Benefits of Htwo™ Hydrogen Water™

Drink one pouch a day

Purified water infused with molecular hydrogen

Hydrogen For Health And Performance

Boosts Endurance - Reduces Lactic Acid
Reduces Fatigue - Provides Antioxidants

www.HTWO.com
500 ml (1 pt 0.9 fl oz)
NURSING HOME
HTWO® (Hydrogen Water)®

‘Return to Form’™ with HTWO®
a Metabolic Drink that delivers Molecular Hydrogen

Scientific Support & Clinical Trials
...for applications of molecular hydrogen in geriatric populations, with a specific focus in wound healing.
The following are the categories that are briefly presented in this presentation:

• Animal Models of Human Diseases & Disorders

(Visuals) Heart Attack / Stroke / Memory Loss (Confined Conditions)
Alzheimer’s Disease / Atherosclerosis / Traumatic Brain Injury
Diabetes (Fatty Liver & Body Fat)

• Historical Applications for Humans (United States Navy)

• Published Clinical Trials

Pressure Ulcers / Skin Erythematous / Rheumatoid Arthritis / Hepatitis Parkinson’s Disease / Diabetes (Metabolic Syndrome) / Cancer Therapy Dialysis / Stroke / Bladder Syndrome

• HTWO – Medical Developments

FDA Correspondence
Arkansas Heart Hospital – Clinical Research Department
Medical Devices – Element One LLC
For more than four decades, animal models have shown that molecular hydrogen can address the health of human diseases and disorders. Listed below are the more notable citations from the number of examples that are available.

* Dole et al. *Hyperbaric Hydrogen Therapy: A Possible Treatment for Cancer* (1975) *Science*

Dole et al. was first published in *Science*, a prestigious scientific journal that is peer-reviewed. This research demonstrated that exposure to molecular hydrogen could help the regression of skin tumors (squamous cell carcinoma) in mice.
In 2007, Ohsawa et al. indicated a molecular mechanism for the biological benefits of molecular hydrogen in animal models have shown that molecular hydrogen can address the health of human diseases and disorders.


Ohsawa et al. was first published in Nature, a prestigious scientific journal that is peer-reviewed. This article demonstrated that exposure to molecular hydrogen could help prevent the damage from a cerebral ischemia even also known as stroke.
Since the publication of Ohsawa et al., animal models clearly demonstrate that molecular hydrogen can address an array of human diseases and disorders.

A rat model has demonstrated that applications of molecular hydrogen can potentially attenuate the side effects of Parkinson’s Disease. Presented below are images of this rat model. The left image is a control rat, with Parkinson’s-like syndrome, who did not receive Hydrogen Water and thus exhibited symptoms. The right image is a treated rat who received Hydrogen Water and thus did not present with symptoms.
Animal models indicate that molecular hydrogen is beneficial for addressing ...

- Heart Attacks (Myocardial Ischemia)
  - (Control) vs (H₂ Treatment)

- Stroke (Cerebral Ischemia)
  - (Control) vs (H₂ Treatment)
  - MCA

- Memory Impairment (Confined Conditions)
  - (Control) vs (H₂ Treatment)
  - Dead Tissue

- Alzheimer’s Disease (Premature Ageing)
  - (Control) vs (H₂ Treatment)
Animal models indicate that molecular hydrogen is beneficial for addressing:

- Atherosclerosis (Arterial Plaques)
  - (Control)
  - (H₂ Treatment)

- Diabetes (Fatty Liver)
  - (Control)
  - (H₂ Treatment)

- Diabetes (Body Fat)
  - (Control)
  - (H₂ Treatment)
  - (H₂ Treatment)

- Traumatic Brain Injury (Concussion)
  - (Control)
  - (H₂ Treatment)

Recent Studies ...
Htwo™ (Hydrogen Water)™

- Clinical Trials & Medical Applications -
Humans have also historically benefited from the consumption of molecular hydrogen. Listed below are notable citations from the abundant examples that are available in the medical literature.

Medical Applications: Molecular hydrogen has been used as a medical application for over a century, before the direct benefits of the molecule were evident.


Governmental Applications: Applications of molecular hydrogen have been developed by the United States Navy and a French company, Compagnie maritime d’expertises (COMEX), as a breathing gas for deep sea diving.

- “ECG changes during the experimental human dive HYDRA 10 (71 atm/7,200 kPa)” (1995) Undersea and Hyperbaric Medicine Journal
Molecular hydrogen is naturally produced & consumed by the human body, more specifically, by the microbial flora in the alimentary tract.

The quantitative measurement for endogenous production of molecular hydrogen is a diagnostic tool for people with gastrointestinal pathophysiology, including but not limited to irritable bowel syndrome.


Quantitative measurements are also conducted to identify the amount of molecular hydrogen that is delivered into humans who receive exogenous sources of the molecule.


Clinical trials have shown that molecular hydrogen is a safe therapy that addresses a wide variety of human diseases and disorders.

*“Hydrogen water intake via tube-feeding for patients with pressure ulcer and its reconstructive effects on normal human skin cells in vitro” (2013) Molecular Gas Research

*“Hydrogen(H2) treatment for acute erythematous skin diseases. A report of 4 patients with safety data and a non-controlled feasibility study with H2 concentration measurement on two volunteers” (2012) Medical Gas Research

*“Consumption of water containing a high concentration of molecular hydrogen reduces oxidative stress and disease activity in patients with rheumatoid arthritis: an open-label pilot study” (2012) Medical Gas Research


*“Hydrogen-rich water decreases serum LDL-cholesterol levels and improves HDL function in patients with potential metabolic syndrome” (2013) The Journal of Lipid Research

*“Transperitoneal administration of dissolved hydrogen for peritoneal dialysis patients: a novel approach to suppress oxidative stress in the peritoneal cavity” (2013) Medical Gas Research


Clinical Trials have shown that molecular hydrogen is a safe therapy that addresses a wide variety of human diseases and disorders.

“Effect of hydrogen-rich water on oxidative stress, liver function, and viral load in patients with chronic hepatitis” (2013) Clinical and Translational Science

*“Effects of drinking hydrogen-rich water on the quality of life of patients treated with radiotherapy for liver tumors” (2011) Medical Gas Research

*“A novel bioactive haemodialysis system using dissolved dihydrogen (H2) produced by water electrolysis: A clinical trial” (2010) Nephrology Dialysis Transplantation

*“A basic study on molecular hydrogen (H2) inhalation in acute cerebral ischemia patients for safety check with physiological parameters and measurement of blood H2 level” (2012) Medical Gas Research

*“Improved brain MRI indices in the acute brain stem infarct sites treated with hydroxyl radical scavengers, Edaravone and hydrogen as compared to Edaravone alone, A non-randomized study” (2011) Medical Gas Research


*“Open-label trial and randomized, double-blind, placebo-controlled, crossover trial of hydrogen-enriched water for mitochondrial and inflammatory myopathies” (2011) Medical Gas Research

“Effects of intravenous infusion of hydrogen-rich fluid combined with intra-cisternal infusion of magnesium sulfate in severe aneurysmal subarachnoid hemorrhage: study protocol for a randomized controlled trial” BioMedCentral Neurology
Partnerships for Pharmaceutical Applications & Medical Devices

- United States FDA (Food & Drug Administration)
- Arkansas Heart Hospital® - Wound Care Center –
- Element One®
Htwo™ is actively engaged with the FDA to expand the opportunities in which molecular hydrogen can be delivered to consumers. MitoGene, the parent company of Htwo™, recently has received FDA GRAS status.

February 1, 2012

Office of Pre-market approval (HSF-200)
Center for Food safety and Applied Nutrition
Food and Drug Administration
200 C Street, Washington DC 20204

To whom it may concern,

In accordance with the Federal Register 62 FR18937, dtd April 17, 1997, MitoGene, LLC is submitting a notice of a self-determination that the use of molecular hydrogen (H₂) solubilized in water is generally recognized as safe (GRAS). The data and information that are the basis for the GRAS determination are available for the Food and Drug Administration’s (FDA) review.

Sincerely,

Cody C. Cook
Founder, MitoGene, LLC

Dr. Drew R. Jones
Co-Founder, MitoGene, LLC

401 S. Cedar
Little Rock, Arkansas, 72205
CodyCook@MitoGene.com
The FDA is in communication with MitoGene™, the parent company of Htwo™ for consideration of molecular hydrogen as a medical food and/or a pharmaceutical. This regulatory process requires the FDA to review the benefits of Htwo™ in a series of clinical trials that are to be conducted in collaboration with the Arkansas Heart Hospital.

Dear Dr. Cook,

Your inquiry to the FDA has been referred to my office for follow-up. I understand that you were in communication with Shawne Suggs-Anderson in the FDA Center for Food Safety and Applied Nutrition (CFSAN) and that you were informed that your proposal did not appear to fall within the regulatory scheme for medical foods.

Based on the information available to me at this time, your proposed product appears to be appropriate for review in FDA's Center for Drug Evaluation and Research (CDER). Please let me know if you require further assistance to identify the appropriate regulatory pathway and product requirements.

Sincerely,

Kristina J. Lauritsen, PhD
Assistant Ombudsman / Product Jurisdiction Officer
Office of Executive Programs
Center for Drug Evaluation and Research
Food and Drug Administration
Arkansas Heart Hospital is partnered with Htwo™ to provide molecular hydrogen to medical patients who have diseases and disorders that could benefit from medical hydrogen therapy.

Dr. Bruce Murphy, M.D./Ph.D., and CEO/President of Arkansas Heart Hospital has a strong interest in determining how Htwo™ can benefit patients with wounds such as but not limited to decubitus (pressure) ulcers of the elderly, and diabetic ulcerations from peripherals vascular disease.

Arkansas Heart Hospital is a nationally recognized as an award-winning hospital dedicated to the prevention, diagnosis and treatment of cardiovascular disease. The hospital has access to advanced technology and surgical techniques, including a Wound Care and Hyperbaric Center in a comprehensive outpatient center designed for the treatment of non-healing or difficult wounds. The Wound Care Center provides state-of-the-art treatment and features the largest individual patient hyperbaric chambers available, but also debridement, medications, dressings and individualized support services.

www.arheart.com/services/wound-care-center
The Clinical Research Department at the Arkansas Heart Hospital is in communication with the United States FDA to ask if Htwo™ can be provided to medical patients as a medical therapy for diseases and disorders that could benefit from medical hydrogen.

Arkansas Heart Hospital’s® Clinical Research Department is dedicated to providing comprehensive research support to assist sponsors and investigators by coordinating and facilitating clinical research studies. For both patients and physicians, the clinical research trials allow the opportunity to gain access to the latest cutting edge technology and treatments before they are commonly available. Arkansas Heart Hospital® has been the nation’s leading investigative site for various key research trials. The Clinical Research Department is directed by Dr. Gerardo Rodriguez, M.D./Ph.D.

www.arheart.com/services/clinical-research

Htwo™ is partnering with Arkansas Heart Hospital to conduct a set of clinical trials to verify the benefits of Htwo™ for promoting the wound healing of ulcers including but not limited to decubitus (pressure) ulcers and diabetic ulcers.
Element One® LLC, the World’s premier manufacture of sensors for molecular hydrogen, is partnered with Htwo™ for the development of molecular hydrogen sensors in beverage packages and medical devices.

With the **Element One LLC** partnership, Htwo™ will ensure its lead as the authority in packaging of molecular hydrogen for delivery to consumers. The molecular hydrogen sensor will allow consumers to know the concentration of molecular hydrogen that is consumed with each bottle of HTWO™.

Htwo™ is in communication with the FDA to develop these molecular hydrogen sensors into medical devices, which will allow physicians to properly administer and monitor Htwo™ for the individual needs of their patents.