Enhanced induction of mitochondrial damage and apoptosis in human leukemia HL-60 cells due to electrolyzed-reduced water and glutathione.

Tsai CF, Hsu YW, Chen WK, Ho YC, Lu FJ.

Abstract

Electrolyzed-reduced water (ERW) is a higher pH and lower oxidation-reduction potential water. In the present study, we examined the enhanced effect of ERW in the apoptosis of leukemia cells (HL-60) induced by glutathione (GSH). An enhanced inhibitory effect on the viability of the HL-60 cells was observed after treatment with a combination of ERW with various concentrations of GSH, whereas no cytotoxic effect in normal peripheral blood mononuclear cells was observed. The results of apoptotic related protein indicated that the induction of HL-60 cell death was caused by the induction of apoptosis through upregulation of Bax and downregulation of Bcl-2. The results of further investigation showed a diminution of intracellular GSH levels in ERW, and combination with GSH groups. These results suggest that ERW is an antioxidant, and that ERW, in combination with GSH, has an enhanced apoptosis-inducing effect on HL-60 cells, which might be mediated through the mitochondria-dependent pathway.

PMID: 19202298 [PubMed - indexed for MEDLINE]

Inhibitory effect of electrolyzed reduced water on tumor angiogenesis.
Ye J¹, Li Y, Hamasaki T, Nakamichi N, Komatsu T, Kashiwagi T, Teruya K

Abstract
Vascular endothelial growth factor (VEGF) is a key mediator of tumor angiogenesis. Tumor cells are exposed to higher oxidative stress compared to normal cells. Numerous reports have demonstrated that the intracellular redox (oxidation/reduction) state is closely associated with the pattern of VEGF expression. Electrolyzed reduced water (ERW) produced near the cathode during the electrolysis of water scavenged intracellular H(2)O(2) and decreased the release of H(2)O(2) from a human lung adenocarcinoma cell line, A549, and down-regulated both VEGF transcription and protein secretion in a time-dependent manner. To investigate the signal transduction pathway involved in regulating VEGF expression, mitogen-activated kinase (MAPK) specific inhibitors, SB203580 (p38 MAPK inhibitor), PD98059 (ERK1/2 inhibitor) and JNKi (c-Jun N-terminal protein kinase inhibitor) were applied. The results showed that only PD98059 blocks VEGF expression, suggesting an important role for ERK1/2 in regulating VEGF expression in A549 cells. As well, ERW inhibited the activation of extracellular signal-regulated kinase (ERK) in a time-dependent manner. Co-culture experiments to analyze in vitro tubule formation assay revealed that A549 cell-derived conditioned medium significantly stimulated the formation of vascular tubules in all analyzed parameters; tubule total area, tubule junction, number of tubules, and total tubule length. ERW counteracted the effect of A549 cell-conditioned medium and decreased total tube length (p<0.01). The present study demonstrated that ERW down-regulated VEGF gene transcription and protein secretion through inactivation of ERK.

PMID: 18175936 [PubMed - indexed for MEDLINE]
Effects of drinking hydrogen-rich water on the quality of life of patients treated with radiotherapy for liver tumors
Ki-Mun Kang Young-Nam Kang

Cancer patients receiving radiotherapy often experience fatigue and impaired quality of life (QOL). Many side effects of radiotherapy are believed to be associated with increased oxidative stress and inflammation due to the generation of reactive oxygen species during radiotherapy. Hydrogen can be administered as a therapeutic medical gas, has antioxidant properties, and reduces inflammation in tissues. This study examined whether hydrogen treatment, in the form of hydrogen-supplemented water, improved QOL in patients receiving radiotherapy.

Methods
A randomized, placebo-controlled study was performed to evaluate the effects of drinking hydrogen-rich water on 49 patients receiving radiotherapy for malignant liver tumors.

Results: The consumption of hydrogen-rich water for 6 weeks reduced reactive oxygen metabolites in the blood and maintained blood oxidation potential. QOL scores during radiotherapy were significantly improved in patients treated with hydrogen-rich water compared to patients receiving placebo water. There was no difference in tumor response to radiotherapy between the two groups.

Conclusions
Daily consumption of hydrogen-rich water is a potentially novel, therapeutic strategy for improving QOL after radiation exposure. Consumption of hydrogen-rich water reduces the biological reaction to radiation-induced oxidative stress without compromising anti-tumor effects.
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<th>Authors/Year</th>
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<td>Song et al. 2015</td>
<td>Hyperlipidemia</td>
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Supplementation of hydrogen-rich water improves lipid and glucose metabolism in patients with type 2 diabetes or impaired glucose tolerance.

- Oxidative stress is recognized widely as being associated with various disorders including diabetes, hypertension, and atherosclerosis. It is well established that hydrogen has a reducing action. We therefore investigated the effects of hydrogen-rich water intake on lipid and glucose metabolism in patients with either type 2 diabetes mellitus (T2DM) or impaired glucose tolerance (IGT).

- We performed a randomized, double-blind, placebo-controlled, crossover study in 30 patients with T2DM controlled by diet and exercise therapy and 6 patients with IGT. The patients consumed either 900 mL/d of hydrogen-rich pure water or 900 mL of placebo pure water for 8 weeks, with a 12-week washout period. Several biomarkers of oxidative stress, insulin resistance, and glucose metabolism, assessed by an oral glucose tolerance test, were evaluated at baseline and at 8 weeks.

- Intake of hydrogen-rich water was associated with significant decreases in the levels of modified low-density lipoprotein (LDL) cholesterol (ie, modifications that increase the net negative charge of LDL), small dense LDL, and urinary 8-isoprostanes by 15.5% (P < .01), 5.7% (P < .05), and 6.6% (P < .05), respectively. Hydrogen-rich water intake was also associated with a trend of decreased serum concentrations of oxidized LDL and free fatty acids, and increased plasma levels of adiponectin and extracellular-superoxide dismutase.

- In 4 of 6 patients with IGT, intake of hydrogen-rich water normalized the oral glucose tolerance test. In conclusion, these results suggest that supplementation with hydrogen-rich water may have a beneficial role in prevention of T2DM and insulin resistance.


Pubmed
Pilot study of H$_2$ therapy in Parkinson's disease: a randomized double-blind placebo-controlled trial.

Oxidative stress is involved in the progression of Parkinson's disease (PD). Recent studies have confirmed that molecular hydrogen (H$_2$) functions as a highly effective antioxidant in cultured cells and animal models. Drinking H$_2$-dissolved water (H$_2$-water) reduced oxidative stress and improved Parkinson's features in model animals.

METHODS:
In this a placebo-controlled, randomized, double-blind, parallel-group clinical pilot study, the authors assessed the efficacy of H$_2$-water in Japanese patients with levodopa-medicated PD. Participants drank 1,000 mL/day of H$_2$-water or pseudo water for 48 weeks.

RESULTS:
Total Unified Parkinson's Disease Rating Scale (UPDRS) scores in the H$_2$-water group (n=9) improved (median, -1.0; mean ± standard deviation, -5.7 ± 8.4), whereas UPDRS scores in the placebo group (n=8) worsened (median, 4.5; mean ± standard deviation, 4.1 ± 9.2). Despite the minimal number of patients and the short duration of the trial, the difference was significant (P<0.05).

CONCLUSIONS:
The results indicated that drinking H$_2$-water was safe and well tolerated, and a significant improvement in total UPDRS scores for patients in the H$_2$-water group was demonstrated.
Electrolyzed-reduced water reduced hemodialysis-induced erythrocyte impairment in end-stage renal disease patients
KC Huang, CC Yang, SP Hsu, KT Lee, HW Liu… - Kidney …, 2006 - nature.com
Abstract Chronic hemodialysis (HD) patients increase erythrocyte susceptibility to hemolysis and impair cell survival. We explored whether electrolyte-reduced water (ERW) could palliate HD-evoked erythrocyte impairment and anemia. Forty-three patients undergoing...

Preservative Effect of Electrolyzed Reduced Water on Pancreatic. BETA.-Cell Mass in Diabetic db/db Mice
MJ Kim, KH Jung, YK Uhm, KH Leem… - Biological and …, 2007 - jlc.jst.go.jp
Oxidative stress is produced under diabetic conditions and involved in progression of pancreatic β-cell dysfunction. Both an increase in reactive oxygen free radical species (ROS) and a decrease in the antioxidant defense mechanism lead to the increase in...

Electrolyzed and natural reduced water exhibit insulin-like activity on glucose uptake into muscle cells and adipocytes
Abstract In the type 2 diabetes, it has become clear that reactive oxygen species (ROS) cause reduction of glucose uptake by inhibiting the insulin-signaling pathway in muscle cells and adipocytes. We demonstrated that electrolyzed-reduced water (ERW) scavenges ...
Protective mechanism of ERW against alloxan-induced pancreatic β-cell damage: Scavenging effect against reactive oxygen species

Y Li, T Nishimura, K Teruya, T Maki, T Komatsu... - Cytotechnology, 2002 - Springer

Electrolyzed-reduced water (ERW) was prepared by the electrolysis of ultra pure water containing 0.002 N NaOH... The electrolyzing device used was a batch type one and consisted of a vessel. It is reduced extracellularly to dialuric acid in the presence of a reducing agent...

Efficacy of neutral EW for reducing microbial contamination on minimally-processed vegetables

M Abadias, J Usall, M Oliveira, I Alegre... - International Journal of ..., 2008 - Elsevier

Consumption of minimally-processed, or fresh-cut, fruit and vegetables has rapidly increased in recent years, but there have also been several reported outbreaks associated with the consumption of these products. Sodium hypochlorite is currently the most...

Protective effect of ERW on the paraquat-induced oxidative damage of human lymphocyte DNA

EJ Park, KK Ryoo, YB Lee, JK Lee... - Journal of the Korean ..., 2005 - agris.fao.org

Electrolyzed reduced water (ERW), showing extremely negative oxidation-reduction potential, was used to investigate the effects of paraquat-induced damages on DNA from human lymphocyte. The effect of ERW on paraquat-induced oxidative DNA damage in...
and more

Enhanced induction of *mitochondrial damage and apoptosis in human leukemia* HL-60 cells due to *electrolyzed-reduced water* and glutathione

CF Tsai, YW Hsu, WK Chen, YC Ho… - Bioscience, …, 2009 - Taylor & Francis

Electrolyzed-reduced water (ERW) is a higher pH and lower oxidation-reduction potential water. In the present study, we examined the enhanced effect of ERW in the apoptosis of leukemia cells (HL-60) induced by glutathione (GSH). An enhanced inhibitory effect on the ...

**Telomere shortening in cancer cells** by *electrolyzed-reduced water*

S Shirahata, E Murakami, K Kusumoto… - Animal cell technology: …, 2002 - Springer

Abstract Electroly-reduced water (ERW) which is produced near cathode during electrolysis of water scavenges reactive oxygen species and protects DNA from oxidative damage (Shirahata et al., 1997). Most of cancer cells exhibit high telomerase activity to elongate ...

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

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 …