# MOLECULAR HYDROGEN IS A NOVEL ANTIOXIDANT TO EFFICIENTLY REDUCE OXIDATIVE STRESS WITH POTENTIAL FOR THE IMPROVEMENT OF MITOCHONDRIAL DISEASES

Biochim Biophys Acta. 2012 May;1820(5):586-94. doi: 10.1016/j.bbagen.2011.05.006. Epub 2011 May 20. Ohta S.

### Source

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### Abstract

BACKGROUND: Mitochondria are the major source of oxidative stress. Acute oxidative stress causes serious damage to tissues, and persistent oxidative stress is one of the causes of many common diseases, cancer and the aging process; however, there has been little success in developing an effective antioxidant with no side effect. We have reported that molecular hydrogen has potential as an effective antioxidant for medical applications [Ohsawa et al., Nat. Med. 13 (2007) 688-694].

SCOPE OF REVIEW: We review the recent progress toward therapeutic and preventive applications of hydrogen. Since we published the first paper in Nature Medicine, effects of hydrogen have been reported in more than 38 diseases, physiological states and clinical tests in leading biological/medical journals. Based on this cumulative knowledge, the beneficial biological effects of hydrogen have been confirmed. There are several ways to intake or consume hydrogen, including inhaling hydrogen gas, drinking hydrogen-dissolved water, taking a hydrogen bath, injecting hydrogen-dissolved saline, dropping hydrogen-dissolved saline into the eyes, and increasing the production of intestinal hydrogen by bacteria. Hydrogen has many advantages for therapeutic and preventive applications, and shows not only anti-oxidative stress effects, but also has various anti-inflammatory and anti-allergic effects. Preliminary clinical trials show that drinking hydrogen-dissolved water seems to improve the pathology of mitochondrial disorders.

GENERAL SIGNIFICANCE: Hydrogen is a novel antioxidant with great potential for actual medical applications. This article is part of a Special Issue entitled Biochemistry of Mitochondria.

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### HYDROGEN IN DRINKING WATER REDUCES DOPAMINERGIC NEURONAL LOSS IN THE 1-METHYL-4-PHENYL-1,2,3,6-TETRAHYDROPYRIDINE MOUSE MODEL OF PARKINSON'S DISEASE

PLoS One. 2009 Sep 30;4(9):e7247. doi: 10.1371/journal.pone.0007247. Fujita K, Seike T, Yutsudo N, Ohno M, Yamada H, Yamaguchi H, Sakumi K, Yamakawa Y, Kido MA, Takaki A, Katafuchi T, Tanaka Y, Nakabeppu Y, Noda M.

#### Source

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### Abstract

It has been shown that molecular hydrogen (H(2)) acts as a therapeutic antioxidant and suppresses brain injury by buffering the effects of oxidative stress. Chronic oxidative stress causes neurodegenerative diseases such as Parkinson's disease (PD). Here, we show that drinking H(2)-containing water significantly reduced the loss of dopaminergic neurons in PD model mice using both acute and chronic administration of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). The concentration-dependency of H(2) showed that H(2) as low as 0.08 ppm had almost the same effect as saturated H(2) water (1.5 ppm). MPTP-induced accumulation of cellular 8-oxoguanine (8-oxoG), a marker of DNA damage, and 4-hydroxynonenal (4-HNE), a marker of lipid peroxidation were significantly decreased in the nigro-striatal dopaminergic pathway in mice drinking H(2)-containing water, whereas production of superoxide (O(2)\*(-)) detected by intravascular injection of dihydroethidium (DHE) was not reduced significantly. Our results indicated that low concentration of H(2) in drinking water can reduce oxidative stress in the brain. Thus, drinking H(2)-containing water may be useful in daily life to prevent or minimize the risk of life style-related oxidative stress and neurodegeneration.

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# PILOT STUDY: EFFECTS OF DRINKING HYDROGEN-RICH WATER ON MUSCLE FATIGUE CAUSED BY ACUTE EXERCISE IN ELITE ATHLETES

Med Gas Res. 2012; 2: 12. Published online Jul 12, 2012. doi: 10.1186/2045-9912-2-12 Kosuke Aoki, Atsunori Nakao, corresponding author Takako Adachi, Yasushi Matsui, and Shumpei Miyakawa

Source

Medical Gas Research

#### **Abstract**

BACKGROUND: Muscle contraction during short intervals of intense exercise causes oxidative stress, which can play a role in the development of overtraining symptoms, including increased fatigue, resulting in muscle microinjury or inflammation. Recently it has been said that hydrogen can function as antioxidant, so we investigated the effect of hydrogen-rich water (HW) on oxidative stress and muscle fatigue in response to acute exercise.

METHODS: Ten male soccer players aged  $20.9\pm1.3$ years old were subjected to exercise tests and blood sampling. Each subject was examined twice in a crossover double-blind manner; they were given either HW or placebo water (PW) for one week intervals. Subjects were requested to use a cycle ergometer at a 75% maximal oxygen uptake (VO2) for 30min, followed by measurement of peak torque and muscle activity throughout 100 repetitions of maximal isokinetic knee extension. Oxidative stress markers and creatine kinase in the peripheral blood were sequentially measured.

RESULTS: Although acute exercise resulted in an increase in blood lactate levels in the subjects given PW, oral intake of HW prevented an elevation of blood lactate during heavy exercise. Peak torque of PW significantly decreased during maximal isokinetic knee extension, suggesting muscle fatigue, but peak torque of HW didn't decrease at early phase. There was no significant change in blood oxidative injury markers (d-ROMs and BAP) or creatine kinease after exercise.

CONCLUSION: Adequate hydration with hydrogen-rich water pre-exercise reduced blood lactate levels and improved exercise-induced decline of muscle function. Although further studies to elucidate the exact mechanisms and the benefits are needed to be confirmed in larger series of studies, these preliminary results may suggest that HW may be suitable hydration for athletes.

### INTRODUCTION

Since energy demands and oxygen consumption increase during supermaximal exercise, such as intermittent running, sprints, and jumps, production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) also increase, threatening to disturb redox balance and cause oxidative stress. During normal conditions, ROS and RNS are generated at a low rate and subsequently eliminated by the antioxidant systems. However, a greatly increased rate of ROS production may exceed the capacity of the cellular defense system. Consequently, substantial free radicals' attack on cell membranes may lead to a loss of cell

viability and to cell necrosis and could initiate the skeletal muscle damage and inflammation caused by exhaustive exercise. Although well-trained athletes suffer from less oxidative stress reduction because their antioxidant systems adapt, accumulation of intense exercise can provoke an increase in oxidative stress. To mitigate oxidative stress-induced adverse events during sports, antioxidant supplementation among athletes has been well documented. Although results of these studies are often contradictory depending on the antioxidant compounds and quantity, some studies demonstrate the beneficial effects of antioxidants on muscle fatigue or performance.

Recently, the beneficial effects of hydrogen-rich water (HW) have been described in experimental and clinical disease conditions. Although research on the health benefits of HW is limited and there is scant data on long-term effects, pilot studies on humans suggest that consuming HW may help prevent metabolic syndrome, diabetes mellitus, and cancer patients' side effects with radiotherapy. Since hydrogen is known to scavenge toxic ROS and induce a number of antioxidant proteins, we hypothesized that drinking HW may be beneficial for athletes in reducing oxidative stress-induced muscle fatigue following acute exercise. In this study, we evaluated the efficacy of hydrogen-rich water on healthy subjects by measuring muscle fatigue and blood lactate levels after exercise. Although further studies are needed to elucidate the exact mechanisms and benefits, this report suggests that hydrogen-rich water might be an appropriate hydration fluid for athletes.

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### MOLECULAR HYDROGEN IN DRINKING WATER PROTECTS AGAINST NEURODEGENERATIVE CHANGES INDUCED BY TRAUMATIC BRAIN INJURY

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Kim M. Hansen, Gul N. Shah, Nader Sheibani, Therese Salameh, William A. Banks.

### Source

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### Abstract

Traumatic brain injury (TBI) in its various forms has emerged as a major problem for modern society. Acute TBI can transform into a chronic condition and be a risk factor for neurodegenerative diseases such as Alzheimer's and Parkinson's diseases, probably through induction of oxidative stress and neuroinflammation. Here, we examined the ability of the antioxidant molecular hydrogen given in drinking water (molecular hydrogen water; mHW) to alter the acute changes induced by controlled cortical impact (CCI), a commonly used experimental model of TBI. We found that mHW reversed CCI-induced edema by about half, completely blocked pathological tau expression, accentuated an early increase seen in several cytokines but attenuated that increase by day 7, reversed changes seen in the protein levels of aquaporin-4, HIF-1, MMP-2, and MMP-9, but not for amyloid beta peptide 1-40 or 1–42. Treatment with mHW also reversed the increase seen 4 h after CCI in gene expression related to oxidation/carbohydrate metabolism, cytokine release, leukocyte or cell migration, cytokine transport, ATP and nucleotide binding. Finally, we found that mHW preserved or increased ATP levels and propose a new mechanism for mHW, that of ATP production through the Jagendorf reaction. These results show that molecular hydrogen given in drinking water reverses many of the sequelae of CCI and suggests that it could be an easily administered, highly effective treatment for TBI.

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# MOLECULAR HYDROGEN AS AN EMERGING THERAPEUTIC MEDICAL GAS FOR NEURODEGENERATIVE AND OTHER DISEASES

Kinji Ohno(1), Mikako Ito(1), Masatoshi Ichihara(2), and Masafumi Ito(3)

#### Source

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### **Abstract**

Effects of molecular hydrogen on various diseases have been documented for 63 disease models and human diseases in the past four and a half years. Most studies have been performed on rodents including two models of Parkinson's disease and three models of Alzheimer's disease.

Effects of Molecular Hydrogen on Rodent Models of Neurodegenerative Diseases.

Parkinson's disease is caused by death of dopaminergic neurons at the substantia nigra pars compact of the midbrain and is the second most common neurodegenerative disease after Alzheimer's disease.

Alzheimer's disease is the most common neurodegenerative disease and is characterized by abnormal aggregation of \$\beta\$-amyloid (A\$\beta\$) and tau, the large aggregates of which are recognizable as senile plaques and neurofibrillary tangles, respectively. Effects of molecular hydrogen on Alzheimer's disease have been studied in three rodent models. First, Nagata and colleagues made a mouse model of dementia by restricting movement of mice for 10 hrs a day. They analyzed cognitive functions through passive avoidance learning, object recognition tasks, and the Morris water maze and demonstrated that ad libitum administration of hydrogen-rich water efficiently ameliorated cognitive impairment.

They also showed that neural proliferation in the dentate gyrus was restored by hydrogen. Second, Li and colleagues made a rat model of Alzheimer's disease by intracerebroventricular injection of A\u03b41-42. They analyzed cognitive functions by the Morris water maze open field tasks, and electrophysiological measurement of long-term potentiation (LTP) and found that intraperitoneal injection of hydrogen-rich saline for 14 days efficiently ameliorated cognitive decline and preserved LTP. The same team later reported that the protective effects were mediated by suppression of abnormal activation of IL1\u03b4, JNK, and NF?B. Third, Gu and colleagues used a senescence-accelerated mouse strain (SAMP8) that exhibits early aging syndromes including impairment in learning ability and memory.

Ad libitum administration of hydrogen-rich water for 30 days prevented cognitive decline, which was examined by the Morris water maze. Additionally, ad libitum drinking of hydrogen water for 18 weeks showed efficient amelioration of hippocampal neurodegeneration.

Cerebrovascular diseases are the most frequently reported neurological diseases for which hydrogen has prominent effects. As stated in Section 2, current hydrogen research has broken out after Ohsawa reported a prominent effect of 2–4% hydrogen for a rat model of left cerebral artery occlusion in 2007.

In addition to neurodegenerative disorders of Parkinson's disease and Alzheimer's disease, effects of molecular hydrogen have been reported in eight other brain diseases listed under the categories of "brain" and "perinatal disorders" in Table 1. The brain consumes a large amount of oxygen and is predisposed to be exposed to a large amount of radical oxygen species especially under pathological conditions. Molecular hydrogen is thus likely to exert a prominent beneficial effect on brain diseases.

Oxid Med Cell Longev. 2012; 2012: 353152. Published online 2012 Jun 8. doi: 10.1155/2012/353152 PubMed: National Center for Biotechnology Information (NCBI) is a division of the U.S. National Library of Medicine (NLM) at the National Institutes of Health (NIH).

# DRINKING HYDROGEN WATER AMELIORATED COGNITIVE IMPAIRMENT IN SENESCENCE-ACCELERATED MICE

J Clin Biochem Nutr. 2010 May;46(3):269-76. doi: 10.3164/jcbn.10-19. Epub 2010 Apr 23. Gu Y, Huang CS, Inoue T, Yamashita T, Ishida T, Kang KM, Nakao A.

### Source

Graduate School of Health Science, Suzuka University of Medical Science, Suzuka, Mie 510-0293, Japan.

### Abstract

Hydrogen has been reported to have neuron protective effects due to its antioxidant properties, but the effects of hydrogen on cognitive impairment due to senescence-related brain alterations and the underlying mechanisms have not been characterized. In this study, we investigated the efficacies of drinking hydrogen water for prevention of spatial memory decline and age-related brain alterations using senescence-accelerated prone mouse 8 (SAMP8), which exhibits early aging syndromes including declining learning ability and memory. However, treatment with hydrogen water for 30 days prevented age-related declines in cognitive ability seen in SAMP8 as assessed by a water maze test and was associated with increased brain serotonin levels and elevated serum antioxidant activity. In addition, drinking hydrogen water for 18 weeks inhibited neurodegeneration in hippocampus, while marked loss of neurons was noted in control, aged brains of mice receiving regular water. On the basis of our results, hydrogen water merits further investigation for possible therapeutic/preventative use for age-related cognitive disorders.

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### CONSUMPTION OF MOLECULAR HYDROGEN PREVENTS THE STRESS-INDUCED IMPAIRMENTS IN HIPPOCAMPUS-DEPENDENT LEARNING TASKS DURING CHRONIC PHYSICAL RESTRAINT IN MICE

Neuropsychopharmacology. 2009 Jan;34(2):501-8. doi: 10.1038/npp.2008.95. Epub 2008 Jun 18. Nagata K(1), Nakashima-Kamimura N, Mikami T, Ohsawa I, Ohta S.

### Source

(1)Department of Biochemistry and Cell Biology, Institute of Development and Aging Sciences, Graduate School of Medicine, Nippon Medical School, Nakahara-ku, Kawasaki, Japan.

### Abstract

We have reported that hydrogen (H(2)) acts as an efficient antioxidant by gaseous rapid diffusion. When water saturated with hydrogen (hydrogen water) was placed into the stomach of a rat, hydrogen was detected at several microM level in blood. Because hydrogen gas is unsuitable for continuous consumption, we investigated using mice whether drinking hydrogen water ad libitum, instead of inhaling hydrogen gas, prevents cognitive impairment by reducing oxidative stress. Chronic physical restraint stress to mice enhanced levels of oxidative stress markers, malondialdehyde and 4-hydroxy-2-nonenal, in the brain, and impaired learning and memory, as judged by three different methods: passive avoidance learning, object recognition task, and the Morris water maze. Consumption of hydrogen water ad libitum throughout the whole period suppressed the increase in the oxidative stress markers and prevented cognitive impairment, as judged by all three methods, whereas hydrogen water did not improve cognitive ability when no stress was provided. Neural proliferation in the dentate gyrus of the hippocampus was suppressed by restraint stress, as observed by 5-bromo-2'-deoxyuridine incorporation and Ki-67 immunostaining, proliferation markers. The consumption of hydrogen water ameliorated the reduced proliferation although the mechanistic link between the hydrogen-dependent changes in neurogenesis and cognitive impairments remains unclear. Thus, continuous consumption of hydrogen water reduces oxidative stress in the brain, and prevents the stress-induced decline in learning and memory caused by chronic physical restraint. Hydrogen water may be applicable for preventive use in cognitive or other neuronal disorders.

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# HYDROGEN-RICH WATER ATTENUATES EXPERIMENTAL PERIODONTITIS IN A RAT MODEL

First published: 9 October 2011 - DOI: 10.1111/j.1600-051X.2011.01801.x Kasuyama K, Tomofuji T, Ekuni D, Tamaki N, Azuma T, Irie K, Endo Y, Morita M.

### Source

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This work was supported by Grants-in-Aid for Scientific Research (20791642) from the Ministry of Education, Culture, Sports, Science and Technology, Tokyo, Japan.

### **Abstract**

AIM: Reactive oxygen species (ROS) contribute to the development of periodontitis. As molecular hydrogen can act as a scavenger of ROS, we examined the effects of treatment with hydrogen-rich water on a rat model of periodontitis.

MATERIAL & METHODS: A ligature was placed around the maxillary molars for 4 weeks to induce periodontitis, and the animals were given drinking water with or without hydrogen-rich water.

RESULT: The rats with periodontitis which were treated with pure water showed a time-dependent increase in serum ROS level. Compared with the rats without periodontitis, the periodontitis-induced rats which were given pure water also showed polymorphonuclear leucocyte infiltration and alveolar bone loss at 4 weeks. Hydrogen-rich water intake inhibited an increase in serum ROS level and lowered expression of 8-hydroxydeoxyguanosine and nitrotyrosine in the periodontal tissue at 4 weeks. Such conditions prevented polymorphonuclear leucocyte infiltration and osteoclast differentiation following periodontitis progression. Furthermore, inflammatory signalling pathways, such as mitogen-activated protein kinases, were less activated in periodontal lesions from hydrogen-rich water-treated rats as compared with pure water-treated rats.

CONCLUSION: Consuming hydrogen-rich water might be beneficial in suppressing periodontitis progression by decreasing gingival oxidative stress.

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# INHIBITORY EFFECT OF ELECTROLYZED REDUCED WATER ON TUMOR ANGIOGENESIS

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

Ye J, Li Y, Hamasaki T, Nakamichi N, Komatsu T, Kashiwagi T, Teruya K, Nishikawa R, Kawahara T, Osada K, Toh K, Abe M, Tian H, Kabayama S, Otsubo K, Morisawa S, Katakura Y, Shirahata S.

### Source

Graduate School of Systems Life Sciences, Kyushu University, Higashi-ku, Fukuoka 812-8581, Japan.

#### 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 timedependent 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.

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# HYDROGEN-SUPPLEMENTED DRINKING WATER PROTECTS CARDIAC ALLOGRAFTS FROM INFLAMMATION-ASSOCIATED DETERIORATION

Transpl Int. 2012 Dec;25(12):1213-22. doi: 10.1111/j.1432-2277.2012.01542.x. Epub 2012 Aug 14. Noda K, Tanaka Y, Shigemura N, Kawamura T, Wang Y, Masutani K, Sun X, Toyoda Y, Bermudez CA, Nakao A.

#### Source

Department of Cardiothoracic Surgery, University of Pittsburgh, Pittsburgh, PA, USA.

### Abstract

Recent evidence suggests that molecular hydrogen has therapeutic value for disease states that involve inflammation. We hypothesized that drinking hydrogen-rich water (HW) daily would protect cardiac and aortic allograft recipients from inflammation-associated deterioration. Heterotopic heart transplantation with short-course tacrolimus immunosuppression and orthotopic aortic transplantation were performed in allogeneic rat strains. HW was generated either by bubbling hydrogen gas through tap water (Bu-HW) or via chemical reaction using a magnesium stick [Mg + 2H(2) O ? Mg (OH)(2) + H(2)]immersed in tap water (Mg-HW). Recipients were given either regular water (RW), Mg-HW, Bu-HW, or Mg-HW that had been subsequently degassed (DW). Graft survival was assessed by daily palpation for a heartbeat. Drinking Mg-HW or Bu-HW was remarkably effective in prolonging heart graft survival and reducing intimal hyperplasia in transplanted aortas as compared with grafts treated with RW or DW. Furthermore, T cell proliferation was significantly inhibited in the presence of hydrogen in vitro, accompanied by less production of interleukin-2 and interferon-?. Hydrogen treatment was also associated with increased graft ATP levels and increased activity of the enzymes in mitochondrial respiratory chain. Drinking HW prolongs survival of cardiac allografts and reduces intimal hyperplasia of aortic allografts.

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### PROTECTION OF THE RETINA BY RAPID DIFFUSION OF HYDROGEN: ADMINISTRATION OF HYDROGEN-LOADED EYE DROPS IN RETINAL ISCHEMIA-REPERFUSION INJURY

Invest Ophthalmol Vis Sci. 2010 Jan;51(1):487-92. doi: 10.1167/iovs.09-4089. Epub 2009 Oct 15. Oharazawa H1, Igarashi T, Yokota T, Fujii H, Suzuki H, Machide M, Takahashi H, Ohta S, Ohsawa I

### Source

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### Abstract

PURPOSE: Retinal ischemia-reperfusion (I/R) injury by transient elevation of intraocular pressure (IOP) is known to induce neuronal damage through the generation of reactive oxygen species. Study results have indicated that molecular hydrogen (H(2)) is an efficient antioxidant gas that selectively reduces the hydroxyl radical (\*OH) and suppresses oxidative stress-induced injury in several organs. This study was conducted to explore the neuroprotective effect of H(2)-loaded eye drops on retinal I/R injury.

METHODS: Retinal ischemia was induced in rats by raising IOP for 60 minutes. H(2)-loaded eye drops were prepared by dissolving H(2) gas into a saline to saturated level and administered to the ocular surface continuously during the ischemia and/or reperfusion periods. One day after I/R injury, apoptotic cells in the retina were quantified, and oxidative stress was evaluated by markers such as 4-hydroxynonenal and 8-hydroxy-2-deoxyguanosine. Seven days after I/R injury, retinal damage was quantified by measuring the thickness of the retina.

RESULTS: When H(2)-loaded eye drops were continuously administered, H(2) concentration in the vitreous body immediately increased and I/R-induced \*OH level decreased. The drops reduced the number of retinal apoptotic and oxidative stress marker-positive cells and prevented retinal thinning with an accompanying activation of Müller glia, astrocytes, and microglia. The drops improved the recovery of retinal thickness by >70%.

CONCLUSIONS: H(2) has no known toxic effects on the human body. Thus, the results suggest that H(2)-loaded eye drops are a highly useful neuroprotective and antioxidative therapeutic treatment for acute retinal I/R injury.

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# REDUCTION OF PESTICIDE RESIDUES ON FRESH VEGETABLES WITH ELECTROLYZED WATER TREATMENT

J Food Sci. 2011 May;76(4):C520-4. doi: 10.1111/j.1750-3841.2011.02154.x. Hao J, Wuyundalai, Liu H, Chen T, Zhou Y, Su YC, Li L.

#### Source

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### Abstract

Degradation of the 3 pesticides (acephate, omethoate, and dimethyl dichloroviny phosphate [DDVP]) by electrolyzed water was investigated. These pesticides were commonly used as broad-spectrum insecticides in pest control and high-residual levels had been detected in vegetables. Our research showed that the electrolyzed oxidizing (EO) water (pH 2.3, available chlorine concentration:70 ppm, oxidation-reduction potential [ORP]: 1170 mV) and the electrolyzed reducing (ER) water (pH 11.6, ORP: -860 mV) can reduce the pesticide residues effectively. Pesticide residues on fresh spinach after 30 min of immersion in electrolyzed water reduced acephate by 74% (EO) and 86% (ER), omethoate by 62% (EO) and 75% (ER), DDVP by 59% (EO) and 46% (ER), respectively. The efficacy of using EO water or ER water was found to be better than that of using tap water or detergent (both were reduced by more than 25%). Besides spinach, the cabbage and leek polluted by DDVP were also investigated and the degradation efficacies were similar to the spinach. Moreover, we found that the residual level of pesticide residue decreased with prolonged immersion time. Using EO or ER water to wash the vegetables did not affect the contents of Vitamin C, which inferred that the applications of EO or ER water to wash the vegetables would not result in loss of nutrition.

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### HYPOCHLOROUS ACID AS A POTENTIAL WOUND CARE AGENT

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#### Source

J Burns Wounds. 2007; 6: e5. Published online Apr 11, 2007.

### Abstract

Objective: Hypochlorous acid (HOCl), a major inorganic bactericidal compound of innate immunity, is effective against a broad range of microorganisms. Owing to its chemical nature, HOCl has never been used as a pharmaceutical drug for treating infection. In this article, we describe the chemical production, stabilization, and biological activity of a pharmaceutically useful formulation of HOCl. Methods: Stabilized HOCl is in the form of a physiologically balanced solution in 0.9% saline at a pH range of 3.5 to 4.0. Chlorine species distribution in solution is a function of pH. In aqueous solution, HOCl is the predominant species at the pH range of 3 to 6. At pH values less than 3.5, the solution exists as a mixture of chlorine in aqueous phase, chlorine gas, trichloride (Cl3-), and HOCl. At pH greater than 5.5, sodium hypochlorite (NaOCI) starts to form and becomes the predominant species in the alkaline pH. To maintain HOCl solution in a stable form, maximize its antimicrobial activities, and minimize undesirable side products, the pH must be maintained at 3.5 to 5. Results: Using this stabilized form of HOCl, the potent antimicrobial activities of HOCl are demonstrated against a wide range of microorganisms. The in vitro cytotoxicity profile in L929 cells and the in vivo safety profile of HOCl in various animal models are described. Conclusion: On the basis of the antimicrobial activity and the lack of animal toxicity, it is predicted that stabilized HOCl has potential pharmaceutical applications in the control of soft tissue infection.

PMCID: PMC1853323

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# THE HEALING EFFECT OF ELECTROLYTIC-REDUCTION ION WATER ON BURN WOUNDS

Biosci Trends. 2010 Feb;4(1):31-6. Okajima M, Shimokawa K, Ishii F.

### Source

Department of Pharmaceutical Sciences, Meiji Pharmaceutical University, Tokyo, Japan.

### Abstract

We prepared a lotion using electrolytic-reduction ion water (ERI), and evaluated the healing effects of this lotion (ERI lotion) on burn wounds. Third degree burn wounds were induced in the mouse dorsal skin, and ERI lotion or physiological salt (PS) lotion was applied to the wounds from immediately after injury [ERI (+) group and ERI (-) group as a control group, respectively]. The burn wound area was measured, and its serial changes were evaluated. In addition, histological examination of the burn wound site (on day 3) was performed. Comparison of the ERI (+) and (-) groups showed a significant reduction in the burn wound area in the former. Histological examination confirmed many interstitial spaces, blood vessels, and lymphatic vessels in the subcutaneous tissue in the ERI (-) compared with the ERI (+) group. These results suggest the promotion of burn wound healing by ERI lotion.

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### HISTOLOGICAL STUDY ON THE EFFECT OF ELECTROLYZED REDUCED WATER BATHING ON UVB RADIATION-INDUCED SKIN INJURY IN HAIRLESS MICE

Biol Pharm Bull. 2011;34(11):1671-7.

Yoon KS, Huang XZ, Yoon YS, Kim SK, Song SB, Chang BS, Kim DH, Lee KJ.

### Source

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### Abstract

Electrolyzed reduced water (ERW), functional water, has various beneficial effects via antioxidant mechanism in vivo and in vitro. However there is no study about beneficial effects of ERW bathing. This study aimed to determine the effect of ERW bathing on the UVB-induced skin injury in hairless mice. For this purpose, mice were irradiated with UVB to cause skin injury, followed by individually taken a bath in ERW (ERW-bathing) and tap water (TW-bathing) for 21 d. We examined cytokines profile in acute period, and histological and ultrastructural observation of skin in chronic period. We found that UVBmediated skin injury of ERW-bathing group was significantly low compared to TW control group in the early stage of experiment. Consistently, epidermal thickening as well as the number of dermal mast cell was significantly lowered in ERW-bathing group. Defection of corneocytes under the scanning electron microscope was less observed in ERW-bathing group than in TW-bathing group. Further, the level of interleukin (IL)-1\beta, tumor necrosis factor (TNF)-α and IL-12p70 in ERW group decreased whereas those of IL-10 increased. Collectively, our data indicate that ERW-bathing significantly reduces UVB-induced skin damage through influencing pro-/anti-inflammatory cytokine balance in hairless mice. This suggests that ERW-bathing has a positive effect on acute UVB-mediated skin disorders. This is the first report on bathing effects of ERW in UVB-induced skin injury.

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