Molecular hydrogen (H_2) therapy — delivered via **hydrogen-rich water (HRW), gas inhalation, or H_2-saline infusion** — has the strongest clinical evidence for **exercise recovery, metabolic syndrome/lipid improvement, oxidative stress reduction, and radiation-induced side effects**, with emerging data in rheumatoid arthritis, cancer adjunctive care, and aging. H_2 is notable for its **excellent safety profile** and unique mechanism as a selective antioxidant that scavenges cytotoxic hydroxyl radicals while preserving physiologically important ROS.

Delivery Methods

H_2 can be administered through several routes: drinking hydrogen-rich water (most common and practical), inhaling H_2 gas (typically 2–4% concentration), intravenous H_2-saline infusion, and topical/bathing applications. Each route has distinct pharmacokinetics — inhalation provides rapid systemic delivery, while oral HRW has been shown to accumulate in hepatic glycogen, potentially explaining why even small amounts produce measurable effects.

Exercise Performance and Muscle Recovery — Most Consistent Human RCT Data

Multiple double-blind, placebo-controlled crossover trials demonstrate meaningful benefits:

- In resistance-trained men (n = 12), HRW (1,260 mL) **reduced blood lactate by 19–23%** during exercise ($p \leq 0.008$), improved lunge performance speed ($p < 0.001$), and decreased delayed-onset muscle soreness (DOMS) by **37%** at 24 hours (VAS 26 vs. 41 mm, $p = 0.002$).
- In elite fin swimmers (n = 12), 4 days of HRW supplementation **reduced creatine kinase by 18%** (156 vs. 190 U/L, $p = 0.043$), decreased muscle soreness by **19%** ($p = 0.045$), and improved countermovement jump height ($p = 0.014$) at 12 hours post-exercise.
- In trained men (n = 18), 8 days of HRW intake increased **total power output by 9.6%** ($p = 0.032$) and **total repetitions by 11.2%** ($p = 0.019$) during half-squat exercise to failure.

Metabolic Syndrome and Lipid/Glucose Metabolism

A meta-analysis of **7 clinical studies** found HRW consumption produced significant reductions in **total cholesterol** (SMD −0.23), **LDL-cholesterol** (SMD −0.22), and **triglycerides** (SMD −0.38), all with p = 0.01.

Key individual trials:

- In 20 patients with potential metabolic syndrome, 10 weeks of HRW (0.9–1.0 L/day) significantly **decreased serum TC and LDL-C**, reduced apoB100 and apoE, and improved HDL functionality across four independent assays (LDL oxidation protection, monocyte adhesion inhibition, cholesterol efflux stimulation, and endothelial cell protection).
- In 36 patients with type 2 diabetes or impaired glucose tolerance, 8 weeks of HRW (900 mL/day) improved electronegative LDL-cholesterol, small dense LDL, and urinary 8-isoprostanes. Notably, **4 of 6 patients with impaired glucose tolerance had normalized oral glucose tolerance tests**.
- In 73 patients with impaired fasting glucose, 8 weeks of HRW (1,000 mL/day) produced significantly greater fasting glucose reduction than placebo, with **62.5% achieving fatty liver remission** (vs. 31.6% in controls), accompanied by favorable gut microbiota modulation.
- In 181 subjects with metabolic syndrome, 3 months of electrolyzed hydrogen water combined with high physical activity produced a **significant reduction in waist circumference** compared to controls, with trends toward improved HbA1c, blood glucose, and oxidative stress markers.

Oxidative Stress and Inflammation — Foundational Mechanism

A randomized controlled study (n = 37) demonstrated that a single session of hydrogen inhalation therapy produced a **significant reduction in blood reactive oxygen species** (d-ROMs) levels in participants with elevated baseline ROS, with effects persisting at 24 hours.

In healthy adults (n = 38), a double-blind RCT showed 4 weeks of HRW (1.5 L/day) significantly **reduced PBMC apoptosis**, decreased $CD14^+$ monocyte frequency, and — via RNA-sequencing — demonstrated clearly distinct transcriptomes with **significant downregulation of inflammatory response and NF-κB signaling networks**.

The selective antioxidant mechanism is central to H_2's appeal: unlike conventional antioxidants, H_2 preferentially scavenges the highly cytotoxic hydroxyl radical (•OH) and peroxynitrite ($ONOO^-$) while **preserving physiologically important ROS** (H_2O_2, NO, O_2^-) needed for normal cell signaling.

Rheumatoid Arthritis

A randomized, double-blind, placebo-controlled pilot study (n = 24) of IV H_2-saline infusion (500 mL daily × 5 days) in RA patients showed the H_2 group's **DAS28 decreased from 5.18 to 3.74** at 4 weeks (from high to moderate disease activity), while the placebo group showed no significant change. IL-6 decreased by **37.3%**, MMP-3 by **19.2%**, and urinary 8-OHdG by **4.7%** in the H_2 group. An earlier open-label study found that drinking HRW (530 mL/day × 4 weeks) in 20 early RA patients achieved disease remission (DAS28 < 2.6) in a subset, with the effect most pronounced in early-stage disease.

Cancer — Adjunctive Therapy

Clinical evidence remains early-stage but notable:

- A survey of **82 advanced cancer patients** found H_2 inhalation helped control cancer progression and improve quality of life.
- In **55 stage IV colorectal cancer patients**, H_2 inhalation enhanced mitochondrial activity via PGC-1α activation and **reduced the proportion of terminal PD-1$^+$ CD8$^+$ T cells** — a marker associated with improved cancer prognosis.
- A pilot RCT in head and neck cancer patients undergoing radiotherapy/CCRT found HRW gargling significantly **improved oral mucositis at Day 7 (p = 0.04) and Day 14 (p = 0.002)**, reduced pain at Day 14 (p = 0.02), and improved quality of life (p = 0.03).
- H_2 has been shown to reduce side effects of cisplatin and radiotherapy in preclinical models, with the mechanism attributed to selective scavenging of radiation-generated hydroxyl radicals.

Aging and Neuroprotection

A 6-month RCT in **40 older adults (≥70 years)** found HRW (0.5 L/day, 15 ppm) produced a significant **increase in telomere length** (p = 0.049) — telomeres

lengthened in the HRW group while shortening in controls. HRW also significantly increased TET2 expression (an epigenetic regulator, $p = 0.040$), improved brain choline and NAA levels on MRS ($p < 0.05$), and enhanced chair stand performance ($p = 0.01$).

For neurodegenerative diseases, clinical data remain limited. In patients with mild cognitive impairment, H_2 did not change overall ADAS-cog scores at 1 year, but among **APOE4 carriers, 6 of 7 subjects showed improved cognitive scores** — suggesting a genotype-specific benefit.

Skin and Wound Healing

A pilot clinical study (n = 15) of topical HRW application for 4 weeks showed significant reduction in pore visibility, with trends toward improved pigmentation, wrinkle severity, and estimated biological skin age. In animal models, HRW dressing significantly accelerated wound closure in both diabetic and non-diabetic rats, with reduced TNF-α and IL-6 levels.

Cardiovascular Protection

Preclinical and mechanistic evidence supports H_2's cardioprotective effects through anti-inflammatory, antioxidant, and anti-apoptotic pathways, with demonstrated benefits in ischemia-reperfusion injury, atherosclerosis, and radiation-induced cardiac damage models. However, large-scale human cardiovascular outcome trials are lacking.

Safety Profile

H_2 therapy has an **exceptionally favorable safety profile**. Across all reviewed clinical studies and delivery methods, **no serious adverse effects have been reported**. H_2 is mild enough to neither disturb metabolic redox reactions nor affect signaling ROS, and it rapidly diffuses through tissues without residue. H_2 gas is non-flammable below 4% concentration in air at room temperature. The primary safety consideration for inhalation is maintaining concentrations below the flammability threshold.

References

Ahmad, A., Baig, A. A., Hussain, M., Saeed, M. U., Bilal, M., Ahmed, N., Chopra, H., Hassan, M., Rachamalla, M., Putnala, S. K., Khaliq, M., Tahir, Z., & Kamal, M. A. (2022). Narrative on Hydrogen Therapy and its Clinical Applications: Safety and Efficacy. *Current pharmaceutical design*, *28*(31), 2519–2537. https://doi.org/10.2174/1381612828666220728104200

Botek, M., Krejčí, J., McKune, A., Valenta, M., & Sládečková, B. (2022). Hydrogen Rich Water Consumption Positively Affects Muscle Performance, Lactate Response, and Alleviates Delayed Onset of Muscle Soreness After Resistance Training. *Journal of strength and conditioning research*, *36*(10), 2792–2799. https://doi.org/10.1519/JSC.0000000000003979

Chair, M., AlAani, H., Lafci Fahrioglu, S., Ben Hamda, C., Fahrioglu, U., & Degheidy, T. (2024). The impact of hydrogen inhalation therapy on blood reactive oxygen species levels: A randomized controlled study. *Free radical biology & medicine*, *222*, 601–606. https://doi.org/10.1016/j.freeradbiomed.2024.07.010

Debkowska, N., Niczyporuk, M., Surazynski, A., & Wolosik, K. (2025). Topically Applied Molecular Hydrogen Normalizes Skin Parameters Associated with Oxidative Stress: A Pilot Study. *Antioxidants (Basel, Switzerland)*, *14*(6), 729. https://doi.org/10.3390/antiox14060729

Deniz, M., Akkuş, Y., Yıldız, G., Havadar, H. B., & Makav, M. (2026). Effect of hydrogen-enriched water on healing of excisional full-layer skin wounds in diabetic and non-diabetic rats. *Naunyn-Schmiedeberg's archives of pharmacology*, *399*(1), 561–580. https://doi.org/10.1007/s00210-025-04427-x

Fu, Zhiling, Zhang, Jin, Zhang, Yan, Role of Molecular Hydrogen in Ageing and Ageing-Related Diseases, Oxidative Medicine and Cellular Longevity, 2022, 2249749, 17 pages, 2022. https://doi.org/10.1155/2022/2249749

Hu, Q., Zhou, Y., Wu, S., Wu, W., Deng, Y., & Shao, A. (2020). Molecular hydrogen: A potential radioprotective agent. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie*, *130*, 110589. https://doi.org/10.1016/j.biopha.2020.110589

Ishibashi T. (2013). Molecular hydrogen: new antioxidant and anti-inflammatory therapy for rheumatoid arthritis and related diseases. *Current pharmaceutical design*, *19*(35), 6375–6381. https://doi.org/10.2174/13816128113199990507

Ishibashi, T., Sato, B., Shibata, S., Sakai, T., Hara, Y., Naritomi, Y., Koyanagi, S., Hara, H., & Nagao, T. (2014). Therapeutic efficacy of infused molecular hydrogen in saline on rheumatoid arthritis: a randomized, double-blind, placebo-controlled pilot study. *International immunopharmacology*, *21*(2), 468–473. https://doi.org/10.1016/j.intimp.2014.06.001

Kamimura, N., Nishimaki, K., Ohsawa, I., & Ohta, S. (2011). Molecular hydrogen improves obesity and diabetes by inducing hepatic FGF21 and stimulating energy metabolism in db/db mice. *Obesity (Silver Spring, Md.)*, *19*(7), 1396–1403. https://doi.org/10.1038/oby.2011.6

Kura, B., Pavelkova, P., Kalocayova, B., Sykora, M., Vlkovicova, J., Kluknavsky, M., LeBaron, T., Pobijakova, M., Sagatova, A., & Slezak, J. (2026). Comparison of hydrogen administration methods in the treatment of radiation-induced heart disease in rats. *Canadian journal of physiology and pharmacology*, *104*, 1–13. https://doi.org/10.1139/cjpp-2025-0085

Li, Yujie, Shen, Chengcheng, Zhou, Xin, Zhang, Jianghe, Lai, Xiaoyue, Zhang, Yiming, Local Treatment of Hydrogen-Rich Saline Promotes Wound Healing In Vivo by Inhibiting Oxidative Stress via Nrf-2/HO-1 Pathway, Oxidative Medicine and Cellular Longevity, 2022, 2949824, 13 pages, 2022. https://doi.org/10.1155/2022/2949824

Liang, B., Shi, L., Du, D., Li, H., Yi, N., Xi, Y., Cui, J., Li, P., Kang, H., Noda, M., Sun, X., Liu, J., Qin, S., & Long, J. (2023). Hydrogen-Rich Water Ameliorates Metabolic Disorder via Modifying Gut Microbiota in Impaired Fasting Glucose Patients: A Randomized Controlled Study. *Antioxidants (Basel, Switzerland)*, *12*(6), 1245. https://doi.org/10.3390/antiox12061245

Moribe, R., Minami, M., Hirota, R., J-P, N. A., Kabayama, S., Eitoku, M., Yamasaki, K., Kuroiwa, H., & Suganuma, N. (2024). Health Effects of Electrolyzed Hydrogen Water for the Metabolic Syndrome and Pre-Metabolic Syndrome: A 3-Month Randomized Controlled Trial and Subsequent Analyses. *Antioxidants (Basel, Switzerland)*, *13*(2), 145. https://doi.org/10.3390/antiox13020145

Nguyen Puente, B., Habet, V., Wheeler, C. R., & Kheir, J. N. (2026). Emerging Clinical Applications for Molecular Hydrogen. *Respiratory care*, *71*(3), 328–338. https://doi.org/10.1177/19433654251398759

Nguyen, L. D., Peng, S. Y., Mac, C. H., Nguyen, N., Lo, S. K., Lin, P. H., Pham, N. S., Chang, H. H., Lin, Y. J., & Sung, H. W. (2026). Advances in hydrogen delivery strategies for therapeutic applications. *Advanced drug delivery reviews*, *228*, 115734. https://doi.org/10.1016/j.addr.2025.115734

Ohno, Kinji, Ito, Mikako, Ichihara, Masatoshi, Ito, Masafumi, Molecular Hydrogen as an Emerging Therapeutic Medical Gas for Neurodegenerative and Other Diseases, Oxidative Medicine and Cellular Longevity, 2012, 353152, 11 pages, 2012. https://doi.org/10.1155/2012/353152

Ohta S. (2014). Molecular hydrogen as a preventive and therapeutic medical gas: initiation, development and potential of hydrogen medicine. *Pharmacology & therapeutics*, *144*(1), 1–11. https://doi.org/10.1016/j.pharmthera.2014.04.006

Saengsin, K., Sittiwangkul, R., Chattipakorn, S. C., & Chattipakorn, N. (2023). Hydrogen therapy as a potential therapeutic intervention in heart disease: from the past evidence to future application. *Cellular and molecular life sciences : CMLS*, *80*(6), 174. https://doi.org/10.1007/s00018-023-04818-4

Sim, M., Kim, C. S., Shon, W. J., Lee, Y. K., Choi, E. Y., & Shin, D. M. (2020). Hydrogen-rich water reduces inflammatory responses and prevents apoptosis of peripheral blood cells in healthy adults: a randomized, double-blind, controlled trial. *Scientific reports*, *10*(1), 12130. https://doi.org/10.1038/s41598-020-68930-2

Sládečková, B., Botek, M., Krejčí, J., Valenta, M., McKune, A., Neuls, F., & Klimešová, I. (2024). Hydrogen-rich water supplementation promotes muscle recovery after two strenuous training sessions performed on the same day in elite fin swimmers: randomized, double-blind, placebo-controlled, crossover trial. *Frontiers in physiology*, *15*, 1321160. https://doi.org/10.3389/fphys.2024.1321160

Slezak, J., Kura, B., LeBaron, T. W., Singal, P. K., Buday, J., & Barancik, M. (2021). Oxidative Stress and Pathways of Molecular Hydrogen Effects in Medicine. *Current pharmaceutical design*, *27*(5), 610–625. https://doi.org/10.2174/1381612826666200821114016

Song, G., Li, M., Sang, H., Zhang, L., Li, X., Yao, S., Yu, Y., Zong, C., Xue, Y., & Qin, S. (2013). Hydrogen-rich water decreases serum LDL-cholesterol levels and improves HDL function in patients with potential metabolic syndrome. *Journal of lipid research*, *54*(7), 1884–1893. https://doi.org/10.1194/jlr.M036640

Todorovic, N., Fernández-Landa, J., Santibañez, A., Kura, B., Stajer, V., Korovljev, D., & Ostojic, S. M. (2023). The Effects of Hydrogen-Rich Water on Blood Lipid Profiles in Clinical Populations: A Systematic Review and Meta-Analysis. *Pharmaceuticals (Basel, Switzerland)*, *16*(2), 142. https://doi.org/10.3390/ph16020142

Terasaki, Y., Terasaki, M., & Shimizu, A. (2021). Protective Effects of Hydrogen against Irradiation. *Current pharmaceutical design*, *27*(5), 679–686. https://doi.org/10.2174/1381612827666210119103545

Tian, Y., Zhang, Y., Wang, Y., Chen, Y., Fan, W., Zhou, J., Qiao, J., & Wei, Y. (2021). Hydrogen, a Novel Therapeutic Molecule, Regulates Oxidative Stress, Inflammation, and Apoptosis. *Frontiers in physiology*, *12*, 789507. https://doi.org/10.3389/fphys.2021.789507

Tsai, H. T., Huang, C. J., Wang, H. C., Luo, S. D., Rau, K. M., & Chou, P. L. (2026). Effects of Hydrogen Water Gargling on Oral Mucositis and Pain in Head and Neck Cancer Patients: A Randomized Controlled Pilot Study. *Integrative cancer therapies*, *25*, 15347354261463550. https://doi.org/10.1177/15347354261463550

Yang, Mengling, Dong, Yinmiao, He, Qingnan, Zhu, Ping, Zhuang, Quan, Shen, Jie, Zhang, Xueyan, Zhao, Mingyi, Hydrogen: A Novel Option in Human Disease Treatment, Oxidative Medicine and Cellular Longevity, 2020, 8384742, 17 pages, 2020. https://doi.org/10.1155/2020/8384742

Zanini, D., Todorovic, N., Korovljev, D., Stajer, V., Ostojic, J., Purac, J., Kojic, D., Vukasinovic, E., Djordjievski, S., Sopic, M., Guzonjic, A., Ninic, A., Erceg, S., & Ostojic, S. M. (2021). The effects of 6-month hydrogen-rich water intake on molecular and phenotypic biomarkers of aging in older adults aged 70 years and over: A randomized controlled pilot trial. *Experimental gerontology*, *155*, 111574. https://doi.org/10.1016/j.exger.2021.111574

Zhou, K., Yuan, C., Shang, Z., Jiao, W., & Wang, Y. (2024). Effects of 8 days intake of hydrogen-rich water on muscular endurance performance and fatigue recovery during resistance training. *Frontiers in physiology*, *15*, 1458882. https://doi.org/10.3389/fphys.2024.1458882