



Biological and therapeutic benefits of drinking Zamzam water

Jihan Mesfer Alghamdi and Ramesa Shafi Bhat*

Biochemistry Department; Science College of King Saud University, Riyadh, Saudi Arabia

*Correspondence: rbhat@ksu.edu.sa Received: Jan 29, 2025, Revised: March 20, 2025, Accepted: March 25, 2025 e-Published: March 29, 2025

ZumZum water is the most popular drinking water in Saudi Arabia, utilized by millions of people. The safety of the ingredients in Zamzam water is an important health consideration. It has been reported that this water contains a safe level of fluoride. In this review, we highlighted the hydrology, composition, and impact of Zamzam water on human health. It is alkaline and physiologically free from bacterial growth with no toxicity. Numerous disorders are treated using Zamzam water due to its antibacterial, antioxidant, and anticancer properties. It is rich in minerals but its daily intake does not increase any mineral or electrolyte levels in humans. Due to its alkaline nature, Zamzam water is beneficial in many physiological conditions related to toxicity and oxidative stress. Zamzam water is reported as a perfect balance of nutritional composition and minerals for the human body. It tends to strengthen the human body's cell system and increase energy levels. It increases the expression of new aquaporin and stimulates fertilization in both male and female reproductive systems. It is reported as hepatic-protective, nephron-protective, and neuroprotective, and helps in the prevention of cardiovascular diseases. It has the perfect balance of nutritional composition and minerals and helps in the prevention of diseases such as diabetes, congenital cataracts, and nephrogenic problems. It stimulates the reproductive system and has strong anti-inflammatory properties to fight against cancer.

Keywords: Antibacterial; Antioxidants; Anticancer; Fluoridated water; Zamzam.

INTRODUCTION

Drinking water has a potential impact on health and is very important for maintaining the balance of body fluids. The human body is composed of about 60% water and aids in digestion, absorption, circulation, creation of saliva, transportation of nutrients, and maintenance of body temperature. Drinking water should contain chemicals below toxic levels and should not affect overall health. Fluoride is commonly found in groundwater due to weathering and leaching of fluoride-bearing minerals rocks and is reported in the drinking water of Zamzam well with many beneficial properties. Zamzam water is used for both religious and therapeutic purposes and is collected from a well in the Mecca region of Saudi Arabia. Zamzam water has a unique physicochemical property with alkaline pH of 8 and is naturally hard (Al Doghaither et al. 2016). It is high in minerals such as calcium, magnesium, potassium, and sodium. In addition, fluoride, arsenic, and nitrate are present but below the dangerous level for human consumption (Shomar 2012). Some trace metals found in Zamzam water are vanadium, manganese, iron, cobalt, copper, zinc, and molybdenum required for normal biological functions in humans (Shomar 2012). In spite of being rich in minerals, Zamzam water is stable and does not change its taste, odor, and smell with time (Alfadul and Khan, 2012). Daily intake of

Zamzam water has not reported any change in mineral and electrolyte levels in humans (NourEldin et al. 2014). Zamzam water is beneficial in many physiological conditions related to toxicity, mainly in nephrotoxicity and hepatotoxicity. Many studies have reported its healing properties against diabetes and stress. These therapeutic properties of Zamzam water may perhaps be attributed to its alkaline nature which can reduce oxidative stress (Nassini et al. 2010). Recently a study by Moni et al (2022) proved the wound healing properties of Zamzam water more than a standard drug. Zamzam water is hardly contaminated with bacterial growth if exposed to open air as compared to pure water as its purity promptly deteriorates with open air (Ambrosch et al. 2008). In order to determine whether Zamzam water was fit for human consumption, the Saudi Arabian Ministry of Agriculture and Water Resources sent samples of Zamzam water for testing in European laboratories in 1971. According to the findings of water samples examined by European laboratories, Zamzam water has a unique structure that makes it suitable for drinking. The main finding was highlighted as the presence of fluoride as an excellent bactericide the satisfactory concentration of sodium, and the presence of the desired amount of calcium and magnesium protect against Cardio-vascular Disease and cancer (Analytical report, 1971). In this review, we will highlight some therapeutic properties of

Zamzam water (Figure 1).

Wound healing properties of Zamzam water

Zamzam water contains fluorine, arsenic, and zinc as trace elements. Low-level fluoride therapy has become known as a viable method to improve wound healing (Bhawal. 2020; Blee and Arikawa 2015; Lee et al. 2017). In recent years, significant progress has been made in understanding how fluoride treatment affects cells. These effects have been discovered to be concentration-dependent, with mill molar levels of fluoride (high concentration) inducing stress in the endoplasmic reticulum, apoptosis, and DNA fragmentation by the caspase-mediated pathway in enamel organ/epithelial-

derived cell lines while micromolar levels (low concentration) of fluoride increase cell proliferation (Blee and Arikawa 2015). A novel low-level fluorine application has recently come to light as an inventive, practical, and reasonably priced adjunct for wound healing. Studies have examined the effectiveness of low-level fluorine to stimulate osteoblasts and epithelial cells. Yet, little is known about the related molecular regulatory network. Furthermore, the fraction of fluorine in bone marrow mesenchymal stem cell homing has not yet been investigated (Lee et al. 2017). Arsenic and zinc are involved in protein and collagen synthesis and in the angiogenesis process resulting in the healing of a wound.

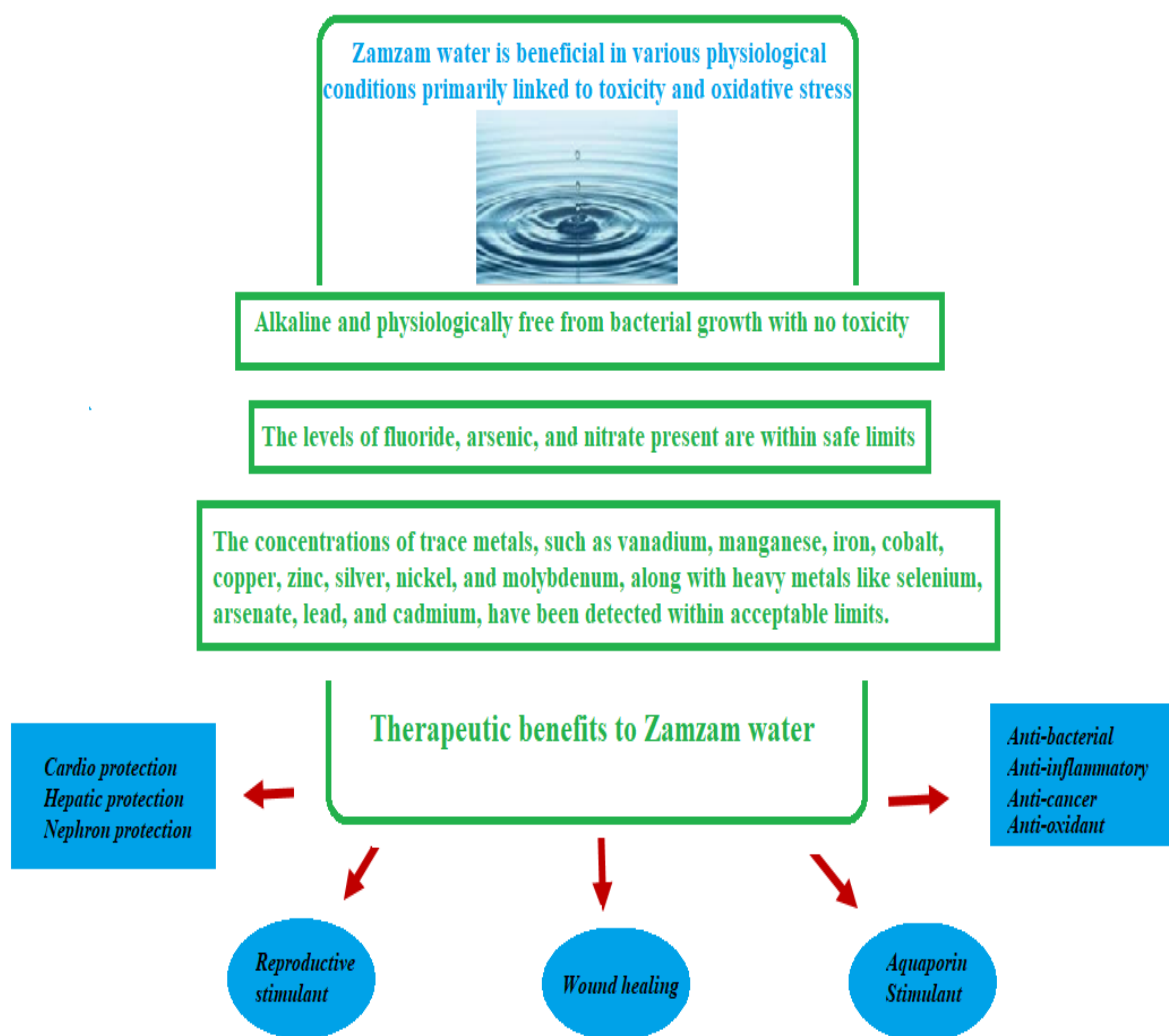


Figure 1: Therapeutic properties of Zamzam water.

Moni et al. (2022) showed a faster healing process

with Zamzam water than with povidone cream in male. Wistar rats. Arsenic in Zamzam water is associated with the downregulation of both (Type 1 T helper) Th1 and

(Type 2 T helper) Th2 cytokines (Ambrosch et al. 2008; YANG et al. 2016). Interleukin-1 beta (IL-1 β) known as a lymphocyte activating factor is an important mediator of inflammatory responses (Tanaka et al. 2014). IL-1 β is associated with human surgical wounds. Interleukin-6 (IL-6) has a key role in the immune response by regulating leukocyte infiltration, angiogenesis, and collagen accumulation to tissue injuries, chronic inflammation, and the level of bacterial infection in wounds (Rose-john et al. 2017; Sun. 2018). TNF- α is a pro-inflammatory cytokine released and induces inflammation at the site wound (Ritsu et al. 2017). Zamzam water treatment decreased the levels of IL-1 β , IL-6, and tumor necrosis factor-alpha (TNF- α) in wounded animals (Moni et al. 2022). Zamzam water has a better immunomodulation effect and exhibited excellent wound-healing properties.

Antioxidant benefits of Zamzam

The imbalance between oxidant and antioxidant mechanisms in the body can lead to oxidative stress. It happens mainly due to a deficiency of essential elements like selenium, zinc, and manganese and dietary deficiencies of vitamin E and, vitamin C. Alkaline water has the capacity to build up the antioxidant capacity and slow down aging (Wasowicz et al. 2003). Drinking water can increase the antioxidant capability in the human body if water is alkaline in nature (Logozzi et al. 2020 and Sun et al. 2022). Zamzam water is a natural alkaline; carbonated; hard water with exceptional chemical and physical characteristics (Waleed et al. 2021). Many studies have acknowledged the antioxidant properties of Zamzam water. It contains 34 diverse elements out of which selenium, zinc, and manganese are essential constituents of the antioxidant enzymes glutathione peroxidase, superoxide dismutase, and catalase (Khalid. 2014). Bamosa et al. (2013) reported a significant elevation of some antioxidant biomarkers like catalase, superoxide dismutase, glutathione, and total serum antioxidant capacity in diabetic patients after consuming Zamzam water for two months. Abdullah et al. (2012) reported elevated levels of catalase, glutathione, and dismutase with total antioxidant capacity in gentamicin-induced stressed models of rats. Zamzam water contains zinc which is a component of more than 2700 enzymes (Z Andreini and Bertini 2012) Zinc is a potent antioxidant agent as it can induce metallothionein (MT), Glutathione (GSH) synthesis, regulation of oxidant production, and regulation of redox signaling (Ganger et al. 2016). Zamzam water contains arsenic but it is not harmful to the body because of the presence of neutralizing antioxidant minerals such as selenium, strontium, and zinc. Additionally, the ideal alkaline pH of Zamzam water enhances its antioxidant benefit as alkaline pH can activate the thiol-dependent antioxidant and can raise serum-reduced GSH (Lee et al. 2000)

Zamzam water is neuroprotective.

The alkaline nature of Zamzam water may be the reason for diminishing oxidative stress and hence relieving the symptoms of many diseases. Riaz et al. (2018) explored the neuroprotective effect of Zamzam water in chlorpromazine-induced Parkinsonism models. Zamzam water significantly decreased the cataleptic score. Regenerative changes in the histopathological study of the rat brain were also revealed by Zamzam water treatment. Oxidative stress is the major cause of many neuro-developmental diseases including Parkinson's disease and the positive effect of Zamzam water may be due to its alkaline nature. Additionally, the neuroprotective effect of Zamzam water can be endorsed to zinc. Zinc is a trace element that plays a major role in the proper functioning of the central nervous system. Zinc can decrease the expression levels of caspase 8, caspase 9, caspase 3, cytochrome-c, caspase 6, BCL2-Associated X Protein (BAX), Apoptotic protease activating factor 1 (Apaf-1), and caspase 7 (Singla and Dhawan 2016) Neuroprotection of Zinc is proposed by anti-apoptotic pathways by reducing oxidative burden (Prasad et al. 2007). Gamma-aminobutyric acid (GABA) and glutamate neurotransmission modulated by zinc are involved in anxiety (Samardzić et al. 2013). Magnesium present in Zamzam water inhibits N-methyl-d-aspartate (NMDA) glutamate receptor (Hou et al. 2020). Zamzam water improves memory and cognition due to the presence of zinc and magnesium. Magnesium has been shown to improve memory by increasing the density of synaptophysin-/synaptobrevin-positive puncta in the dentate gyrus (DG) and CA1 subregions of the hippocampus. An increase in brain magnesium promotes learning and memory processes by enhancing both short-term synaptic facilitation and long-term potentiation (Slutsky et al. 2010). The presence of lithium in Zamzam water may also be responsible for the effect of Zamzam water on stationary rod activity (Shomar. 2012). Lithium has been reported to enhance the levels of phosphoglycogen synthase kinase-3 (GSK3) and Bcl-2 in radiated rats while decreasing the expression of proapoptotic Bax. Lithium is therefore regarded as a neuroprotectant and can therefore enhance learning and memory (Kerr et al. 2013). Since lithium has been shown to lower the phosphorylation of tau proteins that control degeneration, Zamzam water may have a good impact on memory in Alzheimer's patients. But this needs to be tested in an Alzheimer's disease animal model. It also implies that because standard anxiolytics can impair cognitive functions, using Zamzamas an anxiolytic won't affect memory. Zamzam water has been shown to increase serotonin (5HT) levels while decreasing its metabolite, 5-hydroxyindoleacetic acid (5-HIAA), indicating potential antidepressant and anxiolytic effects. Lithium, a component of Zamzam water, acts as an agonist at the 5-hydroxytryptamine receptor 1B (5HT1B), contributing to

its antidepressant action. Massot et al. (1999) proposed that the 5HT_{1B} receptor is the molecular target for lithium's antidepressant effects. While Zamzam water does not significantly affect dopamine, 3,4-Dihydroxyphenylacetic acid (DOPAC), norepinephrine, or Homovanillic acid (HVA) levels, it may interact with selective serotonin reuptake inhibitors (SSRIs), which are used for their anxiolytic and antidepressant effects, potentially enhancing their actions (Mendez-David et al. 2014). SSRIs require 5HT-4 receptor activation for their neurogenic, anxiolytic, and antidepressant effects, and Zamzam water may facilitate these effects by acting as an agonist at the 5HT-4 receptor and increasing 5HT levels. The presence of lithium in Zamzam water might mediate these actions. Additionally, O'Leary et al. (2014) suggested that lithium stimulates neurogenesis in the ventral hippocampus, which plays a critical role in processes related to stress and anxiety. However, further research is needed to fully understand the neurogenic impact of Zamzam water in treating anxiety and depression.

Zamzam water as Aquaporin Stimulant

Aquaporins are integral membranes present in various tissues in humans and are involved in the bidirectional diffusion of water and small solutes. Human consists of 13 Aquaporins, divided into three sub-classes depending on their pore selectivity as orthodox aquaporin; aquaglyceroporin, and super or unorthodox aquaporin. Human aquaporins are functionally diverse and involved in a wide variety of non-infectious diseases including cancer, renal dysfunction, neurological disorder, epilepsy, skin disease, metabolic syndrome, and even cardiac diseases. Zamzam water has the capacity to stimulate all ten kinds of aquaporins present in the human body (28). Fluoride in drinking water can change the expression levels of Aquaporins (Anjomshoaa et al. 2015). Intake of Zamzam water has increased the activity of some endometrial aquaporins in healthy females. Zamzam water also increases the expression of a few new aquaporins which is an important step in fertilization and stimulation of the male and female reproductive system (Ali et al. 2009). Aquaporins 5 which is involved in the pathogenesis of caries are likely to interact with fluoride. Fluoride interact and may act synergistically in certain individuals to protect them against caries.

Zamzam water as anticancer

The crucial signaling molecules known as mitogen-activated protein kinases (MAPKs) are involved in a variety of biological processes, such as cell survival, proliferation, differentiation, and death. Apoptosis resistance and accelerated or unchecked cell proliferation can result from abnormal MAPK signaling. Extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK), and p38-MAP kinase are the three subfamilies of the MAPK family. In a variety of malignancies, including

colorectal and breast cancer, MAPK has been linked to anti-apoptotic mechanisms and the development of chemo-resistance. MEK1/2 has the ability to activate ERK1/2 either temporarily or permanently. While ERK1/2 activation often encourages cell survival, it can also have pro-apoptotic effects. Zamzam water therapy significantly lessened the ability of chemotherapy to prevent the activation of MEK1/2, ERK1/2, and P38 proteins in cancer cell lines and improved cancer cell viability by triggering the MAPK signaling cascade proteins MEK. Many inorganic elements, including Ca²⁺, Mg²⁺, Na⁺, Al, Co, Li, Se, Cl, F, NO₃⁻, HCO₃⁻, and SO₄²⁻ [4-2], were found in ZW. It also contains heavy metals such as As, Cr, Cd, Cu, Zn, and Pb. Arsenic acts as a mitogen and encourages cell survival and proliferation at lower dosages while inducing cytotoxicity at higher concentrations. Zamzam water possesses anticancer properties through its influence on endocrine immunology and the growth system of the body. It can have a strong effect on antitumor necrosis factor (TNF α) and interleukin 1 (IL1). Zamzam water significantly increased cell proliferation in breast, colorectal and ovarian cancer cell lines and suppressed the effect of chemotherapeutic agents by activation of the ERK1/2-MAPK signaling pathway. Zamzam water decreases cell viability and induces apoptosis in cancer cell lines by increasing the phosphorylation of CRAF, MEK1/2, ERK1/2, and P38 proteins. In an experimental mouse model of colon cancer intake of 500 ml of Zamzam water daily for one month, significantly reduces the tumor size (Siraj et al. 2019). In a study by Omar et al. (2017) Zamzam water treatment showed reductions in the cell viability of the human lung cancer (A549) cell line. Incubation of Zamzam water with human colon cancer cell line- HCT-116 inhibits growth, and proliferation and does some morphological changes in cells (Ali et al. 2009b). Minerals like calcium, magnesium, cadmium, zinc, selenium, arsenate, lead, and lithium present in Zamzam water can play important roles in inhibiting the growth of cancer cells (Wark et al. 2012; Remez et al. 1999). Arsenic trioxide and selenium are found cytotoxic against human colon cancer cell lines and cadmium can induce cytotoxicity in a concentration- and time-dependent manner in both colon cancer Caco-2 cells and normal human liver cell line HL-7702 (Aziz et al. 2009). Zamzam water may have both medicinal and preventative benefits, according to several studies. It protects rats from developing kidney stones (Al-Ghamdi. 2012). Moreover, it inhibits the growth of lung cancer cells and lessens the harm that gamma irradiation causes to bone marrow cells (Keramati et al. 2017). One of the most cariogenic infections in the oral cavity is streptococcus mutants, which can be significantly reduced in vitro by a probiotic mouthwash containing Zamzam water (Elgamily et al. 2018).

Zamzam water as Reproductive stimulant

Zamzam water is used to cure and treat unsuccessful

implantation by intracytoplasmic sperm inoculation. Zamzam water is used as an intrauterine injection for embryonal catheter at the time of ovum pickup and for embryo transfer with no fetal or maternal complications (Ali et al. 2009). It acts as a brain-derived neurotrophic factor stimulant and endometrial aquaporins in uterine flushing. Zamzam water is a stimulant for endometrial prolactin, luteinizing hormone (LH), α and β defensin, endometrial vascular endothelial growth factor (VEGF), and angiopoietin receptors (Ali et al. 2006; 2007; 2009). Zamzam water regulates gap junction protein connexin 43 and induces favorable inflammatory reactions in the uterine cavity. The high magnesium and calcium content of Zamzam water stimulates stem cell differentiation and immunoglobulin formation in the endometrium. Intrauterine injection of Zamzam water improves endometrial receptivity and thus controls idiopathic repeated spontaneous early abortion in humans. Peripheral blood mononuclear is activated with Zamzam water which decreases the chance of feto-maternal complications.

Zamzam water and cardiovascular diseases

Deficient serum zinc levels are frequently linked to cardiovascular diseases and death (Knez and Glibetic 2021). Zinc is a crucial micronutrient that has antioxidant potential, participates in a number of signaling pathways, and serves as a critical cofactor for energy transmission and physiological heart function (Choi et al. 2020). Zamzam water treatment dramatically improved heart morphology in dox-induced animals due to the presence of zinc in the alkaline environment which reduced heart toxicity and remodeling. High sensitivity- C-reactive protein (CRP), cytokines, and fibrinogen are some of the inflammatory mediators whose levels are rising during the acute phase of cardiac remodeling. With infection, inflammation, surgery, heart attack, and/or other heart conditions, CRP levels in the serum rise (Kamath et al. 2015). Numerous studies show that inflammation happens when the pH is acidic (Casimir et al. 2018). Lower zinc levels, elevated inflammation, and impaired renal function are all linked to doxorubicin-induced heart remodeling. The very alkaline Zamzam water demonstrated cardio-renal protection by lowering free radical production and inflammation. The anti-inflammatory properties of zinc in the alkaline pH of Zamzam water prevented heart remodeling.

Zamzam water and oral health with antibacterial properties

Zamzam water is very rich in calcium and fluoride. Fluoride balances the calcium levels in the human body and keeps bones and teeth healthy. One of the significant ions that serve as an antibiotic is the fluoride molecule found in Zamzam. Hence, the majority of toothpaste brands place a high priority on including fluoride in their packaging, which is utilized to prevent the buildup of

bacteria that causes dental plaque. Fluoride is a chemical that occurs naturally in varying amounts in Zamzam water. Dental health, in particular, benefits greatly from proportional concentration since it can stop tooth decay. Enamel is strengthened by fluoride chemicals, which make it acid-resistant and stop microorganisms from creating acid. Although fluorine is an antimicrobial, its ineffectiveness can cause gray stains in teeth (Davies and Scully, 2010). Fluoride content in Zamzam water can prevent plaque-causing bacteria from growing. Fluoride toothpaste with herbal ingredients can promote early icariin remineralization, lessen bacteria's capacity to create acid and exhibit antibacterial activity (Davies and Scully 2010).

In addition to fluoride, Zamzam water also has bicarbonate, which has the ability to counteract the acids made by the streptococcus and lactobacillus bacteria that create dental plaque and, due to its hypertonic capabilities, can cause the water to be lost from the hypotonic components of bacterial cells. Bacteria that lose water become dehydrated and eventually perish. Bicarbonate substances have the ability to weaken the link between bacteria and tooth surfaces and harm the bacterial matrix structure. Mutant *Lactobacillus* and *Streptococcus* are the two types of bacteria that can generally result in tooth plaque (Abbate et al. 2014). The two bacteria can then result in the development of caries. Dental caries can be brought on by interactions between bacterial plaque, food, and teeth. Enolase, phosphatase, proton extruding ATPase, and pyrophosphatase are bacterial plaque enzymes that fluoride can block. Consequently, Zamzam water has the potential to be used as a mouthwash to stop the growth of and reduce oral bacteria that form dental plaque as it contains fluoride [69]. According to the findings, gargling with Zamzam water raised salivary pH. High bicarbonate content in Zamzam water may be related to an increase in salivary pH following use. According to numerous research, Zamzam water has a high bicarbonate content of 172 mg/L to 285 mg/L. The bicarbonate content of the Zamzam water raises the salivary pH due to bicarbonate's ability to bind H^+ ions from acids and form carbonic acid, which is quickly converted to water and carbon dioxide (Alawiyah et al. 2021). Salivary pH levels above 7 cause saturated conditions, which cause calcium and phosphate to precipitate and subsequently form calculus. The research by Wulandari et al. revealed that there was a significant link between salivary pH and buffer capacity and calculus buildup (Wulandari et al. 2014).

Dental erosion is dependent on a change in the pH of the saliva. Thus, management should focus on using remineralizing agents in addition to buffering the decreased pH. It has been suggested that Zamzam water can effectively treat early carious lesions (Kaneko et al. 2006). Due to its high mineral content, Zamzam water has a strong buffering capacity (Barbour et al. 2011). Zamzam water has been examined in the dentistry

literature for a variety of applications due to its special composition and quality. In permanent teeth, carious lesions were started by Al-Rawi et al. (2009). The microhardness of enamel increased by 76.36% as a result of the usage of Zamzam water afterwards. Moreover, demineralized surfaces' microhardness values could be increased by agitating Zamzam water. Fluoride, magnesium, and calcium from Zamzam water are incorporated into hunger crystals, which increases the crystals' resilience to acid disintegration (Al-Weheb and Fahad 2012). The outcome of the chemical reaction between Zamzam water constituents and hunger crystals is unknown, however it is caused by the presence of fluoride components in Zamzam water (Al-Weheb and Fahad 2012).

Fluoride content in Zamzam water can prevent plaque-causing bacteria from growing. Fluoride toothpaste can promote early icariin, and decrease the bacterial capacity to create acid and exhibit antibacterial action. Fluoride is one of the significant ions that serve as an antibiotic in Zamzam. Fluoride slows down bacterial metabolism, which has an impact on how quickly acid-producing carbohydrates are broken down. Bacteria that cause dental plaque to multiply in oral microbial communities as a result of the carbohydrate fermentation's acid pH. Fluoride can inhibit the enzyme enolase, which is important for bacterial metabolism. Glycerate-2-phosphate is converted to phosphoenol pyruvate by enolase. Further metabolism of phosphoenolpyruvate results in acids such as lactic acid, formic acid, and pyruvic acid, which can demineralize tooth enamel. The phosphotransferase sugar transport system, which depends on phosphoenolpyruvate and is present in many bacteria, including *Streptococcus* and *Lactobacillus* needs phosphoenolpyruvate as a substrate. In addition to fluoride, Zamzam also contains bicarbonate, which has the ability to counteract the acids produced by the streptococcus and lactobacillus bacteria that create dental plaque as well as to cause the water to be lost from the hypotonic components of bacterial cells (Alfadul and Khan, 2011; Nauman et al. 2014).

Zamzum in hepatic and nephron health

Although Zamzam water has very high calcium and phosphorus concentrations compared to other natural or bottled water, its consumption had no adverse effects on kidney function and did not promote the development of kidney stones like calcium oxalate or calcium phosphate stones. Recently, in an animal-based study by Al Doghithi et al. (2021) tissues of the kidneys showed no discernible alteration upon histopathological analysis after 500 ml treatment of pure Zamzam water for five weeks. It's interesting to note that Al-Ghamdi (2012) previously demonstrated that Zamzam water protected rats from calcium oxalate nephrotoxicity. This shows that the characteristics and constituents of Zamzam water are distinctive. Furthermore, it is widely recognized that heavy

metals including copper, mercury, lead, zinc, and arsenic exhibit hepatotoxicity and are directly hazardous to cells (Hasanein and Emamjomeh, 2019). but recently it was proved that Zamzam water has no harmful impact on liver enzymes and do not induce any kind of histological changes in liver tissue. Zamzam water is reported to show hepatoprotective properties against Carbon tetrachloride (CCl₄)-induced liver damage (Saif et al. 2014). It also induces notable changes in biochemical markers related to liver function. Alkaline water has also been shown to enhance glycemic control in diabetic rats and reduce oxidative stress in individuals with chronic renal impairment (Huang et al. 2003; Jin et al. 2006). Al Meheithif et al. (2012) demonstrated that rats exposed to gentamicin stress had a tendency to have their antioxidant power potentiated by Zamzam water. The high pH and the distinctively well-balanced mineral makeup of Zamzam water may be the cause of its good effects. In addition, this well water has also been reported to normalize blood glucose in experimental diabetic rats

Zamzam water significantly drops the fasting blood glucose levels in animals (Ghadeer et al. 2020). In a study by Abdel-Azeem et al. (2017) Zamzam water significantly reduced blood sugar levels in alloxan-induced diabetic rats, gentamicin-induced nephrotoxic rats, and carbon tetra chloride-induced hepatotoxic rats in comparison to controls. The alkaline pH of Zamzam water may be the cause of Zamzam-induced hypoglycemia because alkaline water has been shown to cause hypoglycemia in a type 2 diabetic possibly by upregulating hexokinase (the primary enzyme of glycolysis that promotes cellular glucose uptake). In research conducted by Mahmoud et al. (2020) consuming Zamzam water for three consecutive months in rodents was found to be safe for overall health and demonstrated a significant decrease in serum uric acid levels due to urine alkalization resulting in easing the excretion of uric acid. Significant decrease in serum cholesterol and serum triglycerides was also reported in the study. Moreover, the hypolipidemic effects of zamzam water is linked to its high mineral content which stimulates lipid metabolism. Nitrates present in Zamzam water could be beneficial, exerting vasodilation, antithrombotic, and immune-regulatory effects, rather than posing harm due to presence of elevated levels of calcium, magnesium, and selenium. Histological studies on mice have confirm that Zamzam water is safe for renal parenchyma (Mahmoud et al. 2020).

CONCLUSIONS

Zamzam water is beneficial in many physiological conditions, its alkaline nature may be the main reason for its therapeutic effect. Zamzam water has a strong buffering capacity and is rich in minerals with play important roles in its antibacterial, anti-inflammatory, and anticancer activity.

Author contributions

Conceptualization, JMA and RSB; data curation, JMA and RSB; writing-original draft preparation, RSB writing-review and editing, RSB funding acquisition JMA. All authors have read and agreed to the published version of the manuscript.

Funding statement

No fund was received for this article.

Informed Consent Statement

Not applicable.

Data Availability Statement

All of the data is included in the article/Supplementary Material.

Conflict of interest

The authors declare no conflict of interest.

Copyrights: © 2025 @ author (s).

This is an **open access** article distributed under the terms of the **Creative Commons Attribution License (CC BY 4.0)**, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Publisher's note/ Disclaimer

All claims stated in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher. ISISnet remains neutral with regard to jurisdictional claims in published maps and institutional affiliations. ISISnet and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

Peer Review: ISISnet follows double blind peer review policy and thanks the anonymous reviewer(s) for their contribution to the peer review of this article.

REFERENCES

- Al Doghaither HA., Al-Ghafari AB, Rahimulddin SA, Al Zahrani SM, Omar AS, Omar U.M. Evaluation of the potential anticancer activity of Zamzam water in human colon cancer cell line. *Cancer and Oncology. Research* 2016;4(3):33–41
- Alfadul SM, Khan MA. Water quality of bottled water in the kingdom of Saudi Arabia: a comparative study with Riyadh municipal and Zamzam water water. *J Environ Sci Health A Tox Hazard Subst Environ Eng.* 2011; 46:1519–1528.
- Ambrosch A, Lobmann R, Pott A, Preissler, J. Interleukin-

Biological and Therapeutic Benefits of Zamzam Water

- 6 concentrations in wound fluids rather than serological markers are useful in assessing bacterial triggers of ulcer inflammation. *International Wound Journal* 2008; 5:99-106.
- A.M. Abdullah, E. Abdelsalam, B. Abdullah, A. Khaled Antioxidant effects of Zamzam in normal rats and those under induced-oxidative stress *J. Med. Plants Res* 2012; 6: 5507-5512
- Andreini C, Bertini I. A bioinformatics view of zinc enzymes. *J Inorg Biochem* 2012: 111:150–156
- Anjomshoa I, Briseño-Ruiz J, Deeley K, Poletta FA, Mereb JC, Leite AL, Barreta PA et al . Aquaporin 5 Interacts with Fluoride and Possibly Protects against Caries. *PLoS One.* 2015 2;10(12): e0143068.
- Ali AF.M, Cosemi, E, Kamel S, Mohammed S, Elhefnawy,M, Farid, L, Shaker, S. Miracle of Zamzam water water: the effect on human endometrial aquaporin. In: 13th International Water Technology Conference, IWTC: Hurghada, Egypt, 2009; 1515–1520.
- Ali, A.F.M., Cosemi, E., Kamel, S., Mohammed, S., Elhefnawy, M., Farid, L., Shaker, S. Oncolytic action of Zamzam water water on azoxymethone (AOM) induced colon tumors in rats. In Thirteenth International Water Technology Conference, IWTC, 13, 1521-1526, 2009.
- Ali, A.F.M.; Hassain, M.; El Hosani, A. Zamzama new modality for failed repeated intra cytoplasmic sperm injection. In: 13th International Water Technology Conference, IWTC: Hurghada, Egypt, 2009, 1557–1560.
- Ali Farid Mohammed Ali et al: miracle of ZamZam water: the effect on human endometrial aquaporin. Thirteenth International Water Technology Conference, IWTC 13 2009, Hurghada, Egypt.P-1515.
- Ali Farid M. Ali: Aquaporin and reproduction; paper presented in the 12 International Conference of Department of Obstetrics and Gynaecology, Ain Shams University, May 2007.
- Ali Farid M. Ali: Secret of ZAM ZAM water, paper presented in the 11International Conference of Department of Obstetrics and Gynaecology, Ain Shams University, May 2006
- Al-Ghamdi S. Inhibition of calcium oxalate nephrotoxicity with Zamzam water. *Open J Prev Med.* 2012; 2:67–71.
- Aziz, R., Rafiq, M.T., Yang, J., Liu, D., Lu, L., He, Z., Daud, M.K., Li, T., Yang, X. Impact assessment of cadmium toxicity and its bioavailability in human cell lines (Caco-2 and HL-7702). *BioMed Research International*, 2014logy Conference, IWTC: Hurghada, Egypt, 2009; 1515–1520.
- Al Doghaither HA, Al-Sohaibani RM, Omar UM, Alharbi HA. Biochemical and histological effects of five weeks ingestion of Zamzam on the liver and kidneys of Wistar rats. *Saudi Pharm J.* 2021 ;29(1):91-95.

- Abbate GM, Levrini L, Caria MP. Salivary pH after a glucose rinse: effect of a new mucoadhesive spray (Cariex) based on sodium bicarbonate and xylitol. *J Clin Dent*. 2014;25(4):71–5.
- Alawiyah, Fadlun & Chairani, Shanty & Anastasia, Danica. Gargling Effect of Zamzam water on Salivary pH. *Insisiva Dental Journal: Majalah Kedokteran Gigi Insisiva* 2021;10: 7-11.
- Al-Rawi NA, Al-Alousi HMR, Al-Obaidy NM. Effect of Zamzam on the microhardness of initial carious lesion of permanent teeth enamel (an in vitro study) *Mustansiria Dent J*. 2009; 6:110–6.
- Al-Weheb AM, Fahad AH. Effect of Zamzam on the microhardness of initial caries-like lesion of permanent teeth, compared to casein phosphopeptide-amorphous calcium phosphate agents. *J Bagh College Dent*. 2012; 24:128–32.
- Alfadul SM, Khan MA. Water quality of bottled water in the Kingdom of Saudi Arabia: A comparative study with Riyadh municipal and Zamzam water. *J Environ Sci Health A Tox Hazard Subst Environ Eng*. 2011; 46:1519–28.
- Al Meheithif A., Elnour A., Bamosa A., Aleissa K. Antioxidant effects of Zamzamin normal rats and those under induced-oxidative stress. *J. Med. Plants Res*. 2012;6(42):5507–5512.
- A.S. Abdel-Azeem, A.E. Mubarak, Y.A. Abd-Elhady, A.G. Badawi Potential role of Zamzamin some chronic diseases in rats *IJPCR* 2017;9 : 571-580
- Barbour ME, Lussi A, Shellis RP. Screening and prediction of erosive potential. *Caries Res*. 2011;45(Suppl 1):24–32.
- Bamosa, A. Elnour, H. Kaatabi, A. Al Meheithif, K. Aleissa, S. Al-Almaie Zamzam ameliorates oxidative stress and reduces hemoglobinA1c in Type 2 diabetic patients. *J. Diabetes Metab* 2013; 4
- Bhawal UK, Li X, Suzuki M, Taguchi C, Oka S, Arikawa K, Tewari N, Liu Y. Treatment with low-level sodium fluoride on wound healing and the osteogenic differentiation of bone marrow mesenchymal stem cells. *Dent Traumatol*. 2020; 36(3):278-284.
- BLee HJ, Arikawa K. Influence of low level sodium fluoride on expression of IGF-1 and IGF-2 protein in experimental Type 2 diabetes with periodontitis model. *J Hard Tissue Biol*. 2015; 24:319–24.
- Casimir GJ, Lefèvre N, Corazza F, Duchateau J, Chamekh M. The Acid-Base Balance and Gender in Inflammation: A Mini-Review. *Front Immunol*. 2018 Mar 7; 9:475.
- Choi S, Hong DK, Choi BY, Suh SW. Zinc in the Brain: Friend or Foe? *Int J Mol Sci*. 2020 25;21(23):8941.
- Davies R, Scully C PA. Dentifrices - update. *Med Oral Pathol*. 2010; 1–7.
- Elgamily H, Mosallam O, El-Sayed H, Mosallam R. Antibacterial effectiveness of probiotic-based experimental mouthwash against cariogenic pathogen: An in vitro study. *Eur J Dent*. 2018; 12:7–14.
- Ganger, R., Garla, R., Mohanty, B.P. et al. Protective Effects of Zinc Against Acute Arsenic Toxicity by Regulating Antioxidant Defense System and Cumulative Metallothionein Expression. *Biol Trace Elem Res* 2016; 169, 218–229.
- Ghadeer F. AlJuwaie, Rabia Latif, Mona H. AlSheikh, Ahmed Al Sunni, Shahanas Chathoth, Effects of Zamzam on glycemic status, lipid profile, redox homeostasis, and body composition in rats, *Journal of Taibah University Medical Sciences* 2020; 15: 14-18,
- Hasanein, P., Emamjomeh, A., 2019. Beneficial effects of natural compounds on heavy metal-induced hepatotoxicity. In: Watson, R.R., Preedy, V.R. (Eds.). *Dietary Interventions in Liver Disease*. Academic Press. 345–355
- Hou H, Wang L, Fu T, Papasergi M, Yule DI, Xia H. Magnesium Acts as a Second Messenger in the Regulation of NMDA Receptor-Mediated CREB Signaling in Neurons. *Mol Neurobiol*. 2020 ;57(6):2539-2550.
- Huang K.C., Yang C.C., Lee K.T., Chien C.T. Reduced hemodialysis-induced oxidative stress in end-stage renal disease patients by electrolyzed reduced water. *Kidney Int*. 2003;64(2):704–714.
- Jin D., Ryu S.H., Kim H.W., Yang E.J., Lim S.J., Ryang Y.S., Chung C.H., Park S.K., Lee K.J. Anti-diabetic effect of alkaline-reduced water on OLETF rats. *Biosci. Biotechnol. Biochem*. 2006; 70:31–37.
- Kaneko N, Yoshihara A, Ida H, Nomura Y, Imai S, Nishizawa T, et al. Influence of a Fluoride Mouthrinse on Mutans Streptococci in Schoolchildren. *Caries Res*. 2006; 40: 501–7.
- Khalid N, A. Ahmad, S. Khalid, A. Ahmed, M. Irfan. Mineral composition and health functionality of Zamzam water: a review *Int. J. Food Prop* 2014; 17: 661-677
- Keramati Yazdi F, Shabestani Monfared A, Tashakkorian H, Mahmoudzadeh A, Borzoueisileh S. Radioprotective effect of Zamzam water (alkaline) water: A cytogenetic study. *J Environ Radioact*. 2017; 167:166–9.
- Knez M, Glibetic M. Zinc as a Biomarker of Cardiovascular Health. *Front Nutr*. 2021 Jul 30; 8:686078.
- Kamath DY, Xavier D, Sigamani A, Pais P. High sensitivity C-reactive protein (hsCRP) & cardiovascular disease: An Indian perspective. *Indian J Med Res*. 2015 ;142(3):261-8.
- Kerr F, Bjedov I, Sofola-Adesakin O. Molecular Mechanisms of Lithium Action: Switching the Light on Multiple Targets for Dementia Using Animal Models. *Front Mol Neurosci*. 2018; 11:297.
- Lee H, Cha MK, Kim IH. Activation of thiol-dependent antioxidant activity of human serum albumin by alkaline pH is due to the B-like conformational

- change. Arch Biochem Biophys. 2000;3 80:309–318.
- Lee M, Arikawa K, Nagahama F. Micromolar levels of sodium fluoride promote osteoblast differentiation through Runx2 signaling. Biol Trace Elem Res. 2017; 178: 283–91
- Logozzi M, Mizzoni D, Di Raimo R, Andreotti M, Macchia D, Spada M, Fais S. In vivo antiaging effects of alkaline water supplementation. J Enzyme Inhib Med Chem. 2020;35(1):657-664.
- Mahmoud HS, Eltahlawi RA, Jan AA, Alhadramy O, Soliman TM, El Sayed SM, Abdallah HI, El-Shazley M, Shafik NM, Mariah RA, El-Dabie N, Abdel-Haleem M, Hassan SMA, Nabo MMH, El-Alaf H, Baghdadi H, Yousef RS, Mahmoud AA, El Sayed SM, Amer SM. Zamzam water is pathogen-free, uricosuric, hypolipidemic and exerts tissue-protective effects: relieving BBC concerns. Am J Blood Res. 2020 Dec 15;10(6):386-396.
- Massot O, Rousselle JC, Fillion MP, Januel D, Plantefol M, Fillion G. 5-HT_{1B} receptors: a novel target for lithium. Possible involvement in mood disorders. Neuropsychopharmacology. 1999 ;21(4):530-41
- Mendez-David I, David DJ, Darcet F, et al. Rapid anxiolytic effects of a 5-HT₄ receptor agonist are mediated by a neurogenesis-independent mechanism. Neuropsychopharmacology. 2014;39(6):1366-1378.
- Moni SS, Sultan MH, Alshahrani S, Tripathi P, Assiri A, Alqahtani SS, Bakkari MA, Madkhali OA, Alam MF, Alqahtani AH, Tripathi R, Pancholi SS, Ashafaq M, Elmobark ME. Physical characterization and wound healing properties of Zamzam water water. Braz J Biol. 2022; 15: 82:e262815.
- Nassini, R., Andr, egrave, Eunice, Gazzieri, D., Siena, G.D., Zanasi, A., Geppetti, P., Materazzi, S., 2010. A Bicarbonate-Alkaline Mineral Water Protects from Ethanol-Induced Hemorrhagic Gastric Lesions in Mice. Biolog. Pharmaceut. Bull. 33; 8: 1319–1323.
- Nauman, Asif Ahmad, Sumera Khalid, Anwaar Ahmed & Muhammad Irfan (2014) Mineral Composition and Health Functionality of Zamzam water Water: A Review, International Journal of Food Properties, 17:3, 661-677
- NourEldin EM, Assiri AM, Fatani SH, Babakr AT. Effect of water intake pattern on serum mineral and electrolyte levels in Makkah people. AARJMD. 2014; 1:442–456.
- Omar UM, Al Doghaither HA, Rahimulddin SA, Al Zahrani SM, Al-Ghafari AB. In Vitro Cytotoxic and Anticancer Effects of Zamzam water in Human Lung Cancer (A594) Cell Line. Malays J Med Sci. 2017;24(3):15-25.
- O'Leary OF, Cryan JF. A ventral view on antidepressant action: roles for adult hippocampal neurogenesis along the dorsoventral axis. Trends Pharmacol Sci. 2014;35(12):675-87.
- Prasad AS, Beck FW, Bao B, Fitzgerald JT, Snell DC, Steinberg JD and Cardozo LJ. Zinc supplementation decreases incidence of infections in the elderly: effect of zinc on generation of cytokines and oxidative stress. The American Journal of Clinical Nutrition 2007; 85(3): 837-844
- Remez, I., Rabkin, L., Veksler, H., Bauman, M. Cytotoxicity of cadmium, selenium, zinc and copper to mouse myeloma Sp2/0 cells as measured by the MTT Assay. Alternatives to Laboratory Animals: ATLA 1999, 28(3), 473-476.
- Rose-john S, Winthro P K, Calabrese L, The role of IL-6 in host defence against infections: immunobiology and clinical implications. nature reviews. rheumatology 2017; 13:399-409.
- Ritsu M, Kawakami K, Kanno E, Tanno, H, Ishii K, Imai, Y, Maruyama, R. Tachi, M, Critical role of tumor necrosis factor- α in the early process of wound healing in skin. The Journal of Dermatologic Surgery 2017; 21: 14-19.
- Riaz B, Ikram R, Sikandar B. Anticatalytic activity of Zamzamin chlorpromazine induced animal model of Parkinson disease. Pak J Pharm Sci. 2018;31(2):393-397.
- Singla N and Dhawan DK Zinc Improves Cognitive and Neuronal Dysfunction During Aluminium-Induced Neurodegeneration. Mol. Neurobiol 2016; 54(1): 406-422.
- Samardžić J, Savić K, Stefanović N, Matunović R, Baltezarević D, Obradović M, Jancić J, Oprić D, Obradović D. Anxiolytic and antidepressant effect of zinc on rats and its impact on general behavioural parameters. Vojnosanit Pregl. 2013;70(4):391-5.
- Slutsky I, Abumaria N, Wu LJ, Huang C, Zhang L, Li B, Zhao X, Govindarajan A, Zhao MG, Zhuo M, Tonegawa S, Liu G. Enhancement of learning and memory by elevating brain magnesium. Neuron. 2010 28;65(2):165-77.
- Ślifirski G, Król M, Turło J. 5-HT Receptors and the Development of New Antidepressants. Int J Mol Sci. 2021;22(16):9015. P
- Sun, Q., xin, F., Wen, X., Lu, c., Chen, R and Ruan, G. Protective effects of different kinds of filtered water on hypertensive mouse by suppressing oxidative stress and inflammation. Oxidative Medicine and Cellular Longevity 2018; 2917387.
- Sun Y, Zheng J. Yi J. Cai S. Investigation on the Effects and Mechanisms of Alkaline Natural Mineral Water and Distilled Water on Ethanol-Induced Gastric Ulcers In Vivo and In Vitro. Processes 2022; 10:498.
- Shomar B. Zamzam water water: concentration of trace elements and other characteristics. Chemosphere. 2012; 86:600–605.
- Siraj AK, Begum R, Melosantos R, Albalawy W, Abboud J, Siraj N, Al-Kuraya KS. Zamzam protects cancer cells from chemotherapy-induced apoptosis via mitogen-activated protein kinase-dependent

- pathway. *Biomed Pharmacother.* 2019; 118:109376.
- Saif A., Sarhan O.M., Elmogy M., Mutwally H. Hepatoprotective effects of Zamzam against carbon tetrachloride induced liver damage in rats: biochemical, histopathological, and molecular evidences. *Life Sci. J.* 2014;11(10):300–308.
- Tanaka, T., Narazaki, M. Kishimoto, T. IL-6 in inflammation, immunity, and disease. *Cold Spring Harbor Perspectives in Biology* 2014; 6:10, a016295.
- W. Wasowicz, E. Reszka, J. Gromadzinska & K. Rydzynski the Role of Essential Elements in Oxidative Stress, *Comments on Toxicology* 2003; 9:1:39-48,
- Waleed El Maleky, Amal M. Mahfoz, Afaf O. Osman, Hekma A. Abd El-Latif. Investigation of the impacts of Zamzam on streptozotocin-induced diabetic nephropathy in rats. In-vivo and in-vitro study, *Biomedicine & Pharmacotherapy* 2021; 138:111474,
- Wark, P.A., Lau, R., Norat, T., Kampman, E. Magnesium intake and colorectal tumor risk: A case-control study and meta-analysis. *The American Journal of Clinical Nutrition* 2012, 96(3), 622-631.
- Wulandari P, Lestari F. pH dankapasitas buffer saliva dalamhubungannya terhadap pembentukankalkulus pada pasien di instalasiperiodonsia RSGM USU. *dentika Dent J.* 2014;18(2):116–9.
- Yang L, LI D. and Chen, S, Hydrogen water reduces NSE, IL-6, and TNF- α levels in hypoxic-ischemic encephalopathy. *Open Medicine* 2016; 11:399-406.