

# Onderzoek naar anti carcinogene eigenschappen

Biosci Biotechnol Biochem.2009 Feb;73(2):280-7. Epub 2009 Feb 7.

**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](#).

## Author information

### 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]

Biol Pharm Bull 2008 Jan;31(1):19-26.

**Inhibitory effect of electrolyzed reduced water on tumor angiogenesis.**

Ye J<sup>1</sup>, 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<sub>2</sub>O<sub>2</sub> and decreased the release of H<sub>2</sub>O<sub>2</sub> 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]

# QoL during Radiation therapy

Med Gas Res. 2011; 1: 11. Published online 2011 Jun [71-11](#)

## **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.**

# Pub Med Clinical trials

Authors/ Year	Disease	Sample size	OL, DB, SB	Hydrogen administration	Summary of the outcome
Kajiyama et al. 2008	Diabetes mellitus type II	30	DB	Water	Improvement of fractions of low-density lipoprotein (LDL)-cholesterol and a glucose tolerance test.
Nakao et al. 2010	Metabolic syndrome	20	OL	Water	Improvement of urinary markers for oxidative stress such as SOD and TBARS, and increase of high-density lipoprotein (HDL)-cholesterol.
Nakayama et al. 2010	Chronic renal failure	29	OL	Dialysis	Amelioration of hypertension and improvement of markers for oxidative stress and inflammation.
Ito et al. /2011	Inflammatory and mitochondrial myopathies	31	OL/DB	Water	OL: Improvement of the serum lactate/pyruvate ratio in mitochondrial myopathies and the serum matrix metalloproteinase-3 level in polymyositis/dermatomyositis.  DB: Improvement of the serum lactate.
Kang et al. / 2011	Radiation-induced adverse effects for liver tumors	49	OL	Water	Improvement of quality of life (QOL) scores during radiotherapy. Reduction of blood reactive oxygen metabolites and maintenance of blood oxidation potential.
Ishibashi et al/2012	Rheumatoid arthritis	20	OL	Water	Improvement of disease activity score for rheumatoid arthritis (DAS28). Decrease of urinary 8-OHdG.
Aoki et al. / 2012	Muscle fatigue	10	DB	Water	Improvement of muscle fatigue in young athletes
Li et al. / 2013	Pressure skin ulcer	22	OL	Water	Wound size reduction and early recovery from skin pressure ulcer.

Matsumoto et al. /2013	<b>Interstitial cystitis</b>	30	DB	Water	<small>No significant effect on symptoms.</small> Reduction of the bladder pain score in 11 % of patients.
Nagatani et al. /2013	<b>Cerebral ischemia</b>	38	OL	Intravenous infusion	Confirmation of safety of intravenous H <sub>2</sub> infusion. Decrease of MDA-LDL, a serum marker for oxidative stress, in a subset of patients.
Shin et al. 2013	<b>UV-induced skin injury</b>	28	OL	Gas	Prevention and modulation of UV-induced skin inflammation, intrinsic skin aging, and photo aging process through reduction of MMP-1, IL-6, and IL-1b mRNA expression.
Song et al. 2013	<b>Hyperlipidemia</b>	20	OL	Water	Decrease of total serum cholesterol, LDL-cholesterol, apolipoprotein (apo) B100, and apoE
Xia et al. 2013	<b>Chronic hepatitis B</b>	60	DB	Water	Attenuation of oxidative stress
Yoritaka et al. 2013	<b>Parkinson disease</b>	17	DB	Water	Improvement of Total Unified Parkinson's Disease Rating Scale (UPDRS) and exacerbation after termination of H <sub>2</sub> water.
Ishibashi et al. 2014	<b>Rheumatoid arthritis</b>	24	DB	Intravenous saline infusion	Improvement of DAS28. Decrease of serum IL-6, MMP3, CRP, and urinary 8-OHdG.
Ostojic et al. /2014	<b>Sports-related soft tissue injury</b>	36	SB	H <sub>2</sub> -rich tablets and topical H <sub>2</sub> packs	Decrease of plasma viscosity. Faster recovery from soft tissue injury.
Ostojic et al. /2014	<b>Exercise-induced metabolic acidosis</b>	52	DB	Water	Increased blood alkalinity in physically active men.
Sakai et al. /2014	<b>Vascular endothelial function.</b>	34	DB	Water	Increased flow-mediated dilation of brachial artery, suggesting that H <sub>2</sub> can serve as a modulator of vasomotor function of vasculature.
Song et al. 2015	<b>Hyperlipidemia</b>	68	DB	Water	Down-regulation of plasma levels of total cholesterol, and LDL-cholesterol, followed by increased plasma pre-β -HDL, apoM, and decreased plasma oxidized-LDL, apoB100.

## **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.** [Nutr Res.](#) 2008 Mar;28(3):137-43. doi: 10.1016/j.nutres.2008.01.008.
- **Pubmed**

# Pilot study of H<sub>2</sub> 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<sub>2</sub>) functions as a highly effective antioxidant in cultured cells and animal models. **Drinking H<sub>2</sub>-dissolved water (H<sub>2</sub>-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<sub>2</sub> -water in Japanese patients with levodopa-medicated PD. Participants drank **1,000 mL/day of H<sub>2</sub>-water or pseudo water for 48 weeks.**

## **RESULTS:**

Total Unified Parkinson's Disease Rating Scale (**UPDRS**) **scores in the H<sub>2</sub>-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<sub>2</sub>-water was safe and well tolerated, and a significant improvement in total UPDRS scores for patients in the H<sub>2</sub>-water group was demonstrated.*

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# And more...

## **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  $\beta$ -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**

M Oda, K Kusumoto, K Teruya, T Hara, T Maki... - Animal cell technology: ..., 1999 - Springer

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 ...

# and more...

Protective mechanism of **ERW** against alloxan-induced **pancreatic  $\beta$ -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 ...