates content in Zamzam water. BBC reported that Zam Zam water also contains twice the legal level of nitrates, which can affect infants (**Figure 1B**). Nitrates have also been found to increase the risk of cancer (**Figure 1A**, **1D**).

For the authors, BBC concerns are not supported by reality facts. Makkah and Al-Madinah cities in Saudi Arabia have a large human population with a huge enormous daily consumption of Zamzam water compared to other cities in Saudi Arabia. There is no acute or chronic arsenic or nitrate toxicity reports in Makkah and Al-Madinah or any Saudi city.

Table 1. BBC concerns regarding arsenic content in Zamzam water and simple relieving answers

- 1. Any water on sale that is labelled as Zam Zam water is of unknown origin and poses a risk (Figure 1A). This concern can be relieved by some facts:
 - There is no research study to prove any health risks after drinking Zamzam water.
 - There are many research studies to prove beneficial safe effects of Zamzam water [2, 5, 7, 22-23] in addition to data of this study.
 - Antioxidant minerals in Zamzam water (e.g. selenium and strontium) in Zamzam water abolish arsenic effects.
 - There are no arsenic toxicity reports in Saudi Arabia (having massive daily Zamzam water consumption).
- Excess arsenic in Zamzam water is selectively lethal to cancer cells (having deficient antioxidant system), sparing normal cells with better antioxidant systems.
 - Arsenic concentration in Zamzam water is having anticancer effects and is safe to normal cells.
- 2. Zam Zam' water contains high levels of arsenic-almost three times the legal limit (Figure 1A). This concern can be relieved by some facts:
- Arsenic-induced oxidative stress is antagonized by high antioxidant minerals (e.g. strontium, selenium, magnesium, sulfate...) in Zamzam water
- No arsenic-related toxicity was associated to Zamzam water consumption.
- 3. Fake Zam Zam water contains high levels of arsenic (Figure 1C).
 - First prove if it is fake or genuine Zamzam water.
 - Analyze other mineral constituents. Excess antioxidant minerals are protective against arsenic effects.
- 4. Zamzam water contains high levels of arsenic almost three times the legal limit (Figure 1D). Same reliving answers as concern #1.

BBC reported that any water on sale that is labelled as Zam Zam water is of unknown origin and poses a risk (**Table 1**). Actually, this is not based on valid research reports. It is a mere concern. There is no research report or study to support any health risks due to consumption of Zamzam water. If Zamzam water (for sale in UK) is genuine, it is safe for health evidenced by lack of any health harms reports from Saudi Arabia. Zamzam water contains zinc and other antioxidant minerals [1] that protect against arsenic toxicity [12]. Zamzam water is rich in strontium [1] that removes arsenic from aqueous media [13].

Zamzam water consumption lead to decreased serum uric acid i.e. Zamzam water may exert a uricosuric effect (Figure 3A). This may be due to the alkaline nature of Zamzam water [1], which may alkalinize the urine facilitating uric acid excretion. Zamzam water-induced significant decrease in serum uric acid (p < 0.05) may be promising for its future use in treatment of gout. Although none of the mice got hyperuricemia during the whole period (90 days) of the study, mice drinking Zamzam water exclusively exhibited a significant lowering of serum uric acid (p < 0.05). That can be explained by the fact that Zamzam water has an alkaline pH that lowers the acidity of mice urine and facilitates urinary excretion of uric acid. Based on that, Zamzam water facilitates ridding the body of urate and prevents the formation of urates stones.

The synthetic power of hepatocytes (total proteins synthesis) was quite intact and not disturbed by prolonged administration of any of the given water types (Figure 3B). There were no significant differences in serum total proteins levels among the three experimental groups (Figure 3B). Our data confirmed safety of prolonged use of Zamzam water comparable to other drinking water types regarding the metabolic and synthetic functions of the liver (Figure 3B). Our data relieves much of the concerns raised by the BBC regarding fears of a relatively high arsenic in Zamzam water. In other words, the high arsenic content (source of oxidative stress) in Zamzam water does not harm the tissues (Figure 3A, 3B). This may be due to the presence of counteracting antioxidant minerals (selenium, strontium, zinc....) [1] in addition to the alkaline pH of Zamzam water (confers antioxidant benefit). Alkaline pH (as in Zamzam water) was reported to activate thioldependent antioxidant activity of human serum albumin [14].

Regarding serum cholesterol and triglycerides, all mice in all experimental groups exhibited a normal serum level of cholesterol and triglycerides in all the experimental groups (drinking Zamzam water, tap water and distilled water) (Figure 4A, 4B). Serum levels of cholesterol were kept in the normal range (< 200 mg/dl) during the whole study period in the three monthly readings of mice exclusively drinking Zamzam water. Interestingly, serum cholesterol

Table 2. BBC concerns regarding nitrate content in Zamzam water and simple relieving answers

- 1. Nitrates have also been found, which may increase the risk of cancer (Figure 1A). This concern can be relieved by some facts:
 - There is no report proving a relationship between Zamzam water and malignancy.
 - Colorectal cancer (related to nitrates) is lower in Makkah (major consumer of Zamzam water) than other cities.
 - High calcium and magnesium (as in Zamzam water [1]) interfere with nitrate-malignancy relationships [20, 21].
- 2. Nitrates increase the risk of cancer (Figure 1D). This concern can be relieved by some facts:
 - Nitrates in Zamzam water are opposed by high calcium, magnesium and selenium.
 - Nitrates in Zamzam may carry potential benefits e.g. vasodilatation, antithrombotic, and immunoregulatory effects.
- 3. Zam Zam also contained twice the legal level of nitrates, which can affect infants (Figure 1B). Same reliving answers as concern # 1 and 2.
- 4. People have been told not to buy Zam Zam water after tests showed three times the permitted level of arsenic (Figure 1B). This concern can be relieved by some facts:
 - Other antioxidant (tissue-protective) constituents of Zamzam water should be considered.
 - Proving any evidence-based health harms is needed before doing this step.
- 5. Zamzam water cannot legally be exported (Figure 1B).
 - Zamzam water carried by international pilgrims has no reported health harms.
 - Proven therapeutic benefits (versus no proven harms) of Zamzam water should be in favour of allowing its international use.
- 6. The penalty for selling false Zam Zam water is an unlimited fine or two years imprisonment (Figure 1A). However, this can be relieved by some facts:
 - This should be done after proving any harmful health effects.
 - Currently available research results confirming safety of zamzam water should be considered.
 - As long as Zamzam water has proven therapeutic benefits, it should be allowed.

levels were significantly lower in mice drinking Zamzam water (p < 0.05) than the other two groups (drinking tap water and distilled water) in the three time points that we measured (after one month, two months and three months) (**Figure 4A**). This can be explained by the high mineral contents in Zamzam water that act as enzyme cofactors catalysing the metabolism of lipids and consumption of lipid alcohols (cholesterol and glycerol). This may reduce serum lipids and related health consequences.

A similar picture was found regarding serum triglycerides that significantly decreased (p < 0.05) in the same three time points compared to mice drinking tap water and distilled water (**Figure 4B**). The persistently decreased serum triglycerides in Zamzam water drinking group compared to tap water drinking group may reflect the effects of the high content of enzyme cofactors (in Zamzam water) on reducing serum triglycerides. This relieves much of the BBC concerns.

As for BBC concerns regarding cancer risk, Zamzam water was reported to be a miraculous water that is capable of exerting potent anticancer effects and inhibiting liver cancer cells proliferation in vitro using HepG2 cell line. That is due to the balanced mineral and nutritional composition of Zamzam water, which synergizes with other anti-cancer components

to stop cancer progression [15]. Human breast cancer cells treated with different pH values of Zamzam water samples (7.2 or 8) exhibited a significant apoptosis-induced decrease in cancer cell viability. Cancer cells were arrested in the G2/M phase while cancer cells counts were decreased in the G1 phase [16]. Zamzam water significantly decreased viability and induced necrotic death (acute massive group cell death) of human lung cancer cells. Cell cycle arrest occurred in the G0/G1 phases [17].

As for BBC concerns regarding nitrates (Table 2), nitrate levels in different water resources have increased in many areas of the world largely due to increased applications of inorganic fertilizer and animal manure in agricultural areas. Risk of specific cancers and birth defects may be increased when nitrate is ingested under conditions that increase formation of N-nitroso compounds [18]. However, this is not the case for Zamzam water as it is not near agricultural areas to be affected by fertilizers. Zamzam well is located in a dry arid and desert geography away from any contaminants. Moreover, our data proved that Zamzam water is devoid of bacterial contamination (Figure 2) i.e. there is no bacterial contamination to explain the relatively high nitrate content in Zamzam water. Interestingly, Zamzam water is rich in calcium and magnesium [1]. We think that nitrates in Zamzam water is an original constit-

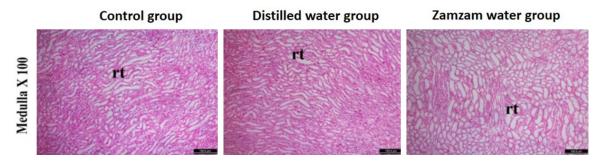


Figure 5. Zamzam water is not nephrotoxic. Normal renal cortex in animals exclusively drinking Zamzam water was confirmed in our recent study [7]. The kidneys of the control group revealed preserved tissue architecture of renal medulla. The renal tubules (rt) in renal medulla were normal and intact. The distilled water & Zamzam water groups had normal histological picture of the medulla with normal intact renal tubules (rt). Histological examination revealed normal renal interstitium with unremarkable blood vessels (no pathological abnormality) (H&E × 100).

uent that may pose health benefits. Potential health benefits of nitrate intake in drinking water include decreasing blood pressure (owing to production of nitric oxide in the acidic stomach resulting in vasodilation, antithrombotic, and immunoregulatory effects) [18]. In experimental animals, nitrates were beneficial in treating vascular hypertrophy, heart failure, myocardial infarction and increasing blood flow in certain parts of the brain. Moreover, nitrate-induced reduction to nitrite enhanced the protection against bacterial infections exerted by enteric bacteria where nitrite in drinking water was associated with both preventive and therapeutic effects [18].

Nitrates in Zamzam water are thought to be harmless. Selenium was reported to exert protective effects against nitrate effects via activating seleno-enzymes/compounds, which reduce the tissue damaging peroxynitrites (ONOO-) formed due to combination of nitrate and superoxide anion [19]. Selenium is a constituent of Zamzam water minerals [1]. High calcium in drinking water (as in Zamzam water [1]) was reported to modify the association between nitrate in drinking water and the risk of death from colon cancer [20]. High magnesium in potable water (as in Zamzam water [1]) is interfering with nitrate effects and is decreasing the incidence of colorectal cancer [21]. On the other hand, acquired methemoglobinemia occurs as a result of exposure to nitrates in drinking water and is of particular importance in infants. Badr et al. reported a recent study in which rat pups dependent on drinking Zamzam water showed a significantly higher total hemoglobin by the end of the study compared to baselines in rats consuming ordinary

water and mineral water groups. Methemoglobin levels were comparable among rats drinking the three different water sources with no significant differences throughout the whole study period i.e. prolonged use of Zamzam water did not induce any significant differences in methemoglobin concentration in rat pups, which might indicate that Zamzam water is safe for infants [22]. This in agreement with another report confirming safety of exclusive Zamzam water consumption on maternal and neonatal outcomes during labour stages in human [23]. Consistent with that is the report that Zamzam water exerted no teratological effects in animal studies. Zamzam water was given from the first day of pregnancy and continued until the 15th postnatal day after delivery. All offspring pups were subjected to various tests. The rate of body weight gain was higher in the last week in Zamzam water group. The sensory and motor reflexes in Zamzam exposed pups after birth and during the first two weeks of weaning period were significantly increased [24].

Histologically, our data confirmed that Zamzam water was quite safe to renal parenchyma and comparable to other types of drinking water (Figure 5).

Conclusion

Health concerns raised by BBC regarding Zamzam water safety were a good chance for fruitful scientific research investigations that confirmed safety and beneficial effects of Zamzam water for human health.

Disclosure of conflict of interest

None.

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