Magna Scientia Advanced Biology and Pharmacy

eISSN: 2582-8363

Cross Ref DOI: 10.30574/msabp

Journal homepage: https://magnascientiapub.com/journals/msabp/

(RESEARCH ARTICLE)

An investigation into the use of electrolyzed reduced water in overall health and wellness

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Magna Scientia Advanced Biology and Pharmacy, 2023, 09(01), 077–086

Publication history: Received on 15 February 2023; revised on 11 June 2023; accepted on 14 June 2023

Article DOI: https://doi.org/10.30574/msabp.2023.9.1.0028

Abstract

Electrolyzed reduced water (ERW) recreates natural ground springs containing a large amount of molecular hydrogen and a small amount of platinum nanoparticles through the process of electrolysis. Extensive research was carried out to investigate the correlation between Electrolyzed Reduced Water (ERW) and overall health, as well as, the prevention of diseases. ERW scavenges active oxygen species and protects DNA from oxidative damage. Both physical and mental diseases, as well as the aging process, can be attributed to oxidative stress. ERW is a novel option to supplement the health and therapeutic practices in the overall American lifestyle.

With much research being done on animals and more research beginning in clinical settings, there is hope that ERW will be studied and implemented as a part of a treatment and prevention strategies for a multiplicity of diseases. Treatment of a disease should never be one-dimensional. Scientists and physicians work together to create a finely tuned combination of many strategies. For the average American, Electrolyzed Reduced Water is a much needed additive for overall health and wellness as seen in this study.

Keywords: Electrolyzed Reduced Water; Oxidative stress; Natural ground water; Electrolysis; treatment; Overall health

1. Introduction

Water is life. Water makes up more than two-thirds of the human body. The human brain is made up of 95 percent water, human blood is 82 percent water, and human lungs are 90 percent water (Khalifa M. 2018). There are stories and legends of men and women searching the earth for a fabled “miracle water.” One of the more famous legends being the Fountain of Youth. Could it be possible that these legends are based in truth?

What if I were to say that these waters exist? Scientists have discovered ground waters from all over the earth that have such qualities. Ground waters such as The Hita Tenryosui Water in Japan, The Nordenau Water in Germany, and The Tracote Water in Mexico have all been called “miracle water” because they can improve various diseases (Shirahata S, Teruya K, Katakura Y, et al. 2002). These natural ground springs are antioxidative waters containing active hydrogen. The water in these springs has the ability to scavenge intracellular reactive oxygen species (ROS) (Shirahata S, Teruya K, Katakura Y, et al. 2002).

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Electrolyzed reduced water (ERW) recreates these natural ground springs through the process of electrolysis (Shirahata S, Teruya K, Katakura Y, et al. 2002). ERW can be described as functional drinking water containing a large amount of molecular hydrogen and a small amount of platinum nanoparticles (Yan H, Kashiwaki T, Hamasaki T, et al. 2011). ERW is produced during water electrolysis near the cathode (Choi Y, Lee D, Cho D, et al. 2020). ERW exhibits a high pH, low dissolved oxygen, extremely high dissolved molecular hydrogen, and extremely negative redox potential values (Shirahata S, Teruya K, Katakura Y, eds. 2002). ERW scavenges active oxygen species and protects DNA from oxidative damage (Shirahata S, Kabayama S, Nakano M, et al. 1997).

What makes both these natural ground waters and water created through electrolysis so special is their effect on oxidative stress? Oxidative stress can be defined as an imbalance between the cellular production of reactive oxygen species and the counteracting antioxidant mechanisms (Salim S. 2014). Active oxygen species, or free radicals, cause extensive oxidative damage to biological macromolecules (Shirahata S, Kabayama S, Nakano M, et al. 1997). Continual oxidative stress is the cause of many common diseases, cancers, and aging (Ohta S 2012). Oxidative stress is also implicated in depression, anxiety, schizophrenia, and bipolar disorders (Salim S. 2014). Both physical and mental diseases, as well as the aging process, can be attributed to oxidative stress.

These natural ground waters can only be found in a few places around the world, making it difficult to access for the general population. ERW is a novel option to investigate because of the accessibility in providing similar water with these properties that reduce oxidative stress. Active hydrogen that is found in both the natural ground waters of the world and in the electrically produced ERW is a key player in the battle against oxidative stress and its effect on physical diseases, mental diseases and the aging process. As previously stated, the human brain is made up of 95 percent water, human blood is 82 percent water, and human lungs are 90 percent water (Khalifa M. 2018), which means without proper hydration the human body cannot function at its most optimum potential.

Purpose of the study

Oxidative stress is a known factor of many diseases and health issues. The purpose of this study is to investigate the use of Electrolyzed Reduced Water (ERW) in overall health and wellness.

2. Material and methods

Extensive research was carried out over six months to investigate the Electrolyzed Reduced Water (ERW) and overall health, as well as, the prevention of diseases. The articles referenced within this thesis contain information, studies, and research results of ERW on overall health and various diseases from a diversity of sources. Databases including Google Scholar and PubMed Central were explored thoroughly. Articles and journals were investigated and reviewed from Redox Biology, Biochimica et Biophyscia Acta - Molecular Basis of Disease, Current Opinion in Clinical Nutrition and Metabolic Care, Oxidative Stress and Cellular Longevity, Antioxidants, Antioxidants & Redox Signaling, Diabetes Care, Journal of Cellular and Molecular Medicine, Hindawi, Biochemical Journal, Biological and Pharmaceutical Bulletin, Medical Gas Research, Scholar Journal of Applied Sciences and Research, Life Sciences, Cytotechnology, Psychoneuroendocrinology, Gut, Brain Behavior and Immunity, Current Neuropharmacology, Biochemical and Biophysical Research Communications, Animal Cell Technology, Oxidative Medicine and Cellular Longevity, World Journal of Diabetes, The Canadian Journal of Cardiology, BMC Complementary Medicine and Therapies, BMC Proceedings, and Biophysical Reviews.

3. Discussion (literature review)

3.1. Oxidative Stress and Electrolyzed Reduced Water (ERW)

Oxidative stress can be defined as the imbalance of cellular production of reactive oxygen species and the counteracting antioxidant mechanisms. (Salim S. 2014). Cellular damage caused by oxidative stress triggers complex defense mechanisms involving antioxidants that have evolved to help protect body tissues (Zhazykbayeva S, Pabel S, Mügge A, et al. 2020). Oxidative damage to biological macromolecules is caused by active oxygen species, also known as free radicals (Shirahata S, Kabayama S, Nakano M, et al. 1997). Free radicals are highly unstable and reactive atoms or molecules because they have unpaired electrons found in their outer orbit (Choi Y, Lee D, Cho D, et al. 2020). Free radicals and antioxidants are both produced during the normal metabolic process in cells which leads to neutralization of the free radicals in the body (Zhazykbayeva S, Pabel S, Mügge A, et al. 2020). A balance between free radicals and antioxidants is usually maintained in the normal equilibrium of the body (Zhazykbayeva S, Pabel S, Mügge A, et al. 2020). Continual oxidative stress is a cause of many common diseases, cancers and aging (Ohta S 2012). Oxidative stress is also implicated in depression, anxiety, schizophrenia, and bipolar disorders (Salim S. 2014).

ERW scavenges active oxygen species and protects DNA from oxidative damage (Shirahata S, Kabayama S, Nakano M, et al. 1997). The high pH, low dissolved oxygen, extremely high dissolved molecular hydrogen, and extremely negative redox potential values that ERW exhibits can be utilized for prevention and therapy of various diseases (Shirahata S, Teruya K, Katakura Y, eds. 2002). According to a study conducted in 2020, ERW has been shown to suppress oxidative stress in multiple ways. These effects include ERW's action on improving the function of antioxidant enzymes in the U937 cell line, protecting neural cells from oxidative damage, inhibiting tumor angiogenesis, and enhancing apoptosis of leukemia cells (Choi Y, Lee D, Cho D, et al. 2020).

3.2. Comparison of Mechanism of Action of Antioxidants and ERW

Antioxidants can be defined as substances that delay or prevent oxidative damage caused by the presence of reactive oxygen species (Bouayed J, Bohn T. 2010). The antioxidant defense system works by eliminating harmful reactive oxygen/nitrogen species (Zhazykbayeva S, Pabel S, Mügge A, et al. 2020). Natural sources of antioxidants come from plant food such as apples, plums, bananas, tomatoes, potatoes, onions, broccolis, etc. (Bouayed J, Bohn T. 2010). There are very few developments of an antioxidant supplement that can be implemented without a side effect (Ohta S 2012). Synthetic antioxidant additives include compounds such as butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), tert-butyl hydroquinone (TBHQ) and propyl, octyl and dodecyl gallates (preserve shelf-life of processed foods) (Bouayed J, Bohn T. 2010).

According to a 2014 review, antioxidant supplements do not seem to prevent cancer, cardiovascular diseases, or death while some antioxidants such as beta-carotene, vitamin A, and vitamin E may increase mortality. (Bjelakovic G, Nikolova D, Gluud C. 2014). Antioxidants found in plant food are considered safer and healthier than antioxidant supplements (Bouayed J, Bohn T. 2010). Therapeutic and preventative uses of hydrogen include anti-oxidative stress effects, anti-inflammatory effects, and anti-allergic effects (Ohta S 2012). Molecular hydrogen is different from traditional antioxidants. The antioxidant effect of molecular hydrogen directly eliminates hydroxyl radicals and peroxynitrite, can easily penetrate biofilms, and does not affect the normal metabolic redox reaction due to its small molecular weight and selective capability to only affect the strongest oxidant (Yang M, Dong Y, He Q, et al. 2020).

3.3. Lifestyle Applications

Daily ERW consumption may also be a consideration for a simple and sustainable lifestyle modification. In both animal and human experiences, the beneficial protective effects of hydrogen-rich water on the body have been gradually confirmed (Sha J, Zhang S, Lu Y, et al. 2019). This has led to studies conducted on healthy individuals to observe the effects of ERW. A 2019 study concluded that the consumption of electrolyzed reduced water long-term enhances diversity and abundance of gut flora, while also exerting antioxidant and anti-inflammatory effects (Sha J, Zhang S, Lu Y, et al. 2019). ERW also increased exercise endurance on healthy athletes (Sha J, Zhang S, Lu Y, et al. 2019). In a study done at the workplace of healthy individuals (no existing uncontrolled medical conditions or excessive alcohol consumption), it was concluded that ERW helped to reduce oxidative stress, increased antioxidant potential, and decreased fat mass over a period of 8 weeks (Choi Y, Lee D, Cho D, et al. 2020). ERW also showed a more significant decrease in total, visceral, and subcutaneous fat mass in body comparison analysis as compared to the placebo group (Choi Y, Lee D, Cho D, et al. 2020).

3.4. Mental Disorders

Anxiety is an aversive emotional state, in which the feeling of fear is disproportionate to the nature of the threat (Bouayed J, Rammal H, Soulimani R. 2009). Anxiety levels are linked to the oxidative status in neuronal and glial cells in the cerebellum and hippocampus, in neurons of the cerebral cortex, and in peripheral leukocytes (Rammal H, Bouayed J, Younos C, et al. 2008). In an extensive study involving anxious mice, oxidative stress was discovered in the central and peripheral nervous systems (Rammal H, Bouayed J, Younos C, et al. 2008). There is a relationship between reactive oxygen species in peripheral blood cells and anxiety-related behavior in mice (Bouayed J, Rammal H, Soulimani R. 2009). Oxidative metabolism can affect the regulation of anxiety (Salim S. 2014).

According to the Centers for Disease Control and Prevention website, depression affects 1 in 6 adults at some point in their lifetime and 16 million American adults every year. Depression is a complex and heterogeneous disorder that has a negative impact on the quality of life, morbidity/mortality, and cognitive function (Salim S. 2014). Increased inflammation and oxidative stress have been shown in Major Depressive Disorder (MDD). In addition, poorer antidepressant treatment response was related to higher baseline levels of the major oxidative stress marker (Lindqvist D, Dhabhar F, James S et al. 2017). Oxidative and nitrosative stress, increased reactive oxygen species and reactive nitrogen species, and altered levels of antioxidant defenses have all been implicated in MDD (Salim 2014).

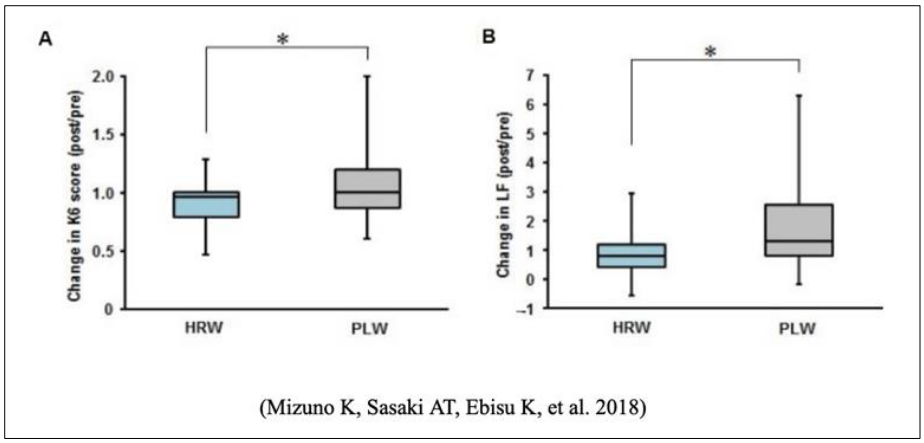

Figure 1 Comparison of hydrogen Rich Water and Placebo water

Figure 1: "Comparison of change ratios (post-treatment/pre-treatment) for parameters related to quality of life with administration of hydrogen-rich water (HRW) or placebo water (PLW) for 4 weeks. Note: Change ratios for K6 score for mood (A) and anxiety and the low-frequency component power (LF) for autonomic nerve function (B). *P < 0.05." (Mizuno K, Sasaki AT, Ebisu K, et al. 2018).

As seen in Figure 1, it was concluded that ERW in adults could improve mood, anxiety, and autonomic nerve function within 4 weeks, which suggests that ERW may help adults maintain good health and a high quality of life (Mizuno K, Sasaki AT, Ebisu K, et al. 2018).

3.5. Physical Diseases

According to the Centers for Disease Control and Prevention website, each year 655,000 Americans die from cardiovascular disease alone (which is every 1 in 4 deaths). Cardiovascular disease is linked to chronic inflammatory disorders which are influenced by vascular oxidative stress (Steven S, Frenis K, Oelze M, et al. 2019). Oxidative stress in cardiovascular disease occurs in the myocardium and plasma and also correlates with left ventricular dysfunction as seen in the signaling pathways of Figure 2 (Zhazykbayeva S, Pabel S, Mügge A, et al. 2020).

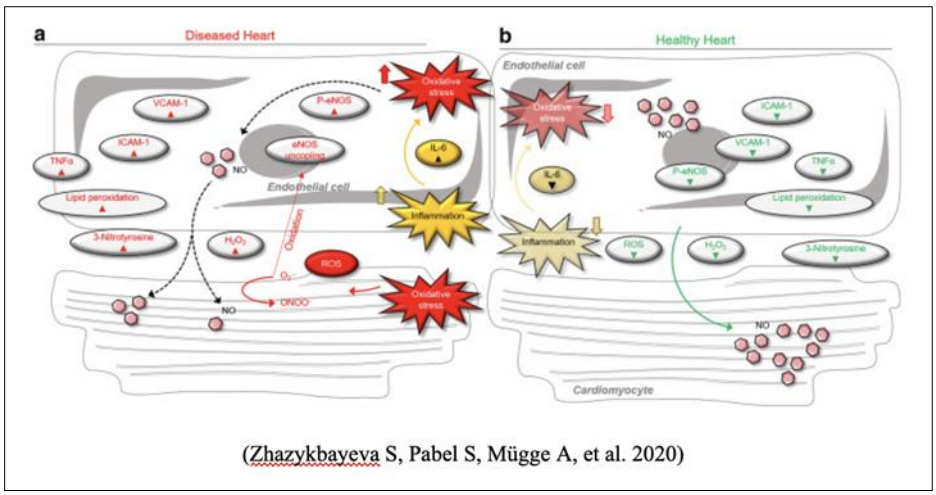

Figure 2 Signling pathways of endothelial cells in oxidative and healthy condition

Figure 2: "Scheme for the signaling pathways of endothelial cells in diseased heart under oxidative (right) and healthy (left) conditions. A Represents a heart under oxidative condition with impaired endothelial function via increased inflammatory cytokines and oxidative stress (red arrow pointing upwards means increase and red arrow pointing down means decrease). B Represents a healthy condition showing a normal endothelial function via normal/low inflammatory cytokines and oxidative stress (green arrow pointing upwards means increase and green arrow pointing down means decrease). Abbreviations: H2O2, hydrogen peroxide; ICAM-1, intercellular cell adhesion molecule-1; IL-6, interleukin-6; NO, nitric oxide; NOX2, NADPH phagocyte oxidase isoform; ONOO-, peroxynitrite; ROS, reactive oxygen

species; sGC, soluble guanylyl cyclase; TNF-α, tumor necrosis factor-alpha; VCAM-1, vascular cell adhesion molecule-1; P-eNOS, phospho-endothelial nitric oxide synthase" (Zhazykbayeva S, Pabel S, Mügge A, et al. 2020).

Hypertension affects nearly half of all adults in the United States (108 million or 45%) according to the Centers for Disease Control and Prevention website. Increases of reactive oxygen species that are triggered by immune cells when a hemodynamic insult is absent can lead to pathologic increases in blood pressure, ultimately leading to hypertension (Crowley S. 2014). Hypertension is commonly found to have an underlying pathophysiologic process of oxidative stress (Touyz R, Rios F, Alves-Lopes R, et al. 2020).

Gastroesophageal reflux disease (GERD) is characterized by reflux of gastroduodenal contents into the esophagus (Franceschelli, S, Gatta, DMP, Pesce, M, et al. 2018). The primary cause of the mucosal damage in GERD is mediated by oxygen-derived free radicals (Oh T, Lee J, Ahb B, et al. 2001).

According to a 2020 study, molecular hydrogen protects against cardiovascular disease and improves cardiac function in the following ways. Molecular hydrogen, consumed as ERW, has been proven to reduce the volume of atherosclerotic lesions derived from macrophage accumulation in apolipoprotein E knockout mice (ApoE-/- mice), decrease the numbers of endothelial cells in the atheroma expressing the senescence factors p16INK4a and p21, suppress macrophage infiltration and TNF-α expression in the atheroma which suggests that vascular aging can be suppressed by HW, and increase flow-mediated dilation in the high-H2 group which indicates that H2 may protect the vasculature from shear stress-derived ROS that is detrimental (Yang M, Dong Y, He Q, et al. 2020).

A 2014 study concluded that ERW can inhibit aspirin-HCl-induced stomach injury in a dose-dependent manner (as seen in Figure 3) and that drinking ERW may prevent gastric damage caused by oxidative stress in healthy individuals (Xue J, Shang G, Tanaka Y, et al. 2014). Likewise, a 2018 study concluded that integration of ERW in GERD patients can lead to a restored optimal oxidative balance and symptoms can be reduced rapidly (Franceschelli S, Gatta D, Pesce M, et al. 2018).

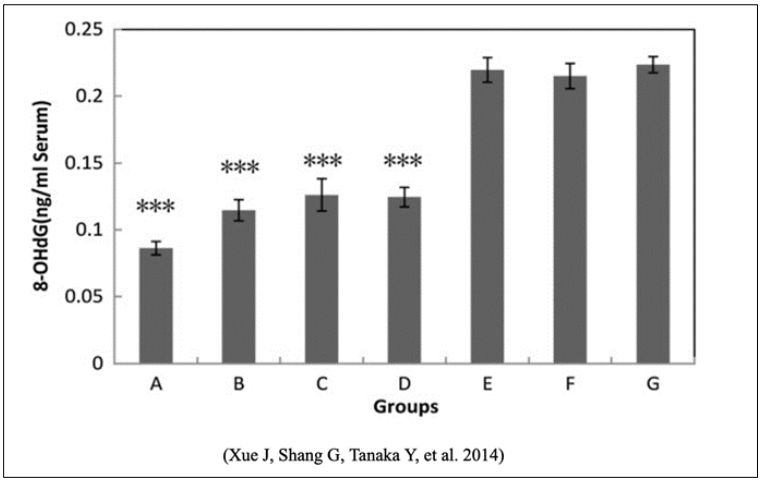

Figure 3 Serum 8-OHdg Leval in different groups

Figure 3: The serum 8-OHdG level (biomarker for oxidative stress and carcinogenesis) in different groups. Values are the mean ± SE for 6 to 8 animals. ***: $p < 0.001$, compared with group E (low hydrogen and low pH group), F (neutral water control), or G (no injury control). (Xue J, Shang G, Tanaka Y, et al. 2014).

3.6. Diabetes

According to the 2020 National Diabetes Statistics Report from the Centers for Disease Control and Prevention, 34.2 million Americans have diabetes (10.5% of the US population) and 88 million Americans aged 18 years or older have prediabetes (34.5% of the adult US population). While Type 1 Diabetes Mellitus (T1DM) cases are included in these statistics, 90-95% of all cases are Type 2 Diabetes Mellitus (T2DM). Systemic oxidative stress is present in T1DM upon early onset and is increased by early adulthood (Domínguez C, Ruiz E, Gussinye M, et al. 1998). High levels of oxidative stress is a damaging factor on the body leading to insulin resistance, dyslipidemia, β-cell dysfunction, impaired glucose tolerance and ultimately leading to T2DM (Tangvarasittichai S. 2015). Clinical complications during the course of diabetes mellitus can be attributed to oxidative injury due to decreased antioxidant defenses (Domínguez C, Ruiz E,

Gussinye M, et al. 1998). Diabetic conditions and the progression of pancreatic β-cell dysfunction is produced from oxidative stress. An increase in reactive oxygen free radical species (ROS) along with a decrease in the antioxidant defense mechanism both lead to the increase in oxidative stress in diabetes (Kim M, Jung K, Uhm Y, et al. 2007).

In a 2006 study, ERW was provided to mice that represented TIDM and T2DM and significantly reduced the blood glucose concentration and improved glucose tolerance in both animal models (Kim M, Kim H. 2006). In a 2002 study, ERW was found to protect pancreatic β-cells from alloxan-induced cell damage by preventing alloxan-derived reactive oxygen species generation. They also concluded that ERW could be useful in preventing alloxan-induced T1DM (Li Y, Nishimura T, Teruya K, et al. 2002). A 2011 study was also conducted that concluded, "electrolyzed reduced water can prevent apoptosis of pancreatic β-cells and the development of symptoms in type 1 diabetes model mice by alleviating the alloxan-derived generation of reactive oxygen species" (Li Y, Hamasaki T, Nakamichi N, et al. 2011). In 2007, a study found that "blood glucose levels of diabetic mice (DC) were significantly higher than non-diabetic control mice (NC), and ERW consumption significantly lowered (41%) the blood glucose levels in hyperglycemic db/db mice (DE) without any effect in non-diabetic control mice (NE)." as seen in Figure 4 (Kim M, Jung K, Uhm Y, et al. 2007).

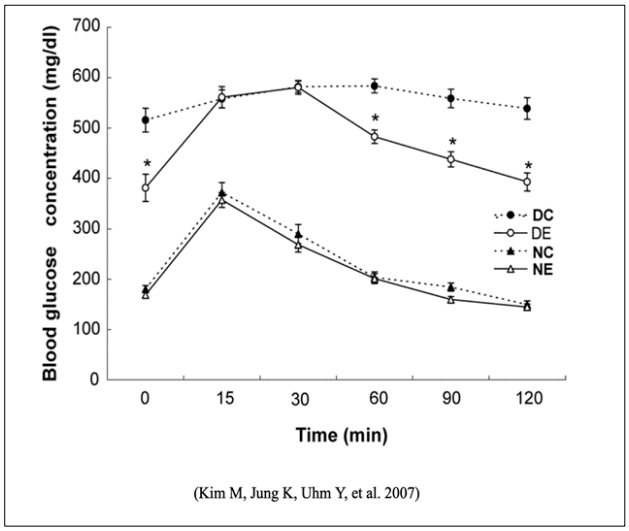

Figure 4 Effect of Electrolyzed reduced water on glucose tolerance in Mice

Figure 4: Effect of Electrolyzed Reduced Water (ERW) on Glucose Tolerance in Genetically Diabetic db/db Mice. Normal db/- mice fed tap water (NC); normal db/- mice fed ERW (NE); db/db mice fed tap water (DC); db/db mice fed ERW (DE). Data are expressed as mean ± S.E.M. (Kim M, Jung K, Uhm Y, et al. 2007).

3.7. Cancer

More than one hundred types of malignant neoplasms affect humans and are commonly denoted as cancer (Andrisic L, Dudzik D, Barbas C, et al. 2018). Reactive species of various types are formed in vivo, and many are powerful oxidizing agents capable of damaging DNA and other biomolecules (Halliwell B 2007). Oxidative stress plays a crucial role in cancer development and progression (Andrisic L, Dudzik D, Barbas C, et al. 2018). Increased formation of reactive species can promote the development of malignancy, and the normal rates of reactive species generation may account for the increased risk of cancer development in the aged (Halliwell B 2007).

Figure 5: "Effect of ERW on death of breast cancer cell lines. Trypan blue exclusion test was performed to determine the percentage of cell death of breast cancer cells treated with ERW, autoclaved ERW, or control medium (CTR) after 24, 48, and 72 hours of treatment. The results are expressed as the mean ± SD of six independent experiments performed in triplicate (∗p ≤ 0.01, #p ≤ 0.001 compared with the cultures treated with 1CTR and 2autoclaved ERW)" (Frajese GV, Benvenuto M, Mattera R, et al. 2018).

In a 2018 study, it was concluded that "ERW treatment inhibited cell survival, induced cell apoptosis, decreased ErbB2/neu expression, and impaired pERK1/ERK2 activation in breast cancer cells…" (Frajese GV, Benvenuto M, Mattera R, et al. 2018). The effect of ERW on death of breast cancer cell lines can be seen in Figure 5 (Frajese GV, Benvenuto M, Mattera R, et al. 2018). A study conducted in 2002, concluded that ERW led to a decreased effect on the telomere binding activities of telomere binding proteins in cancer cells, which would suggest that ERW results in a

shortened telomere length (Shirahata S, Murakami E, Kusumoto K, et al. 2002). Another 2008 study concluded that ERW down-regulated VEGF gene transcription (a mediator of tumor angiogenesis) and protein secretion through inactivation of ERK (Jun Y, Yuping L, Takeki H, et al. 2008).

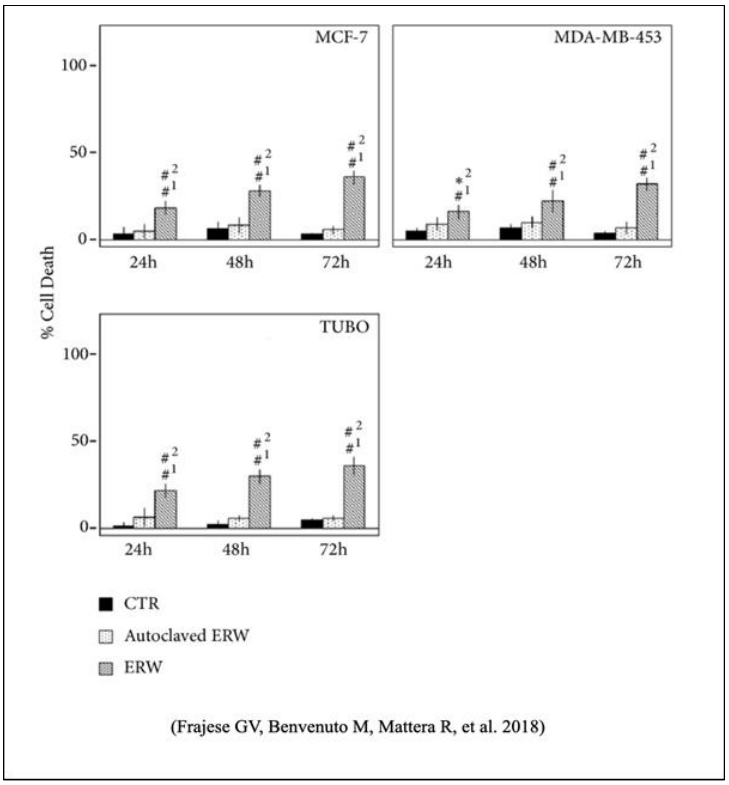

Figure 5 Effect of ERW on death of breast cancer cell lines

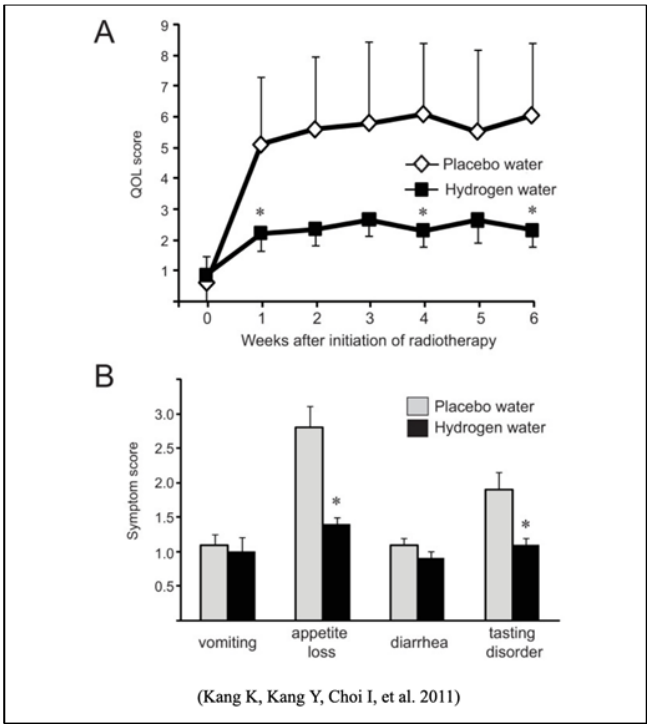

Figure 6 Placebo water and hydrogen water improved QOL in Radiotherapy patients

Not only has ERW been studied as a part of a cancer treatment protocol, it has also been studied as a treatment for the side effects seen in chemotherapy and radiation. A 2011 study concluded that daily consumption of hydrogen-rich water is a therapeutic strategy for improving quality of life after radiation exposure in cancer radiotherapy patients as seen in Figure 6 (Kang K, Kang Y, Choi I, et al. 2011). Consumption of hydrogen-rich water reduces the biological reaction to radiation-induced oxidative stress without compromising anti-tumor effects (Kang K, Kang Y, Choi I, et al. 2011).

Figure 6: "Placebo water and hydrogen water improved the QOL of patients receiving radiotherapy. A. Weekly assessment of the patients' QOL. B. Scoring system of GI symptoms after 6 weeks of radiotherapy with or without hydrogen water."(Kang K, Kang Y, Choi I, et al. 2011).

4. Conclusion

Throughout this study, extensive research was carried out to investigate the use of Electrolyzed Reduced Water (ERW) in overall health and wellness. ERW can be described as functional drinking water containing a large amount of molecular hydrogen and a small amount of platinum nanoparticles (Li Y Hamasaki T, et al. 2011). Oxidative stress can be defined as an imbalance between the cellular production of reactive oxygen species and the counteracting antioxidant mechanisms (S Salim. 2014). Active oxygen species, or free radicals, cause extensive oxidative damage to biological macromolecules Research articles referenced within this thesis point to oxidative stress as being a cause for diseases including, but not limited to, anxiety, depression, cardiovascular disease, hypertension, gastroesophageal reflux disease (GERD), diabetes and cancer. Research articles referenced within this thesis also point to ERW being able to scavenge active oxygen species and protect DNA from oxidative damage (S Shirahata, et al. 1997).

ERW can be used as a supplemental antioxidant with none of the side effects seen in other antioxidant supplements. A 2020 study was conducted in the workplace because the majority of healthy adults spend most of their waking hours at work, so the workplace appears to be the ideal place to adopt a healthy lifestyle (Choi Y, et al. 2020). Adopting the habit of drinking 1.5 L of ERW daily may lead to all of the benefits seen in multiple studies. After only four to eight weeks of drinking this 1.5 L of ERW, these benefits may be seen. After four weeks, healthy changes were seen in healthy individuals drinking 1.5 L to 2L of ERW daily (Sha J, Zhang S, Lu Y, et al. 2019). After 8 weeks, healthy changes were seen in individuals drinking 1.5 L of ERW daily (Choi Y, et al. 2020). ERW being produced from platinum coated titanium electrode plates is already commonly used and known to be effective for electrolysis but with further research on new material ERW may be able to be more cost-effective and will allow more individuals to benefit from drinking ERW (Choi Y, et al. 2020).

With much research being done on animals and more research beginning in clinical settings, there is hope that ERW will be studied and implemented as a part of a treatment and prevention strategies for a multiplicity of diseases. Treatment of a disease should never be one-dimensional. Scientists and physicians work together to create a finely tuned combination of many strategies. For the average American, Electrolyzed Reduced Water is a much needed additive for overall health and wellness.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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