

WELLNESS

BEAUTY

OXIDANT

INFEL

AI

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SP



**YOU NEED
OXYGEN TO LIVE
BUT HYDROGEN
TO LIVE WELL**



**MOLECULAR HYDROGEN
FOR WELLNESS BEAUTY AND SPORTS**

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HOHH

01

WHAT IS MOLECULAR H₂ GAS

Molecular hydrogen (H₂) or diatomic hydrogen is a tasteless, odourless, non-toxic, flammable gas.

02

WHY MOLECULAR H₂ GAS

Molecular H₂ is small which can easily penetrate the biomembrane/blood-brain barrier by diffusion and enter into our cell and can efficiently affect the bad elements of our body. Intense research suggests that molecular H₂ gas possesses anti-allergic, anti-aging, anti-inflammatory, antiapoptotic (anti-cell death) properties in addition to antioxidant properties¹.

03

HOW DO YOU INTAKE MOLECULAR H₂ IN YOUR BODY?

Molecular H₂ can be inhaled by cannula, through drinking Hydrogenated water² or bathing in hydrogenated water. Elicare provides all these options efficiently and with utmost safety.



¹ Ge L, Yang M, Yang NN, Yin XX, Song WG. Molecular hydrogen: a preventive and therapeutic medical gas for various diseases. *Oncotarget*. 2017;8(60):102653-102673; Abisso TG, Adzavon YM, Zhao P, Zhang X, Liu M, Ma X, et al. Current Progress In Molecular Hydrogen Medication: Protective And Therapeutic Uses Of Hydrogen Against Different Disease Scenarios. *Intern Med* 2020 10:314

² Asada R, Saitoh Y, Miwa N. Effects of hydrogen-rich water bath on visceral fat and skin blotch, with boiling-resistant hydrogen bubbles. *Med Gas Res*. 2019;9(2):68-73.



04

IS MOLECULAR H₂ IS SAFE TO DRINK, INHALE OR BATHING?

Hydrogen is very natural to our body, as we are exposed to it on a daily basis as a result of normal bacterial metabolism in our intestinal flora upon digestion of fibers³. Additionally, hydrogen gas has also been used in deep sea diving since the 1940s to prevent decompression sickness⁴. The hundreds of studies on hydrogen from bacterial production, deep sea diving, and recent medical applications have not revealed any direct toxic side effects of hydrogen administration at biologically therapeutic levels⁵. Recently, the US Food and Drug Administration (FDA) acknowledged H₂ gas as generally safe food additives when used in drinking water or beverages⁶.

05

WHO CAN INTAKE MOLECULAR H₂?

Molecular H₂ are recommended to use by “healthy” person. It helps to reduce oxidative stress which may be result of the pollution/food habits/smoking/drinking⁷. “Your need oxygen to live but hydrogen to live well”⁸.

³ Conlon MA, Bird AR. The impact of diet and lifestyle on gut microbiota and human health. *Nutrients*. 2014;7(1):17-44

⁴ Dougherty JH Jr. Use of H₂ as an inert gas during diving: pulmonary function during H₂-O₂ breathing at 7.06 ATA. *Aviat Space Environ Med*. 1976;47(6):618-626.

⁵ Ono H, Nishijima Y, Ohta S, et al. Hydrogen Gas Inhalation Treatment in Acute Cerebral Infarction: A Randomized Controlled Clinical Study on Safety and Neuroprotection. *J Stroke Cerebrovasc Dis*. 2017;26(11):2587-2594 and <https://clinicaltrials.gov/ct2/show/NCT03971617>

⁶ <https://wayback.archive-it.org/7993/20170606194850/https://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/NoticeInventory/ucm432907.htm>

⁷ Atsunori Nakao, Yoshiya Toyoda, Prachi Sharma, Malkanthi Evans, and Najla Guthrie Effectiveness of Hydrogen Rich Water on Antioxidant Status of Subjects with Potential Metabolic Syndrome—An Open Label Pilot Study *J Clin Biochem Nutr*. 2010 Mar; 46(2): 140–149.

⁸ <https://www.youtube.com/watch?v=OYB2UFm2Fp8>

WHAT ARE THE BENEFITS OF MOLECULAR H₂

A. Wellness

- ▷▷ Reduce oxidative stress that accumulates in everyday's life⁷.
- ▷▷ Improve mood, anxiety, and autonomic nerve function in daily life⁹.
- ▷▷ Protects from the pollution¹⁰.
- ▷▷ Control body fat and weight without changing the food habit¹¹.
- ▷▷ Improve the quality of life¹².
- ▷▷ Improve your muscle fatigue¹³.
- ▷▷ Improve sleep¹⁴.



⁷ Atsunori Nakao, Yoshiya Toyoda, Prachi Sharma, Malkanthi Evans, and Najla Guthrie Effectiveness of Hydrogen Rich Water on Antioxidant Status of Subjects with Potential Metabolic Syndrome—An Open Label Pilot Study *J Clin Biochem Nutr.* 2010 Mar; 46(2): 140–149.

⁹ Mizuno K, Sasaki AT, Ebisu K, et al. Hydrogen-rich water for improvements of mood, anxiety, and autonomic nerve function in daily life. *Med Gas Res.* 2018;7(4):247-255.

¹⁰ Gong ZJ, Guan JT, Ren XZ, et al. Zhonghua Jie He He Hu Xi Za Zhi. Protective effect of hydrogen on the lung of sanitation workers exposed to haze 2016;39(12):916-923. Choi J, Suk An E, Ban YH, et al. Hydrogen-enriched water eliminates fine particles from the lungs and blood by enhancing phagocytic activity. *J Biomed Res.* 2017;31(6):503-511. doi:10.7555/JBR.31.20170066

¹¹ Kamimura N, Nishimaki K, Ohsawa I, Ohta S. Molecular hydrogen improves obesity and diabetes by inducing hepatic FGF21 and stimulating energy metabolism in db/db mice. *Obesity (Silver Spring).* 2011;19(7):1396-1403. Korovljevic D, Trivic T, Drid P, Ostojic SM Molecular hydrogen affects body composition, metabolic profiles, and mitochondrial function in middle-aged overweight women *Irish Journal of Medical Science*, 30 May 2017, 187(1):85-89. Song G, Li M, Sang H, et al. Hydrogen-rich water decreases serum LDL-cholesterol levels and improves HDL function in patients with potential metabolic syndrome. *J Lipid Res.* 2013;54(7):1884-1893.

¹² Kang, K., Kang, Y., Choi, I. et al. Effects of drinking hydrogen-rich water on the quality of life of patients treated with radiotherapy for liver tumors. *Med Gas Res* 1, 11 (2011)

¹³ Aoki K, Nakao A, Adachi T, Matsui Y, Miyakawa S. Pilot study: Effects of drinking hydrogen-rich water on muscle fatigue caused by acute exercise in elite athletes. *Med Gas Res.* 2012;2:12.

¹⁴ <https://drinkhrw.com/blogs/news/hydrogen-sleep>

B. Beauty

- ▷▷ Reduce the wrinkles due to anti-ageing effect of molecular hydrogen.
- ▷▷ Oxidation-reduction potential of the skin increases by oxidative damage and also by aging¹⁵.
- ▷▷ Molecular hydrogen decreased the oxidation reduction potential (ORP) of human skin¹⁶. Improve the elasticity.
- ▷▷ Protect against UV-induced skin cell damage/sun burn¹⁷.
- ▷▷ Daily skin care to repress UVA-induced skin damage by scavenging free radicals and promoting type-1 collagen synthesis¹⁸.
- ▷▷ Improves cosmetic effects such as skin-blotch repression and the visceral-fat-based slimming effects¹⁹.
- ▷▷ Improve fluency and gloss of hair²⁰.



C. Molecular H₂ in anti-oxidant action on our body

▷▷ **Protect from oxidative stress:**

The free radicals can cause oxidative stress in our body. Many disease such as cancer, asthma, cardio vascular, Alzheimer's disease, Parkinson's disease, diabetes, rheumatoid arthritis etc is strongly related to oxidative stress. Regular use of molecular hydrogen protects you from these diseases.

¹⁵ Shiochi Okouchi, et al. Relationships between ORP (Redox Potentials) and pH in Hot and Cold Spring Waters and in Human Skins. Journal of the Balneological Society of Japan. V 49. No. 2, p. 59-64. 1999

¹⁶ Shiochi Okouchi, et al. Electrolyzed-Reduced Water as Artificial Hot Spring Water. Journal of the Balneological Society of Japan. V 53, No. 1, p. 1-9 2003)

¹⁷ Ignacio, R. M., Yoon, Y. S., Sajo, M. E. J., Kim, C. S., Kim, D. H., Kim, S. K. & Lee, K. J. (2013). The balneotherapy effect of hydrogen reduced water on UVB-mediated skin injury in hairless mice. Molecular & Cellular Toxicology 9, 15-21.

¹⁸ Kato, S., Saitoh, Y., Iwai, K. & Miwa, N. (2012). Hydrogen-rich electrolyzed warm water represses wrinkle formation against UVA ray together with type-I collagen production and oxidative-stress diminishment in fibroblasts and cell-injury prevention in keratinocytes. J Photochem Photobiol B 106, 24-33.

¹⁹ Asada R, Saitoh Y, Miwa N. Effects of hydrogen-rich water bath on visceral fat and skin blotch, with boiling-resistant hydrogen bubbles. Med Gas Res. 2019;9(2):68-73.

²⁰ Shochi Ocouchi, Hideyuki Ohnami, et al. Effect of Electrolyzed-Reduced Water as Artificial Hot Spring Water on Human Skin and Hair. Journal of the Balneological Society of Japan. V 55. No. 2, p. 55-63. 2005

▷▷ **Regulate antioxidant system:**

Molecular hydrogen can protect against oxidative damage also by the activation of the Nrf2-Keap1 system and subsequent induction of the antioxidant response element (ARE) pathway, which leads to the production of various cytoprotective proteins like glutathione, catalase, superoxide dismutase, glutathione peroxidase, heme-1 oxygenase, etc²¹.

▷▷ **Protect your DNA:**

Molecular hydrogen protect DNA damage by scavenging hydroxyl radical²².

▷▷ **Protect us from fatigue (boost energy):**

Mitochondria is the power house of the cell. H₂ is smallest molecule and possess high penetrability which accessible by subcellular structure including shown that the H₂ can protect mitochondria from acute oxidative stress. It also preserve the membrane potential, increase ATP production thus provide us energy and protect us from day to day fatigue^{23,24}.



D. Molecular H₂ in anti-inflammatory action on our body

▷▷ H₂ inhibits oxidative stress-induced inflammatory tissue damage via down regulation of pro-inflammatory and inflammatory cytokines. Thus may have significant role in respiratory diseases such as asthma²⁶, COVID-19²⁷, SARS, MARS, many auto immune disease such as psoriasis and parapsoriasis en plaques²⁸.

²¹ W. Fang., L. Tang., G. Wang., J. Lin. , W. Pan., J. Xu.,Molecular Hydrogen Protects Human Melanocytes from Oxidative Stress by Activating Nrf2 Signaling Journal of Investigative Dermatology (2020)

²² Abou-Hamdan M, Gardette B, Cadet J, et al. Molecular hydrogen attenuates radiation-induced nucleobase damage to DNA in aerated aqueous solutions. Int J Radiat Biol. 2016;92(9):536-541.

²³ S. M. Ostojic Targeting molecular hydrogen to mitochondria: Barriers and gateways; Pharmacological Research 94, 2015, 51-53 and Gvozdjčková A, Kucharská J, Kura B, et al. A new insight into the molecular hydrogen effect on coenzyme Q and mitochondrial function of rats. Can J Physiol. Pharmacol. 2020; 98(1):29-34.

²⁴ Ohta, S. Molecular hydrogen is a novel antioxidant to efficiently reduce oxidative stress with potential for the improvement of mitochondrial diseases. Biochimica et Biophysica Acta 1820 (2012) 586–594

²⁵ Gharib B, Hanna S, Abdallahi OM, Lepidi H, Gardette B, De Reggi M. Anti-inflammatory properties of molecular hydrogen: investigation on parasite-induced liver inflammation. C R Acad Sci III. 2001;324(8):719-724.

²⁶ Zhang N, Deng C, Zhang X, Zhang J, Bai C. Inhalation of hydrogen gas attenuates airway inflammation and oxidative stress in allergic asthmatic mice. Asthma Res Pract. 2018; 4: 3

²⁷ Wei-Jie Guan, Chun-Hua Wei, Ai-Lan Chen, Xiao-Cong Sun, Guang-Yun Guo, Xu Zou, Jin-Dong Shi, Pei-Zhen Lai, Ze-Guang Zheng, Nan-Shan Zhong Hydrogen/oxygen mixed gas inhalation improves disease severity and dyspnea in patients with Coronavirus disease 2019 in a recent multicenter, open-label clinical trial J Thorac Dis 2020;12(6):3448-3452. Wei-jie Guan, Rong-chang Chen, Nan-shan Zhong Strategies for the prevention and management of coronavirus disease 2019, European Respiratory Journal Jan 2020, 2000597

²⁸ Zhu, Q., Wu, Y., Li, Y. et al. Positive effects of hydrogen-water bathing in patients of psoriasis and parapsoriasis en plaques. Sci Rep 8, 8051 (2018).

E. Molecular H₂ as anti-allergic

▷▷ H₂ inhalation may improve nasal allergic symptoms, reduce inflammatory cell infiltration in nasal mucosa, and regulate Th1/Th2 responses. Molecular H₂ also attenuates allergic inflammation and suppresses the release and activation of eosinophils in allergic rhinitis²⁹.

▷▷ **Protection from pollution:**

Eliminate both the ultrafine and fine particles from the lungs and blood by enhancing phagocytic activity, but also attenuated the lung tissue injuries by inhibiting lipid peroxidation. Thus showing anti-allergic action³⁰.

F. Molecular H₂ is anti-aging

▷▷ Scientific study showed that molecular hydrogen enhances telomerase activity, thus providing great potential in anti-aging application³¹. Molecular hydrogen is a powerful antioxidant that helps to defend cells and genes from damage and death caused by harmful free radicals. These properties, in combination with its anti-inflammatory properties help enhance longevity because aging is caused by tissue degeneration, oxidative stress and inflammation³².

▷▷ **H₂ Protect your skin:**

The studies suggested that hydrogen water bath might serve as a daily skin care to repress UVA-induced skin damage by scavenging free radicals and promoting type-1 collagen synthesis anti-allergic action³³.

²⁹ Zhao C, Yu S, Li J, Xu W, Ge R. Changes in IL-4 and IL-13 expression in allergic-rhinitis treated with hydrogen-rich saline in guinea-pig model. *Allergol Immunopathol (Madr)* 2017;45:350–355. and Fang S, Li X, Wei X, et al. Beneficial effects of hydrogen gas inhalation on a murine model of allergic rhinitis. *Exp Ther Med.* 2018;16(6):5178-5184. doi:10.3892/etm.2018.6880 and Niu, Y., Nie, Q., Dong, L. et al. Hydrogen Attenuates Allergic Inflammation by Reversing Energy Metabolic Pathway Switch. *Sci Rep* 10, 1962 (2020)

³⁰ Choi J, Suk An E, Ban YH, et al. Hydrogen-enriched water eliminates fine particles from the lungs and blood by enhancing phagocytic activity. *J Biomed Res.* 2017;31(6):503-511

³¹ Settineri, R. Ji, J. Luo, C. Ellithorpe, R. R. Mattos, G. Ferreira de Rosenblatt, S. LaValle, J. Jinenez, A. Ohta, S. Nicolson, G. L. Effects of Hydrogenized Water on Intracellular Biomarkers for Antioxidants, Glucose Uptake, Insulin Signaling and SIRT 1 and Telomerase Activity *American Journal of Food and Nutrition* 4(4 6):161-168 (2016)

³² <https://bioresonance.com/hydrogen-water-for-anti-wrinkle-and-smoother-skin-goals/>

³³ Kato, S., Saitoh, Y., Iwai, K. Miwa, N. Hydrogen-rich electrolyzed warm water represses wrinkle formation against UVA ray together with type-I collagen production and oxidative-stress diminishment in fibroblasts and cell-injury prevention in keratinocytes. *J Photochem Photobiol B* 106, 24-33, (2012).



G. Molecular H₂ as Anti-apoptosis

▷▷ H₂ employs anti-apoptotic properties by up- or down regulating apoptosis - related factors. H₂ inhibits production of pro-apoptotic factors such as B-cell lymphoma-2-associated X-protein, caspase-3, caspase-8, and caspase-12³⁴. H₂ also up regulates the anti-apoptotic factors, B-cell lymphoma-2 and B-cell lymphoma-extra large³⁵.

H. Molecular H₂ in sports

▷▷ Molecular hydrogen was seen to possess effect in the health of athletes. It helps to improve endurance, improves cardiovascular parameters and it helps further to recover quickly from injury³⁶. The points are discussed in details:

▷▷ **Improve endurance:**

The human clinical studies were conducted to observe the effect of H₂ consumption on the endurance³⁷. The group of athletes receiving hydrogenated water, peak power output (PPO) remained constant throughout the trial period in comparison the placebo group reported significantly lower PPO.

▷▷ **Speedy recovery:**

Muscle contraction during intense exercise results in oxidative stress which further alleviate muscle injury or inflammation. Studies shows that adequate pre-exercise hydration with hydrogen-rich water decrease lactate level of blood and enhance muscle function³⁸.

▷▷ **Improves cardiovascular parameters:**

On consumption of hydrogenated water enhances VO₂ max, time to exhaustion and total work completed in comparison to placebo³⁹.



³⁴ Kawamura T, Huang CS, Tochigi N, Lee S, Shigemura N, Billiar TR, Okumura M, Nakao A, Toyoda Y. Inhaled hydrogen gas therapy for prevention of lung transplant-induced ischemia/reperfusion injury in rats. *Transplantation*. 2010;90:1344–51 and reference (33 and 34) in Ge L, Yang M, Yang NN, Yin XX, Song WG. Molecular hydrogen: a preventive and therapeutic medical gas for various diseases. *Oncotarget*. 2017;8(60):102653-102673

³⁵ Hong Y, Shao A, Wang J, Chen S, Wu H, McBride DW, Wu Q, Sun X, Zhang J. Neuroprotective effect of hydrogen-rich saline against neurologic damage and apoptosis in early brain injury following subarachnoid hemorrhage: possible role of the Akt/GSK3beta signaling pathway. *PLoS One*. 2014;9:e96212

³⁶ Jonatas E.Nogueira, Patricia Passaglia, Clarissa M.D.Mota, Bruna M.Santos, Marcelo E.Batalhão, Evelin C.Carnio, Luiz G.S.Branco, Molecular hydrogen reduces acute exercise-induced inflammatory and oxidative stress status *Free Radical Biology and Medicine* 129, 2018, 186-193

³⁷ Da Ponte A, et al. Effects of hydrogen rich water on prolonged intermittent exercise. *J Sports Med Phys Fitness*. 2018 May;58(5):612-621.

³⁸ Kawamura T, et al. Effects of hydrogen bathing on exercise-induced oxidative stress and delayed-onset muscle soreness. *Jpn J Phys Fit Sport Med*. 2016;65:297–305. Aoki K, Nakao A, Adachi T, Matsui Y, Miyakawa S. Pilot study: Effects of drinking hydrogen-rich water on muscle fatigue caused by acute exercise in elite athletes. *Med Gas Res*. 2012;2:12.

³⁹ Ostojic S, et al. 28-days hydrogen-rich water supplementation affects exercise capacity in mid-age overweight women. *ASCM Poster Presentation*. 2018 Jun 15;7

07

HOW MOLECULAR H₂ WORKS IN OUR BODY

H₂ has emerged as a novel medical gas with potentially broad applications. Dole, et al. first reported the therapeutic effects of H₂ in 1975 in a skin squamous carcinoma mouse model⁴⁰. Thereafter, inhaling high pressure H₂ was demonstrated as a treatment for liver parasite infection-induced hepatitis⁴¹. In 2007, Ohsawa and colleagues discovered that H₂ has antioxidant properties that protect the brain against I/R injury and stroke by selectively neutralizing hydroxyl radicals ($\cdot\text{OH}$) and peroxynitrite(ONOO^-)⁴².

▷▷ Mechanism of antioxidant properties of molecular H₂

Antioxidants are molecules that destroy the reactive oxygen species (ROS), free radicals which is continuously being produced by the biochemical oxidation of our body. The known ROS are $\cdot\text{OH}$, $\cdot\text{ONOO}$, $\text{O}_2^{\cdot-}$, H_2O_2 , NO^\cdot . The vitamin C is one of the best known antioxidant. Molecular H₂ exhibited better antioxidant properties than that of Vitamin C as it only selectively trap the “dangerous” cytotoxic free radical, $\cdot\text{OH}$, keeping aside beneficial antioxidants (Figure 1)⁴³. The molecular hydrogen trap $\cdot\text{OH}$ with an added advantage that no other species are formed, as described in the following equations⁴⁴:



H $^\cdot$ atoms are converted to hydrated electrons:



⁴⁰ Dole M, Wilson FR, Fife WP. Hyperbaric hydrogen therapy: a possible treatment for cancer. Science. 1975;190:152–4

⁴¹ Gharib B, Hanna S, Abdallahi OM, Lepidi H, Gardette B, De Reggi M. Anti-inflammatory properties of molecular hydrogen: investigation on parasite-induced liver inflammation. C R Acad Sci III. 2001;324:719–24

⁴² Ohsawa, I., Ishikawa, M., Takahashi, K. et al. Hydrogen acts as a therapeutic antioxidant by selectively reducing cytotoxic oxygen radicals. Nat Med 13, 688–694 (2007)

⁴³ Ohsawa, I., Ishikawa, M., Takahashi, K. et al. Hydrogen acts as a therapeutic antioxidant by selectively reducing cytotoxic oxygen radicals. Nat Med 13, 688–694 (2007)

⁴⁴ Matheson M.S., Rabani J., Pulse radiolysis of aqueous hydrogensolutions. I. rate constants for reaction of eaq^- with itself and othertransients. II. The interconvertibility of eaq^- and H_1 , J. Phys. Chem. 69(1965) 1324–1335. Bielski B.H.J., Gebicki J.M., Application of radiation chemistry tobiology, Pryor W.A., Free radicals in biology, vol. III, Academic Press, NY,1977, p. 35

Mechanism of Antioxidant Property

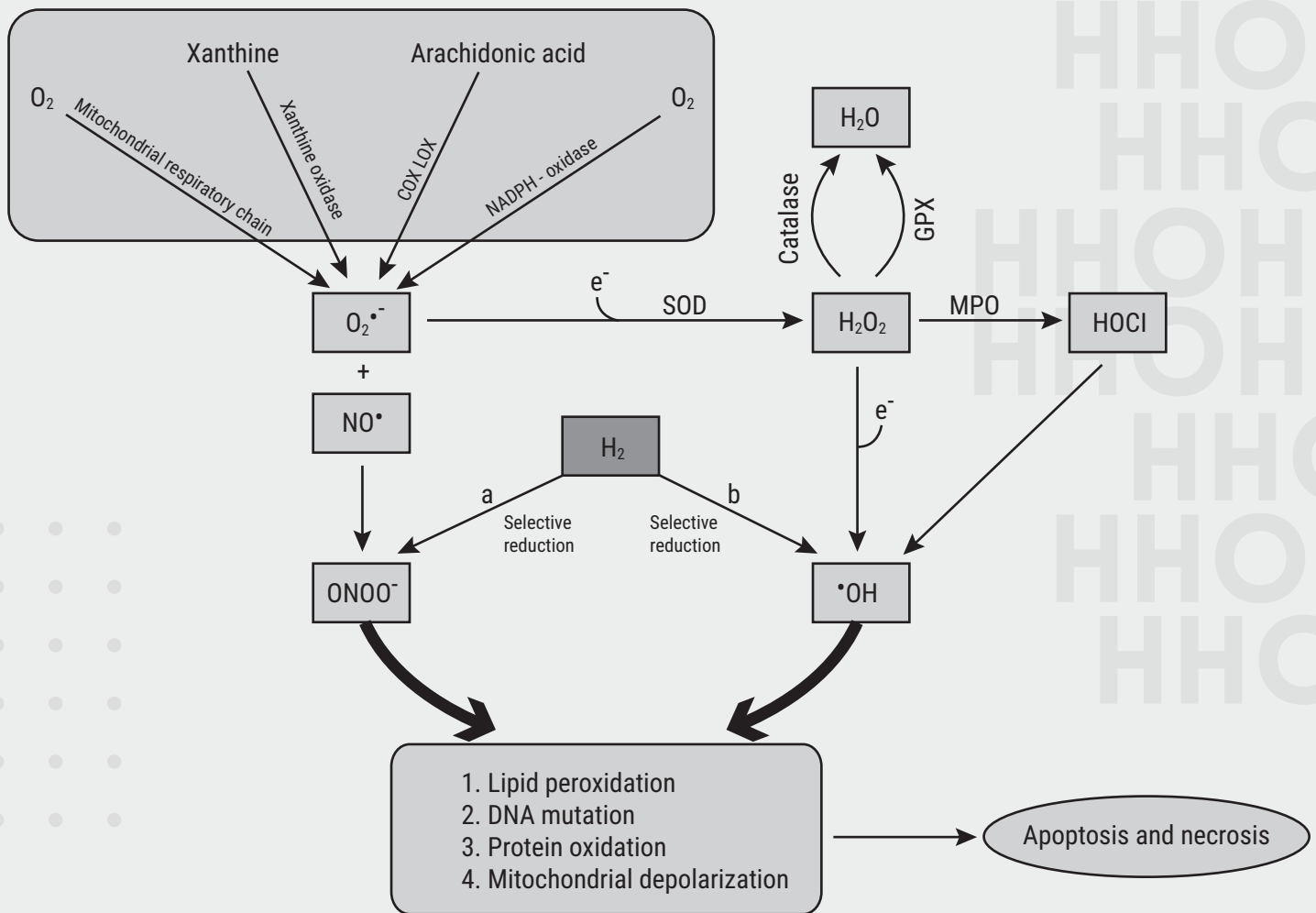


Figure 1: The reactive oxygen species (ROS) production pathway and the selective reduction of •OH and ONOO⁻ by hydrogen, showing that ROS are produced in various ways; one type of ROS can be converted into another type by electron transmission. •OH and ONOO⁻ are much more toxic than other ROS. Hydrogen selectively reduces •OH (b) and ONOO⁻ (a), but does not influence physiological ROS, including O₂^{•-} and H₂O₂ (COX, cyclo-oxygenase; LOX, 5-lipo-oxygenase; NO•, nitric oxide radical; NADPH, reduced nicotinamide adenine dinucleotide phosphate; SOD, superoxide dismutase; GPX, glutathione peroxidase 1; MPO, myeloperoxidase; HOCl, hypochlorous acid; H₂O₂ →• superoxide anion; •OH, hydroxyl radical; H₂O₂, hydrogen peroxide; ONOO⁻, peroxynitrite). Source: Y Hong, S Chen, J-M Zhang *The Journal of International Medical Research* 2010; 38: 1893 – 1903.

▷▷ Mechanism of anti-inflammatory properties of molecular H₂

Reactive Oxygen Species (ROS) play a central role both upstream and downstream of NF-κB and TNFα pathways, which are located at the center of the inflammatory response. Among the ROS, the hydroxyl radical is the most harmful, and H₂ is a selective scavenger for this species. Recently, it has been shown that H₂ is useful when administered along with the conventional therapy in chronic inflammatory diseases such as Rheumatoid arthritis (RA) (mechanism as given in Figure 2)⁴⁵, Liver inflammation⁴⁶ as it acts to reduce oxidative stress in the patients. Especially in the early stage, H₂ showed significant therapeutic potential, which also seemed to assist diagnosis and treatment decisions of RA.

Mechanism of anti-inflammatory action in Rheumatoid Arthritis

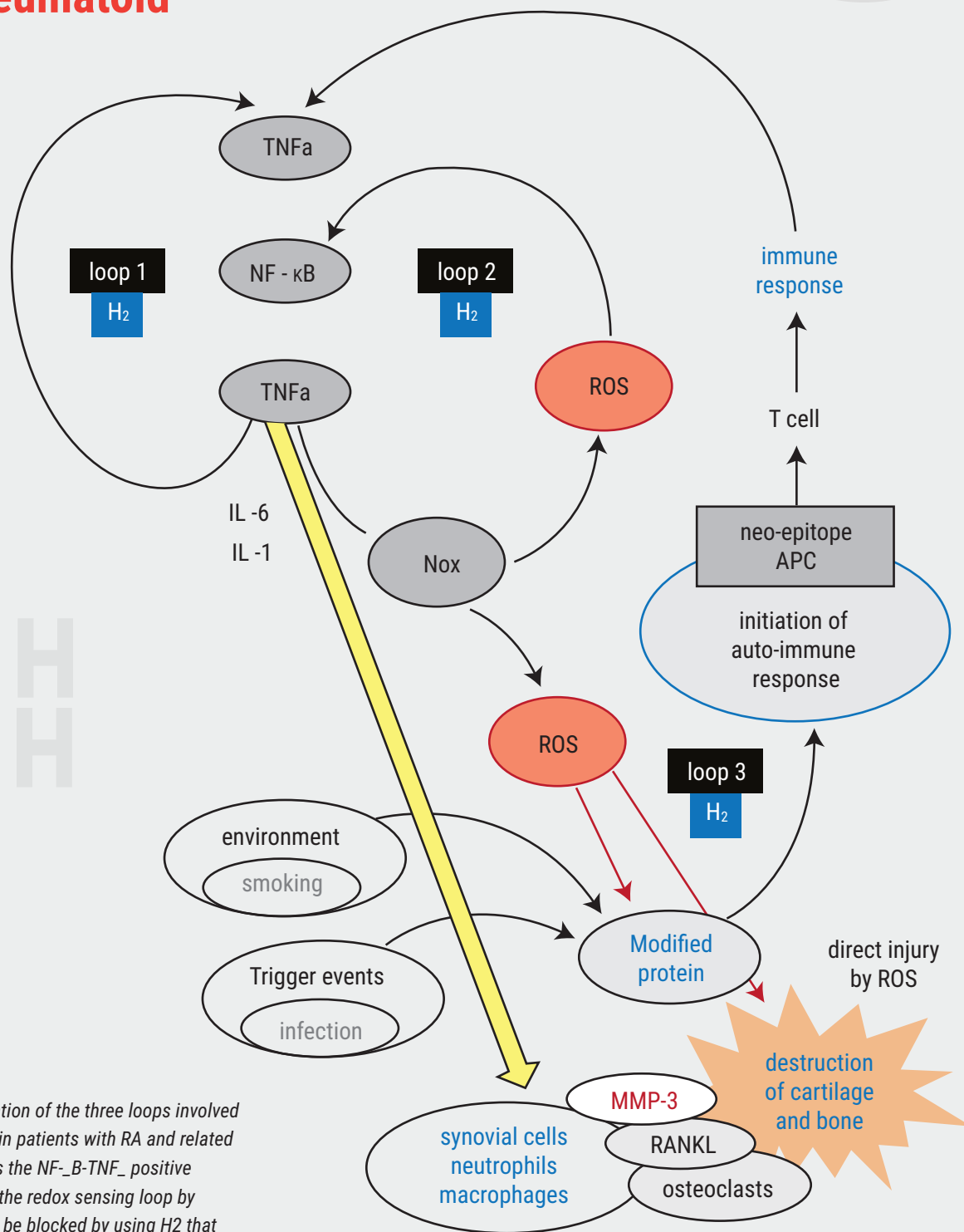


Figure 2: A schematic representation of the three loops involved in amplification of inflammation in patients with RA and related atherosclerosis. Loop 1 indicates the NF- κ B-TNF α positive feedback loop. Loop 2 indicates the redox sensing loop by ROS-NF- κ B-TNF α . Both loops can be blocked by using H₂ that scavenges hydroxyl radicals directly or via NF- κ B pathways.

ROS, which are generated by NOx system and amplified through these loops, then stimulate synovial fibroblasts, neutrophils, and macrophages, which promote cartilage and bone erosion via MMP-3 or RANKL expression. In addition, the modified proteins by ROS may generate a loop 3 which may promote the auto-immune response by feeding back into loops 1 and 2. Source: Toru Ishibashi, *Molecular Hydrogen: New Antioxidant and Anti-inflammatory Therapy for Rheumatoid Arthritis and Related Diseases Current Pharmaceutical Design*, 2013, 19, 6375-6381

⁴⁵ Toru Ishibashi *Molecular Hydrogen: New Antioxidant and Anti-inflammatory Therapy for Rheumatoid Arthritis and Related Diseases Current Pharmaceutical Design*, 2013, 19, 6375-6381

⁴⁶ Bouchra Gharib, Stéphane Hanna, Ould M.S. Abdallahi, Hubert Lepidi, Bernard Gardette, MaxDe Reggi, *Anti-inflammatory properties of molecularhydrogen: investigation on parasite-induced liverinflammation Comptes Rendus de l'Académie des Sciences - Series III - Sciences de la Vie* 2001, 324, 719-724

EXAMPLES OF CLINICAL TRIAL ON MOLECULAR H₂ BASED TREATMENT

Sr.no	Country	Treatment
1	Japan	Cardiac arrest: post-cardiac arrest syndrome, for which a 360 patient, multi-center, clinical study is being conducted ⁴⁷ .
2	China, Korea, USA, UK	COVID-19: Multi-center randomized clinical trial that verifies the efficacy and safety of H ₂ -O ₂ inhalation in patients with COVID-19 ^{48,49,50,51,52,27} .
3	China	Psoriasis and Parapsoriasis en plaques ¹⁷
4	Japan	Haemodialysis ⁵³
5	Japan	Mood, anxiety, autonomic nerve function in daily life ⁵⁴
6	Japan	Arthritis ⁵⁵
7	China	Cancer ⁵⁶

References (<http://www.molecularhydrogeninstitute.com/registered-clinical-studies>)



⁴⁷ Tamura T (2017) Efficacy of inhaled Hydrogen on neurological outcome following Brain Ischemia During post-cardiac arrest care (HYBRID II trial): study protocol for a randomized controlled trial. *Trials* 18: 488

⁴⁸ Wei-Jie Guan, Chun-Hua Wei, Ai-Lan Chen, Xiao-Cong Sun, Guang-Yun Guo, Xu Zou, Jin-Dong Shi, Pei-Zhen Lai, Ze-Guang Zheng, Nan-Shan Zhong Hydrogen/oxygen mixed gas inhalation improves disease severity and dyspnea in patients with Coronavirus disease 2019 in a recent multicenter, open-label clinical trial *J Thorac Dis* 2020;12(6):3448-3452

⁵⁰ <https://clinicaltrials.gov/ct2/show/NCT04336462>

⁵¹ S Westaby From Wuhan to Westminster: can NHS critical care cope with coronavirus? *The Bulletin of the Royal College of Surgeons of England* 2020 102:4, 120-125

⁵² <https://www.cebm.net/covid-19-registered-trials-and-analysis/?fbclid=IwAR2TnDjSpDYcrF-yeq3cv2wtLTfd7vbglo4VIT340tjz9-AN5BiRJJnp-z0>

⁵³ Nakayama M, Itami N, Suzuki H, et al. Novel haemodialysis (HD) treatment employing molecular hydrogen (H₂)-enriched dialysis solution improves prognosis of chronic dialysis patients: A prospective observational study. *Sci Rep.* 2018;8(1):254.

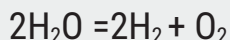
⁵⁴ Mizuno K, Sasaki AT, Ebisu K, et al. Hydrogen-rich water for improvements of mood, anxiety, and autonomic nerve function in daily life. *Med Gas Res.* 2018;7(4):247-255.

⁵⁵ Ishibashi T, Sato B, Shibata S, et al. Therapeutic efficacy of infused molecular hydrogen in saline on rheumatoid arthritis: a randomized, double-blind, placebo-controlled pilot study. *Int Immunopharmacol.* 2014;21(2):468-473

⁵⁶ Chen JB, Kong XF, Lv YY, Qin SC, Sun XJ, Mu F, Lu TY, Xu KC. "Real world survey" of hydrogen-controlled cancer: a follow-up report of 82 advanced cancer patients. *Med Gas Res.* 2019 Jul-Sep;9(3):115-121.

HOW MOLECULAR H₂ CAN BE OBTAINED

The best way to obtain H₂ is to electrolyse water. The water can split in to H₂ and O₂ on application of electricity. For large scale water electrolysis, generally a stack of electrodes were utilized. The water split in to molecular H₂ and O₂ gas by the following reactions:



Water splitting is a natural phenomenon, occurring on the plants with the light energy from sun providing glucose and O₂, termed as photosynthesis. This is the basic reason that the life exist in this planet. The machine exactly mimic plants provides H₂ and O₂. The main parts of the machine are (i)power supply, (ii) Stack, (iii) Water storage tank, (iv) non-returnable valve, (v) Bubbler.

(i) Power supply: As clear from the name, the power supply provides continuous DC voltage of 24V to the electrodes stack. The power supply also converts the 220 VAC to 24VDC by step-down transformer.

(ii) Stack: The stack of the electrode is the main part of this machine. Stack convert electrical voltage to chemical energy. H₂O is electrified and splitted to H₂ and O₂. 23 numbers of Stainless steel 317L electrode of size 5 inch×6 inch×1 mm is arranged parallely together to make a stack. The electrical insulation between electrodes was maintained by rubber gasket of thickness 6 mm.

(iii) Water tank: The water tank is mainly required to store the water and collect gas which can then flow through the channel to inhale.

(iv) Non_return valve: This valve ensures the molecular H₂ and O₂ flow only in one direction. This is the safety valve of the machine.

(v) Bubbler: The bubbler is required to bubble the molecular H₂ and O₂ and also works safety valve.



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