

Clinical Studies and Research on Electrolyzed-Reduced Water

Fluid replacement promotes optimal physical performance:

Adequate fluid replacement helps maintain hydration and, promotes the health, safety, and optimal physical performance of individuals participating in regular physical activity.

Med Sci Sports Exercise
1996 Jan;28(1):i-vii.

American College of Sports Medicine position stand. Exercise and fluid replacement.

Convertino VA, Armstrong LE, Coyle EF, Mack GW, Sawka MN, Senay LC Jr, Sherman WM.

It is the position of the American College of Sports Medicine that adequate fluid replacement helps maintain hydration and, therefore, promotes the health, safety, and optimal physical performance of individuals participating in regular physical activity. This position statement is based on a comprehensive review and interpretation of scientific literature concerning the influence of fluid replacement on exercise performance and the risk of thermal injury associated with dehydration and hyperthermia.

Based on available evidence, the American College of Sports Medicine makes the following general recommendations on the amount and composition of fluid that should be ingested in preparation for, during, and after exercise or athletic competition: 1) It is recommended that individuals consume a nutritionally balanced diet and drink adequate fluids during the 24-hr period before an event, especially during the period that includes the meal prior to exercise, to promote proper hydration before exercise or competition.

2) It is recommended that individuals drink about 500 ml (about 17 ounces) of fluid about 2 h before exercise to promote adequate hydration and allow time for excretion of excess ingested water.

3) During exercise, athletes should start drinking early and at regular intervals in an attempt to consume fluids at a rate sufficient to replace all the water lost through sweating (i.e., body weight loss), or consume the maximal amount that can be tolerated.

4) It is recommended that ingested fluids be cooler than ambient temperature [between 15 degrees and 22 degrees C (59 degrees and 72 degrees F)] and flavored to enhance palatability and promote fluid replacement. Fluids should be readily available and served in containers that allow adequate volumes to be ingested with ease and with minimal interruption of exercise.

5) Addition of proper amounts of carbohydrates and/or electrolytes to a fluid replacement solution is recommended for exercise events of duration greater than 1 h since it does not significantly impair water delivery to the body and may enhance performance. During exercise lasting less than 1 h, there is little evidence of physiological or physical performance differences between consuming a carbohydrate-electrolyte drink and plain water.

6) During intense exercise lasting longer than 1 h, it is recommended that carbohydrates be ingested at a rate of 30-60 g.h(-1) to maintain oxidation of carbohydrates and delay fatigue. This rate of carbohydrate intake can be achieved without compromising fluid delivery by drinking 600-1200 ml.h(-1) of solutions containing 4%-8% carbohydrates (g.100 ml(-1)). The carbohydrates can be sugars (glucose or sucrose) or starch (e.g., maltodextrin).

7) Inclusion of sodium (0.5-0.7 g.1(-1) of water) in the rehydration solution ingested during exercise lasting longer than 1 h is recommended since it may be advantageous in enhancing palatability, promoting fluid retention, and possibly preventing hyponatremia in certain individuals who drink excessive quantities of fluid. There is little

physiological basis for the presence of sodium in an oral rehydration solution for enhancing intestinal water absorption as long as sodium is sufficiently available from the previous meal.

Electrolyzed-reduced water scavenges active oxygen species and protects DNA from oxidative damage.

Biochem Biophys Res Commun.
1997 May 8
234(1):269-74.

Shirahata S, Kabayama S, Nakano M, Miura T, Kusumoto K, Gotoh M, Hayashi H, Otsubo K, Morisawa S, Katakura Y.

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Active oxygen species or free radicals are considered to cause extensive oxidative damage to biological macromolecules, which brings about a variety of diseases as well as aging. The ideal scavenger for active oxygen should be 'active hydrogen'. 'Active hydrogen' can be produced in reduced water near the cathode during electrolysis of water.

Reduced water exhibits high pH, low dissolved oxygen (DO), extremely high dissolved molecular hydrogen (DH), and extremely negative redox potential (RP) values. Strongly electrolyzed-reduced water, as well as ascorbic acid, (+)-catechin and tannic acid, completely scavenged O_2 produced by the hypoxanthine-xanthine oxidase (HX-XOD) system in sodium phosphate buffer (pH 7.0). The superoxide dismutase (SOD)-like activity of reduced water is stable at 4 degrees C for over a month and was not lost even after neutralization, repeated freezing and melting, deflation with sonication, vigorous mixing, boiling, repeated filtration, or closed autoclaving, but was lost by opened autoclaving or by closed autoclaving in the presence of tungsten trioxide which efficiently adsorbs active atomic hydrogen.

Water bubbled with hydrogen gas exhibited low DO, extremely high DH and extremely low RP values, as does reduced water, but it has no SOD-like activity. These results suggest that the SOD-like activity of reduced water is not due to the dissolved molecular hydrogen but due to the dissolved atomic hydrogen (active hydrogen).

Although SOD accumulated H_2O_2 when added to the HX-XOD system, reduced water decreased the amount of H_2O_2 produced by XOD. Reduced water, as well as catalase and ascorbic acid, could directly scavenge H_2O_2 . Reduced water suppresses single-strand breakage of DNA by active oxygen species produced by the Cu(II)-catalyzed oxidation of ascorbic acid in a dose-dependent manner, suggesting that reduced water can scavenge not only O_2 and H_2O_2 , but also $1O_2$ and $\cdot OH$.

PMID: 9169001 [PubMed - indexed for MEDLINE]

The mechanism of the enhanced antioxidant effects against superoxide anion radicals of reduced water produced by electrolysis.

Biophys Chem. 2004
Jan 1;107(1):71-82.

Hanaoka K, Sun D, Lawrence R, Kamitani Y, Fernandes G.
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We reported that reduced water produced by electrolysis enhanced the antioxidant effects of proton donors such as ascorbic acid (AsA) in a previous paper.

We also demonstrated that reduced water produced by electrolysis of 2 mM NaCl solutions did not show antioxidant effects by itself. We reasoned that the enhancement of antioxidant effects may be due to the increase of the ionic product of water as solvent. The ionic product of water (pK_w) was estimated by measurements of pH and by a neutralization titration method. As an indicator of oxidative damage, Reactive Oxygen Species- (ROS) mediated DNA strand breaks were measured by the conversion of supercoiled phiX-174 RF I double-strand DNA to open and linear forms. Reduced water had a tendency to suppress single-strand breakage of DNA induced by reactive oxygen species produced by H₂O₂/Cu (II) and HQ/Cu (II) systems. The enhancement of superoxide anion radical dismutation activity can be explained by changes in the ionic product of water in the reduced water.

PMID: 14871602 [PubMed - in process]

Oxygen Radical Absorbance Capacity--High-ORAC Foods May Slow Aging

Agricultural Research Service, USDA, February 8, 1999

Foods that score high in an antioxidant analysis called ORAC may protect cells and their components from oxidative damage, according to studies of animals and human blood at the Agricultural Research Services Human Nutrition Research Center on Aging at Tufts in Boston. ARS is the chief scientific agency of the U.S. Department of Agriculture.

ORAC, short for oxygen radical absorbance capacity, is a test tube analysis that measures the total antioxidant power of foods and other chemical substances. Early findings suggest that eating plenty of high-ORAC fruits and vegetables, such as spinach and blueberries, may help slow the processes associated with aging in both body and brain. If these findings are borne out in further research, young and middle-aged people may be able to reduce risk of diseases of aging (including senility) simply by adding high-ORAC foods to their diets, said ARS Administrator Floyd P. Horn.

In the studies, eating plenty of high-ORAC foods:

- Raised the antioxidant power of human blood 10 to 25%
- Prevented some loss of long-term memory and learning ability in middle-aged rats
- Maintained the ability of brain cells in middle-aged rats to respond to a chemical stimulus—a function that normally decreases with age.
- Protected rats' tiny blood vessels (capillaries) against oxygen damage.

Nutritionist Ronald L. Prior contends, "If we can show some relationship between ORAC intake and health outcome in people, I think we may reach a point where the ORAC value will become a new standard for good antioxidant protection." (See the table at the bottom for ORAC values of fruits and vegetables.)

The thesis that oxidative damage culminates in many of the maladies of aging is well accepted in the health community. The evidence has spurred skyrocketing sales of antioxidant vitamins. But several large trials have had mixed results. It may be that combinations of nutrients found in foods have greater protective effects than each nutrient taken alone, said Guohua (Howard) Cao, a physician and chemist who developed the ORAC assay.

He and Prior have seen the ORAC value of human blood rise in two studies. In the first, eight women gave blood after separately ingesting spinach, strawberries, and red wine (all high-ORAC foods) or taking 1,250 milligrams of vitamin C. A large serving of fresh spinach produced the biggest rise in the women's blood antioxidant scores (up to 25 percent) followed by vitamin C, strawberries, and lastly, red wine. In the second study, men and women had a 13- to 15-percent increase in the antioxidant power of their blood after doubling their daily fruit and vegetable intake compared to what they consumed before the study. Just doubling intake, without regard to ORAC scores of the fruits and vegetables, more than doubled the number of ORAC units the volunteers consumed, Prior reported. Early evidence for the protecting power of these diets comes from rat studies by Prior, Cao, and colleagues. Rats fed daily doses of blueberry extract for six weeks before being subjected to two days of pure oxygen apparently suffered

much less damage to the capillaries in and around their lungs, Prior said. The fluid that normally accumulates in the pleural cavity surrounding the lungs was much lower compared to the group that didn't get blueberry extract. Neuroscientist James Joseph and psychologist Barbara Shukitt-Hale at the center tested middle-aged rats that had eaten diets fortified with spinach, strawberry extract, or vitamin E for nine months.

A daily dose of spinach extract prevented some loss of long-term memory and learning ability normally experienced by the 15-month-old rats, said Shukitt-Hale. Spinach was also the most potent in protecting different types of nerve cells in two separate parts of the brain against the effects of aging. These cells were significantly more responsive when the animals ate diets fortified with high-ORAC foods, especially spinach, compared to unfortified diets, Joseph said. The spinach group scored twice as responsive as the control animals. Why spinach is more effective than strawberries (which score higher in the ORAC assay) is still a mystery. The researchers conjecture that it may be due to specific compounds or a specific combination of them in the greens.

Top-Scoring Fruits and Vegetables ORAC units per 100 grams (about 3.5 ounces) [Prunes 5770](#) [Raisins 2830](#) [Blueberries 2400](#) [Blackberries 2036](#) [Kale 1770](#) [Strawberries 1540](#) [Spinach 1260](#) [Raspberries 1220](#) [Brussels Sprouts 980](#) [Plums 949](#) [Alfalfa Sprouts 930](#) [Broccoli flowers 890](#) [Beets 840](#) [Red Grapes 785](#) [Oranges 750](#) [Red Bell Peppers 710](#) [Cherries 670](#) [Kiwi Fruit 602](#) [Pink Grapefruit 483](#) [Onion 450](#) [Corn 400](#) [Eggplant 390](#)

Use of Ionized water in hypochlorhydria or achlorhydria

Prof. Kuninaka Hironage, Head of Kuninaka Hospital

"Too many fats in the diets, which lead to the deposition of cholesterol on the blood vessels, which in turn constrict the blood flow, cause most illnesses such as high blood pressure. In accordance with the theory of Professor Gato of Kyushu University on Vitamin K (because vitamin K enables the blood calcium to increase), or the consumption of more antioxidant water, the effectiveness of the increase in the calcium in high blood pressure is most significant. The consumption of alkaline antioxidant water for a period of 2 to 3 months, I have observed the blood pressure slowly drop, due to the water's solvent ability, which dissolves the cholesterol in the blood vessels."

Use of Ionized water for gynecological conditions

Prof. Watanabe Ifao, Watanabe Hospital

"Ionized alkaline antioxidant water improves body constituents and ensures effective healing to many illnesses. The uses of antioxidant water in gynecological patients have proved to be very effective. The main reason for its effectiveness is that this water can neutralize toxins.

When given antioxidant water to pre-eclamptic toxemia cases, the results are most significant. During my long years of servicing the pre-eclamptic toxemia cases, I found that the women with pre-eclamptic toxemia who consumed antioxidant water tend to deliver healthier babies with stronger muscles. A survey report carried out on babies in this group showed intelligence above average."

CLINICAL Improvements Obtained From The Intake Of Reduced Water

Extracts from "Presentation At The Eight Annual International Symposium On man And His Environment in Health And Disease" on February 24th 1990, at The Grand Kempinski Hotel, Dalls, Texas, USA by Dr. H. Hayashi, M.D. and Dr. M Kawamura, M.D., on : -

(THE CONCEPT OF PREHEPATIC MEDICINES)

Since the introduction of alkaline ionic water in our clinic in 1985, we have had the following interesting clinical experiences in the use of this type of water. By the use of alkaline ionic water for drinking and the preparation of meals for our in-patients, we have noticed :-

Declines in blood sugar levels in diabetic patients.

Improvements in peripheral circulation in diabetic gangrene.

Declines in uric acid levels in patients with gout.

Improvements in liver function exams in hepatic disorders.

Improvements in gastroduodenal ulcers and prevention of their recurrences.

Improvements in hypertension and hypotension.

Improvements in allergic disorders such as asthma, urticaria, rhinites and atopic dermatitis.

Improvements in persistent diarrhoea which occurred after gastrectomy.

Quicker improvements in post operative bowel paralysis.

Improvements in serum bilirubin levels in new born babies.

Being confirming clinical improvements, we have always observed changes of stools of the patients, with the colour of their feces changing from black-brown colour to a brighter yellow-brown one, and the odour of their feces becoming almost negligible.

The number of patients complaining of constipation also decreased markedly. The change of stool findings strongly suggests that alkaline ionic water intake can decrease the production of putrefied or pathogenic metabolites.

Devices to produce reduced water were introduced into our clinic in May 1985. Based on the clinical experiences obtained in the past 15 years, it can be said that introduction of electrolyzed-reduced water for drinking and cooking purpose for in-patients should be the very prerequisite in our daily medical practices. Any dietary recipe cannot be a scientific one if property of water is not taken by the patients is not taken into consideration.

The Ministry of Health and Welfare in Japan announced in 1965 that the intake of reduced water is effective for restoration of intestinal flora metabolism.

Toxin Neutralization

Prof. Kuwata Keijiroo, Doctor of Medicine

"In my opinion, the wonder of antioxidant water is the ability to neutralize toxins; but it is not a medicine. The difference is that medicine can only apply to individual cases, whereas the antioxidant water can be consumed generally and its neutralizing power is something which is very much unexpected. Now, in brief, let me introduce to you a heart disease case and how it was cured.

The patient was a 35 years old male suffering from vascular heart disease. For 5 years, his sickness deteriorated. He was in the Setagays Government Hospital for treatment.

During those 5 years, he had been in and out of the hospital 5 to 6 times. He had undergone high tech examinations such as angiogram by injecting VINYL via the vein into the heart. He consulted and sought treatment from many good doctors where later he underwent a major surgical operation. Upon his discharge from the hospital, he quit his job to convalesce. However, each time when his illness relapsed, the attack seemed to be even more severe.

Last year, in August, his relatives were in despair and expected he would not live much longer. It so happened at that time that the victim's relative came across antioxidant water processor. His illness responded well and he is now on the road to recovery."

(In the United States, cardiovascular diseases account for more than one-half of the approximate 2 million deaths occurring each year.... It is estimated that optimal conditioning of drinking water could reduce this cardiovascular disease mortality rate by as much as 15 percent in the United States) From: Report of the Safe Drinking Water Committee of the National Academy of Sciences, 1977

Eczema

Prof. Tamura Tatsuji, Keifuku Rehabilitation Center

"Eczema is used to describe several varieties of skin conditions, which have a number of common features. The exact causes of eczema are not fully understood. In many cases, eczema can be attributed to external irritants. Let me

introduce a patient who recovered from skin disease after consuming the antioxidant water. This patient suffered 10 years of eczema and could not be cured effectively even under specialist treatment. This patient, who is 70 years of age, is the president of a vehicle parts company. After the war, his lower limbs suffered acute eczema, which later became chronic. He was repeatedly treated in a specialist skin hospital.

The left limb responded well to treatment, but not so on the right limb. He suffered severe itchiness, which, when scratched led to bleeding. During the last 10 years, he was seen and treated by many doctors. When I first examined him, his lower limb around the joints was covered with vesicles. Weeping occurred owing to serum exuding from the vesicles.

I advised him to try consuming antioxidant water. He bought a unit and consumed the antioxidant water religiously and used the acidic water to bathe the affected areas. After 2 weeks of treatment the vesicles dried up. The eczema was completely cleared without any relapse after 1½ month."

Allergies

Prof. Kuninaka Hironaga, Head of Kuninaka Hospital

"Mr. Yamada, the head of Police Research Institute, suffered from severe allergy. He was treated repeatedly by skin specialist, but with no success. Then he started consuming antioxidant water. The allergy responded very well and was soon completely cured. No relapse had occurred, although he had taken all kinds of food. He was most grateful and excited about this treatment.

As for myself, I had also suffered severe allergy. Ever since I began to consume antioxidant water, the allergy has recovered. Since then, I started a research on the effectiveness of antioxidant water.

I discovered that most allergies are due to acidification of body condition and is also related to consuming too much meat and sugar. In every allergy case, the patient's antioxidant minerals are excessively low which in turn lower the body resistance significantly. The body becomes overly sensitive and develops allergy easily. To stabilize the sensitivity, calcium solution is injected into the vein. Therefore, it is clear that the antioxidant water has ionic calcium, which can help alleviate allergy.

The ionic calcium not only enhances the heart, urination, and neutralization of toxins but controls acidity. It also enhances the digestive system and liver function. This will promote natural healing power and hence increase its resistance to allergy. In some special cases of illness, which do not respond to drugs, it is found, it is found to respond well to antioxidant water."

Digestive Problems

Prof. Kogure Keizou, Kogure Clinic of Juntendo Hospital

"The stomach is readily upset both by diseases affecting the stomach and by other general illnesses. In addition, any nervous tension or anxiety frequently causes gastric upset.

The important role of antioxidant water in our stomach is to neutralize the secretion and strengthen its functions. Usually, after consuming the antioxidant water for 1 to 3 minutes, the gastric juice increase to 1½ times. For those suffering from achlorhydria (low in gastric juice) the presence of antioxidant water will stimulate the stomach cells to secrete more gastric juice. This in turn enhances digestion and absorption of minerals. However, those with hyperchlorhydria (high in gastric juice), the antioxidant water neutralizes the excessive gastric juice. Hence, it does not create any adverse reaction. According to the medical lecturer from Maeba University, the pH of the gastric secretion will still remain normal when antioxidant water is consumed. This proves the ability of the antioxidant water to neutralize as well as to stimulate the secretion."

Effects of Alkaline Ionized Water on Spontaneously diabetic GK-rats fed Sucrose

Diabetes

TWO ABSTRACTS and ONE REPORT ON DIABETES / ALKALINE WATER RESEARCH

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This study was carried out to evaluate the effects of alkaline ionized water (AIW) on spontaneously diabetic GK-rats fed sucrose for aggravation of diabetes mellitus.

One half of the 32 GK rats was given AIW and the other was given tap water (TW). These two groups were further divided into two subgroups by fed with or without 30% sucrose solution (8 in each group). In blood glucose level, sucrose fed TW group was significantly higher than the other groups. Sucrose fed both AIW and TW groups were significantly increased in body weight as compared to TW group. In serum malondialdehyde (MDA), a marker of lipid peroxide, sucrose fed TW group was significantly higher than AIW and TW groups.

It is suggested that AIW (Alkaline Ionized Water) supplementation may inhibit the increase of blood glucose and lipid peroxide levels in diabetes mellitus.

Protective mechanism of reduced water against alloxan-induced pancreatic β -cell damage: Scavenging effect against reactive oxygen species

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Abstract

Reactive oxygen species (ROS) cause irreversible damage to biological macromolecules, resulting in many diseases. Reduced water (RW) such as hydrogen-rich electrolyzed reduced water and natural reduced waters like Hita Tenryosui water in Japan and Nordenau water in Germany that are known to improve various diseases, could protect a hamster pancreatic β cell line, HIT-T15 from alloxan-induced cell damage. Alloxan, a diabetogenic compound, is used to induce type 1 diabetes mellitus in animals. Its diabetogenic effect is exerted via the production of ROS. Alloxan-treated HIT-T15 cells exhibited lowered viability, increased intracellular ROS levels, elevated cytosolic free Ca^{2+} concentration, DNA fragmentation, decreased intracellular ATP levels and lowering of glucose-stimulated release of insulin. RW completely prevented the generation of alloxan-induced ROS, increase of cytosolic Ca^{2+} concentration, decrease of intracellular ATP level, and lowering of glucose-stimulated insulin release, and strongly blocked DNA fragmentation, partially suppressing the lowering of viability of alloxan-treated cells. Intracellular ATP levels and glucose-stimulated insulin secretion were increased by RW to 2–3.5 times and 2–4 times, respectively, suggesting that RW enhances the glucose-sensitivity and glucose response of β -cells. The protective activity of RW was stable at 4 °C for over a month, but was lost by autoclaving. These results suggest that RW protects pancreatic β -cells from alloxan-induced cell damage by preventing alloxan-derived ROS generation. RW may be useful in preventing alloxan-induced type 1-diabetes mellitus.

Diabetes

Prof. Kuwata Keijiroo, Doctor of Medicine

"When I was serving in the Fire Insurance Association, I used to examine many diabetic patients. Besides treating them with drugs, I provided them with antioxidant water. After drinking antioxidant water for one month, 15 diabetic patients were selected and sent to Tokyo University for further test and observations. Initially, the more serious patients were a bit apprehensive about the treatment. When the antioxidant water was consumed for some time, the sugar in the blood and urine ranged from a ratio of 300 mg/l to 2 mg / dc. There was a time where the patient had undergone 5 to 6 blood tests a day and detected to be within normal range. Results also

showed that even 1 1/2 hour after meals, the blood sugar and urine ratio was 100 mg/dc: 0 mg/dc . The sugar in the urine has completely disappeared."

NOTE: More Americans than ever before are suffering from diabetes, with the number of new cases averaging almost 800,000 each year. The disease has steadily increased in the United States since 1980, and in 1998, 16 million Americans were diagnosed with diabetes (10.3 million diagnosed; 5.4 million undiagnosed). Diabetes is the seventh leading cause of death in the United States, and more than 193,000 died from the disease and its related complications in 1996. From: U. S. Department of Health and Human Services, October 13, 2000 Fact Sheet.

Use of Ionized water in treating Acidosis

Prof. Hatori Tasutaroo, Head of Akajiuji Blood Centre, Yokohama Hospital, Faitama District
"Due to a higher standard of living, our eating habits have changed. We consume too much proteins, fats and sugar. The excess fats and carbohydrates are in the body as fats. In the present lifestyles, Americans are more extravagant on food compared to the Japanese. Due to this excessive intake obesity is a significant problem. Normally, one out of five males and one out of four females is obese.

The degree of "burn-out" in food intake largely depends on the amount on intake of vitamins and minerals. When excessive intake of proteins, carbohydrates and fats occurs, the requirement for vitamins and minerals increases. However, there is not much research carried out pertaining to the importance of vitamins and minerals.

Nowadays, many people suffer from acidification that leads to diabetes, heart diseases, cancer, live and kidney diseases. If our food intake can be completely burned off, then there is no deposition of fats. Obviously, there will be no acidification problem and hence there should not be any sign of obesity.

The antioxidant water contains an abundance of ionic calcium. This ionic calcium helps in the "burn-off" process. By drinking antioxidant water, it provides sufficient minerals for our body. As a result, we do not need to watch our diet to stay slim.

Hence, antioxidant water is a savior for those suffering from obesity and many adult diseases, providing good assistance in enhancing good health."

REDUCED WATER FOR PREVENTION OF DISEASES

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It has long been established that reactive oxygen species (ROS) cause many types of damage to biomolecules and cellular structures, that, in turn result in the development of a variety of pathologic states such as diabetes, cancer and aging. Reduced water is defined as anti-oxidative water produced by reduction of water. Electrolyzed reduced water (ERW) has been demonstrated to be hydrogen-rich water and can scavenge ROS in vitro (Shirahata et al., 1997). The reduction of proton in water to active hydrogen (atomic hydrogen, hydrogen radical) that can scavenge ROS is very easily caused by a weak current, compared to oxidation of hydroxyl ion to oxygen molecule. Activation of water by magnetic field, collision, minerals etc. will also produce reduced water containing active hydrogen and/or hydrogen molecule. Several natural waters such as Hita Tenryosui water drawn from deep underground in Hita city in Japan, Nordenau water in Germany and Tlacote water in Mexico are known to alleviate various diseases. We have developed a sensitive method by which we can detect active hydrogen existing in reduced water, and have demonstrated that not only ERW but also natural reduced waters described above contain active hydrogen and scavenge ROS in cultured cells. ROS is known to cause reduction of glucose uptake by

inhibiting the insulin-signaling pathway in cultured cells. Reduced water scavenged intracellular ROS and stimulated glucose uptake in the presence or absence of insulin in both rat L6 skeletal muscle cells and mouse 3T3/L1 adipocytes. This insulin-like activity of reduced water was inhibited by wortmannin that is specific inhibitor of PI-3 kinase, a key molecule in insulin signaling pathways. Reduced water protected insulin-responsive cells from sugar toxicity and improved the damaged sugar tolerance of type 2 diabetes model mice, suggesting that reduced water may improve insulin-independent diabetes mellitus. Cancer cells are generally exposed to high oxidative stress. Reduced water cause impaired tumor phenotypes of human cancer cells, such as reduced growth rate, morphological changes, reduced colony formation ability in soft agar, passage number-dependent telomere shortening, reduced binding abilities of telomere binding proteins and suppressed metastasis. Reduced water suppressed the growth of cancer cells transplanted into mice, demonstrating their anti-cancer effects in vivo. Reduced water will be applicable to not only medicine but also food industries, agriculture, and manufacturing industries.

Shirahata, S. et al.: Electrolyzed reduced water scavenges active oxygen species and protects DNA from oxidative damage. *Biochem. Biophys. Res. Commun.*, 234, 269174, 1997.

Clinical evaluation of alkaline ionized water for abdominal complaints: Placebo controlled double blind tests

by Hirokazu Tashiro, Tetsuji Hokudo, Hiromi Ono, Yoshihide Fujiyama, Tadao Baba (National Ohkura Hospital, Dept. of Gastroenterology; Institute of Clinical Research, Shiga University of Medical Science, Second Dept. of Internal Medicine)

Effect of alkaline ionized water on abdominal complaints was evaluated by placebo controlled double blind tests. Overall scores of improvement using alkaline ionized water marked higher than those of placebo controlled group, and its effect proved to be significantly higher especially in slight symptoms of chronic diarrhoea and abdominal complaints in cases of general malaise. Alkaline ionized water group did not get interrupted in the course of the test, nor did it show serious side effects nor abnormal test data. It was confirmed that alkaline ionized water is safer and more effective than placebos.

Summary

Effect of alkaline ionized water on abdominal complaints was clinically examined by double blind tests using clean water as placebo. Overall improvement rate was higher for alkaline ionized water group than placebo group and the former proved to be significantly more effective than the other especially in cases of slight symptoms. Examining improvement rate for each case of chronic diarrhoea, constipation and abdominal complaints, alkaline ionized water group turned out to be more effective than placebo group for chronic diarrhoea, and abdominal complaints. The test was stopped in one case of chronic diarrhoea, among placebo group due to exacerbation, whereas alkaline ionized water group did not stop testing without serious side effects or abnormal test data in all cases. It was confirmed that alkaline ionized water is more effective than clean water against chronic diarrhoea, abdominal complaints and overall improvement rate (relief of abdominal complaints) and safer than clean water.

Introduction

Since the approval of alkaline ionized water electrolyzers by Pharmaceutical Affairs Law in 1966 for its antacid effect and efficacy against gastrointestinal disorders including hyperchylia, indigestion, abnormal gastrointestinal fermentation and chronic diarrhoea, they have been extensively used among patients. However, medical and scientific evaluation of their validity is not established. In our study, we examined clinical effect of alkaline ionized water on gastrointestinal disorders across many symptoms in various facilities. Particularly, we studied safety and usefulness of alkaline ionized water by doubleblind tests using clean water as a control group.

Test subjects and methods

163 patients (34 men, 129 women, age 21 to 72, average 38.6 years old) of indigestion, abnormal gastrointestinal fermentation (with abnormal gas emission and rugitus) and abdominal complaints caused by irregular defecation (chronic diarrhoea, or constipation) were tested as subjects with good informed consent. Placebo controlled double blind tests were conducted using alkaline ionized water and clean water at multiple facilities. An alkaline ionized water electrolyzer sold commercially was installed with a pump driven calcium dispenser in each of the subject

homes. Tested alkaline ionized water had pH at 9.5 and calcium concentration at 30ppm. Each subject in placebo group used a water purifier that has the same appearance as the electrolyzer and produces clean water.

The tested equipment was randomly assigned by a controller who scaled off the key code which was stored safely until the tests were completed and the seal was opened again.

Water samples were given to each patient in the amount of 200ml in the morning with the total of 500ml or more per day for a month. Before and after the tests, blood, urine and stool were tested and a log was kept on the subjective symptoms, bowel movements and accessory symptoms. After the tests, the results were analyzed based on the log and the test data.

Test Results

1. Symptom

Among 163 tested subjects, alkaline ionized water group included 84 and placebo group 79. Background factors such as gender, age and basal disorders did not contribute to significant difference in the results.

2. Overall improvement rate

As to overall improvement rate of abdominal complaints, alkaline ionized water group had 2 cases of outstanding improvement (2.5%), 26 cases of fair improvement (32.1%), 36 cases of slight improvement (44.4%), 13 cases of no change (16%) and 4 cases of exacerbation (4.9%), whereas placebo group exhibited 4 (5.2%), 19 (24.7%), 27 (35.1%), 25 (32.5%) and 2 cases (2.6%) for the same category. Comparison between alkaline ionized water and placebo groups did not reveal any significant difference at the level of 5% significance according to the Wilcoxon test, although alkaline ionized water group turned out to be significantly more effective than placebo group at the level of p value of 0.22.

Examining overall improvement rates by a 7, 2 test (with no adjustment for continuity) between the effective and noneffective groups, alkaline ionized water group had 64 (79%) of effective cases and 17 cases (21%) of non effective cases, whereas placebo group had 50 (64.9%) and 27 (35.1%) cases respectively. The result indicated that alkaline ionized water group was significantly more effective than placebo group at the level of p value of 0.048.

Looking only at 83 slight cases of abdominal complaints, overall improvement rate for alkaline ionized water group (45 cases) was composed of 11 cases (24.2%) of fair improvement, 22 cases (48.9%) of slight improvement, 17 cases (44.7%) of no change and 3 cases (6.7%) of exacerbation, whereas placebo group (38 cases) had 3 (7.8%), 17 (44.7%), 17 (44.7%) and 1 (2.6%) cases for the same category. Alkaline ionized water group was significantly more effective than placebo group according to the comparison between the groups (p value = 0.033).

3. Improvement rate by basal symptom

Basal symptoms were divided into chronic diarrhea, constipation and abdominal complaints (dyspepsia) and overall improvement rate was evaluated for each of them to study effect of alkaline ionized water. In case of chronic diarrhoea, alkaline ionized water group resulted in 94.1% of effective cases and 5.9% of non effective cases. Placebo group came up with 64.7% effective and 35.3% non effective. These results indicate alkaline ionized water group proved to be significantly more effective than placebo group. In case of slighter chronic diarrhoea, comparison between groups revealed that alkaline ionized water group is significantly more effective than placebo group (p=0.015). In case of constipation, alkaline ionized water group consisted of 80.5% of effective and 19.5% of non effective cases, whereas placebo group resulted in 73.3% effective and 26.3 non effective. As to abdominal complaints (dyspepsia), alkaline ionized water group had 85.7% of effective and 14.3% non effective cases while placebo group showed 47.1% and 62.9% respectively. Alkaline ionized water group proved to be significantly more effective than placebo group (p=0.025).

4. Safety

Since one case of chronic diarrhoea, in placebo group saw exacerbation, the test was stopped. There was no such cases in alkaline ionized water group. Fourteen cases of accessory symptoms, 8 in alkaline ionized water group and 6 in placebo group, were observed, none of which were serious. 31 out of 163 cases (16 in alkaline ionized water group, 15 in placebo group) exhibited fluctuation in test data, although alkaline ionized water group did not have any problematic fluctuations compared to placebo group. Two cases in placebo group and one case in alkaline ionized water group have seen K value of serum climb up and resume to normal value after re testing which indicates the value changes were temporary.

Conclusion

As a result of double blind clinical tests of alkaline ionized water and clean water, alkaline ionized water was proved to be more effective than clean water against chronic diarrhea, abdominal complaints (dyspepsia) and overall improvement rate (relief from abdominal complaints). Also, safety of alkaline ionized water was confirmed which clinically verifies its usefulness.

Selective stimulation of the growth of anaerobic microflora in the human intestinal tract by electrolyzed reducing water

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96-99% of the "friendly" or residential microflora of intestinal tract of humans consists of strict anaerobes and only 1-4% of aerobes. Many diseases of the intestine are due to a disturbance in the balance of the microorganisms inhabiting the gut. The treatment of such diseases involves the restoration of the quantity and/or balance of residential microflora in the intestinal tract. It is known that aerobes and anaerobes grow at different oxidation-reduction potentials (ORP). The former require positive E(h) values up to +400 mV. Anaerobes do not grow unless the E(h) value is negative between -300 and -400 mV. In this work, it is suggested that prerequisite for the recovery and maintenance of obligatory anaerobic microflora in the intestinal tract is a negative ORP value of the intestinal milieu. Electrolyzed reducing water with E(h) values between 0 and -300 mV produced in electrolysis devices possesses this property. Drinking such water favours the growth of residential microflora in the gut. A sufficient array of data confirms this idea. However, most researchers explain the mechanism of its action by an antioxidant properties destined to detox the oxidants in the gut and other host tissues. Evidence is presented in favour of the hypothesis that the primary target for electrolyzed reducing water is the residential microflora in the gut.

Physiological effects of alkaline ionized water: Effects on metabolites produced by intestinal fermentation

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We have found that long-term ingestion of alkaline ionized water (AIW) reduces cecal fermentation in rats that were given highly fermentable commercial diet (MF: Oriental Yeast Co., Ltd.). In this experiment, rats were fed MF and test water (tap water, AIW with pH at 9 and 10) for about 3 months. Feces were collected on the 57th day, and the rats were dissected on the 88th day. The amount of ammonium in fresh feces and cecal contents as well as fecal free-glucose tended to drop down for the AIW group. In most cases, the amount of free-amino acids in cecal contents did not differ significantly except for cysteine (decreased in AIW with pH at 10) and isoleucine (increased in AIW with pH at 10).

Purpose of tests

Alkaline ionized water electrolyzers have been approved for manufacturing in 1965 by the Ministry of Health and Welfare as medical equipment to produce medical substances. Alkaline ionized water (AIW) produced by this equipment is known to be effective against gastrointestinal fermentation, chronic diarrhea, indigestion and hyperchylia as well as for controlling gastric acid.*1 This is mainly based on efficacy of the official calcium hydroxide. *2 By giving AIW to rats for a comparatively long time under the condition of extremely high level of

intestinal fermentation, we have demonstrated that AIW intake is effective for inhibition of intestinal fermentation when its level is high based on some test results where AIW worked against cecal hypertrophy and for reduction in the amount of short-chain fatty acid that is the main product of fermentation.*3 We have reported that this is caused by the synergy between calcium level generally contained in AIW (about 50ppm) and the value of pH, and that frequency of detecting some anaerobic bacteria tends to be higher in alkaline ionized water groups than the other, although the bacteria count in the intestine does not have significant difference. Based on these results, we made a judgment that effect of taking AIW supports part of inhibition mechanism against abnormal intestinal fermentation, which is one of the claims of efficacy that have been attributed to alkaline ionized water electrolyzers.*4 On the other hand, under the dietary condition of low intestinal fermentation, AIW uptake does not seem to inhibit fermentation that leads us to believe that effect of AIW uptake is characteristic of hyper-fermentation state. Metabolites produced by intestinal fermentation include indole and skatole in addition to organic acids such as short-chain fatty acid and lactic acid as well as toxic metabolites such as ammonium, phenol and p-cresol. We do not know how AIW uptake would affect the production of these materials. In this experiment, we have tested on ammonium production as explained in the following sections.

Testing methods

Four-week-old male Wistar/ST Clean rats were purchased from Japan SLC Co., Ltd. and were divided into 3 groups of 8 each after preliminary breeding. AIW of pH 9 and 10 was produced by an electrolyzer Mineone ROYAL NDX3 1 OH by Omco Co., Ltd. This model produces AIW by electrolyzing water with calcium lactate added. On the last day of testing, the rats were dissected under Nembutal anesthesia to take blood from the heart by a heparin-treated syringe. As to their organs, the small intestines, cecum and colon plus rectum were taken out from each of them. The cecum was weighed and cleaned with physiological saline after its contents were removed, and the tissue weight was measured after wiping out moisture. Part of cecal contents was measured its pH, and the rest was used to assay ammonium concentration. The amount of ammonium contained in fresh feces and cecal contents was measured by the Nessler method after collecting it in the extracted samples using Conway's micro-diffusion container. Fecal free-glucose was assayed by the oxygen method after extraction by hot water. Analysis of free amino acids contained in cecal contents was conducted by the Waters PicoTag amino acid analysis system.

Test results and analyses

No difference was found in the rats' weight gain, water and feed intake and feeding efficiency, nor was any particular distinction in appearance identified. The length of the small intestines and colon plus rectum tended to decline in AIW groups. PH value of cecal contents was higher and the amount of fecal free-glucose tended to be lower in AIW groups than the control group. Since there was no difference in fecal discharge itself, the amount of free-glucose discharged per day was at a low level. The amount of discharged free-glucose in feces is greater when intestinal fermentation is more intensive, which indicates that intestinal fermentation is more inhibited in AIW groups than the control group. Ammonium concentration in cecal contents tends to drop down in AIW groups (Fig. 1). This trend was most distinctive in case of fresh feces of one of AIW groups with pH 10 (Fig.2) AIW uptake was found to be inhibitory against ammonium production. In order to study dynamics of amino acids in large intestines, we examined free amino acids in the cecal contents to find out that cysteine level is low in AIW groups whereas isoleucine level is high in one of AIW groups with pH 10, although no significant difference was identified for other amino acids.

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Effects of alkaline ionized water on formation

& maintenance of osseous tissues

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Effects of calcium alkaline ionized water on formation and maintenance of osseous tissues in rats were examined. In the absence of calcium in the diet, no apparent calcification was observed with only osteoid formation being prominent. Striking differences were found among groups that were given diets with 30% and 60% calcium. Rats raised by calcium ionized water showed the least osteogenetic disturbance. Tibiae and humeri are more susceptible to calcium deficiency than femora. These results may indicate that calcium in drinking water effectively supplements osteogenesis in case of dietary calcium deficiency. The mechanism involved in osteoid formation such as absorption rate of calcium from the intestine and effects of calcium alkaline ionized drinking water on maintaining bone structure in the process of aging or under the condition of calcium deficiency is investigated.

Osteoporosis that has lately drawn public attention is defined as "conditions of bone brittleness caused by reduction in the amount of bone frames and deterioration of osseous microstructure." Abnormal calcium metabolism has been considered to be one of the factors to contribute to this problem, which in turn is caused by insufficient calcium take in, reduction in enteral absorption rate of calcium and increase in the amount of calcium in urinal discharge. Under normal conditions, bones absorb old bones by regular metabolism through osteoid formation to maintain their strength and function as supporting structure. It is getting clear that remodeling of bones at the tissue level goes through the process of activation, resorption, reversal, matrix synthesis and mineralization. Another important function of bones is storing minerals especially by coordinating with intestines and kidneys to control calcium concentration in the blood. When something happens to this osteo metabolism, it results in abnormal morphological changes. Our analyses have been focusing mostly on the changes in the amount of bones to examine effects of calcium alkaline ionized water on the reaction system of osteo metabolism and its efficiency. Ibis time, however, we studied it further from the standpoint of histology. In other words, we conducted comparative studies on morphological and kinetic changes of osteogenesis by testing alkaline ionized water, tap water and solution of lactate on rats.

Three week old male Wistar rats were divided into 12 groups by conditions of feed and drinking water. Feeds were prepared with 0%, 30%, 60% and 100% of normal amount of calcium and were given freely. Three types of drinking water, tap water (city water, about 6ppm of Ca), calcium lactate solution (Ca=40ppm) and alkaline ionized water (Ca =40ppm, pH=9, produced by an electrolyzer NDX 4 LMC by Omco OMC Co., Ltd.) were also given keely. Rats' weight, amount of drinking water and feed as well as the content of Ca in drinking water were assayed every day. On the 19th and 25th days of testing, tetracycline hydrochloride was added to the feed for 48 hours so as to bring its concentration to 30mg/kg. On the 30th day, blood samples were taken under Nembutal anesthesia, and tibiae, humeri and femora were taken out to make non decalcified samples. Their conditions of osteoid formation and rotation were observed using Villanueva bone stain and Villanueva goldner stain.

Three groups that were given different types of drinking water and the same amount of Ca in the feed were compared to find out no significant difference in the rate of weight gain and intakes of feed and drinking water. Alkaline ionized water group had significantly greater amount of tibiae and humeri with higher concentration of calcium in the bones.

The group of 0% calcium in the feed saw drastic increase in the amount of osteoid. There was not much difference by types of drinking water. Almost no tetracycline was taken into tibiae and humeri, although a small amount was identified in femora. As a result, osteogenesis went as far as osteoid formation, but it was likely that decalcification has not happened yet, or most of newly formed bones were absorbed.

As to the groups of 30% and 60% calcium in the feed, increase in the area of tetracycline take in was more identifiable with higher clarity in descending order of alkaline ionized water, calcium lactate solution and tap water groups. Especially in case of tap water group, irregularity among the areas of tetracycline take in was distinctive. The group of 100% calcium in the feed saw some improvements in osteogenesis in descending order of alkaline ionized water, calcium lactate solution and tap water. In any case, bone formation seemed to be in good condition at near normal level.

Alkaline ionized water was regarded to be effective for improvements of osteogenesis under the conditions of insufficient calcium in the feed. Also, the extent. of dysosteogenesis differed by the region. That is, tibiae and humeri tend to have more significant dysosteogenesis than femora.

In addition, there is a possibility that osteo metabolism varies depending on enteral absorption rate of calcium, adjustment of discharge from kidneys and functional adjustment of accessory thyroid in the presence of alkaline ionized water. We are now studying its impact on calcium concentration in the blood. We are also examining whether it is possible to deter bone deterioration by testing on fast aging mouse models.

Magnesium and calcium in drinking water and cardiovascular mortality

Excerpt from:

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Data on the hardness of drinking water were collected from 27 municipalities in Sweden where the drinking water quality had remained unchanged for more than 20 years. Analyses were made of the levels of lead, cadmium, calcium, and magnesium. These water-quality data were compared with the age-adjusted mortality rate from ischemic heart and cerebrovascular disease for the period 1969-1978. Lead and cadmium were not present in detectable amounts except in one water sample. A statistically significant inverse relationship was present between hardness and mortality from cardiovascular disease for both sexes. Mortality caused by ischemic heart disease was inversely related to the magnesium content, particularly for the men ($P < 0.01$). The rather small set of data supports results from previous studies suggesting that a high magnesium level in drinking water reduces the risk for death from ischemic heart disease, especially among men, although the possible importance of confounding factors needs further evaluation.

Key terms: cerebrovascular disease, ischemic heart disease, magnesium, water hardness.

Several epidemiologic investigations performed during recent decades have demonstrated an inverse relationship between water hardness and death from cardiovascular disease. The first observation was made in 1957 (1) and was subsequently elaborated upon in investigations in many other countries (2-4). A particularly relevant study was reported by Crawford et al (5), who followed the mortality rate in 11 English cities where the water hardness had changed between 1950 and 1960. Hardness had increased in five cities and decreased in six. Mortality from cardiovascular disease increased about 10% in the general population during the period of study. In the cities where hardness had decreased, mortality had increased by 20%....

Evaluation of ionized calcium as a nutrient

Chen H, Kimura M, Zhu Z, Itokawa Y, The 11th symposium on Trace Nutrients Research, Japan Trace Nutrients Research Society, p131-138, 1994.

Summary: To clarify effect of ionized calcium water for drinking water in rats, 36 Male Wister rats weighing about 50g were randomly divided into 6 groups, and given following diet and drinking water : (1) Ca-sufficient diet, tap-water; (2) Ca-sufficient diet, tap-water;(3) Ca-sufficient diet, calcium lactate added-ionized calcium-water : (4) Ca-deficient diet, calcium lactate added-water ; (5) Ca deficient diet, calcium lactate added-water :(6) Ca-deficient diet, calcium lactate added ionized calcium-water. The diets were given by paired-feeding method 4 weeks and drinking water was ad libitum. The significant change of calcium concentration in the rats were as follows; Ca concentration of plasma, spleen, of plasma, spleen, kidney, testis and tibia in Ca deficient groups (4), (5), (6) were significantly low compared with these in Ca sufficient groups (1),(2),(3) Ca concentration in brain of groups (4),(5),(6) was low compared to these in groups (2), Ca concentration in heart and muscle of group (4) was low compared to Ca deficient groups (1),(2),(3), but these in group (5) drank Ca added-water was recovered and these in group (6) drank ionized-Ca-water was higher than these in any other groups. Ca concentration of liver in groups (4) were significantly lower than that in group (1),(3) and Ca concentration of liver in Ca deficient rats (groups (5),(6)) drank Ca-added-water were high compared to these in group (4). In 24 hours urine discharge of group (2) was high compared with groups (4), (5), (6). These results suggest that ionized Ca in drinking water may be active for intestinal absorption.

Calcium and magnesium in drinking water
and risk of death from cerebrovascular disease.

MEDLINE ABSTRACT

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BACKGROUND AND PURPOSE: Many studies have demonstrated a negative association between mortality from cardiovascular or cerebrovascular diseases and water hardness. This report examines whether calcium and magnesium in drinking water are protective against cerebrovascular disease.

METHODS: All eligible cerebrovascular deaths (17133 cases) of Taiwan residents from 1989 through 1993 were compared with deaths from other causes (17133 controls), and the levels of calcium and magnesium in drinking water of these residents were determined. Data on calcium and magnesium levels in drinking water throughout Taiwan were obtained from the Taiwan Water Supply Corporation. The control group consisted of people who died from other causes, and the controls were pair matched to the cases by sex, year of birth, and year of death.

RESULTS: The adjusted odds ratios (95% confidence interval) were 0.75 (0.65 to 0.85) for the group with water magnesium levels between 7.4 and 13.4 mg/L and 0.60 (0.52 to 0.70) for the group with magnesium levels of 13.5 mg/L or more. After adjustment for magnesium levels in drinking water, there was no difference between the groups with different levels of calcium.

CONCLUSIONS: The results of the present study show that there is a significant protective effect of magnesium intake from drinking water on the risk of cerebrovascular disease. This is an important finding for the Taiwan water industry and human health.

Reduced hemodialysis-induced oxidative stress in end-stage renal disease patients by electrolyzed reduced water

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KIDNEY INTERNATIONAL.

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BACKGROUND: Increased oxidative stress in end-stage renal disease (ESRD) patients may oxidize macromolecules and consequently lead to cardiovascular events during chronic hemodialysis. Electrolyzed reduced water (ERW) with reactive oxygen species (ROS) scavenging ability may have a potential effect on reduction of hemodialysis-induced oxidative stress in ESRD patients. **METHODS:** We developed a chemiluminescence emission spectrum and high-performance liquid chromatography analysis to assess the effect of ERW replacement on plasma ROS (H₂O₂ and HOCl) scavenging activity and oxidized lipid or protein production in ESRD patients undergoing hemodialysis. Oxidized markers, dityrosine, methylguanidine, and phosphatidylcholine hydroperoxide, and inflammatory markers, interleukin 6 (IL-6), and C-reactive protein (CRP) were determined. **RESULTS:** Although hemodialysis efficiently removes dityrosine and creatinine, hemodialysis increased oxidative stress, including phosphatidylcholine hydroperoxide, and methylguanidine. Hemodialysis reduced the plasma ROS scavenging activity, as shown by the augmented reference H₂O₂ and HOCl counts (Rh₂O₂ and Rhocl, respectively) and decreased antioxidative activity (expressed as total antioxidant status in this study). ERW administration diminished hemodialysis-enhanced Rh₂O₂ and Rhocl, minimized oxidized and inflammatory markers (CRP and IL-6), and partly restored total antioxidant status during 1-month treatment. **CONCLUSION:** This study demonstrates that hemodialysis with ERW administration may efficiently increase the H₂O₂- and HOCl-dependent antioxidant defense and reduce H₂O₂- and HOCl-induced oxidative stress.