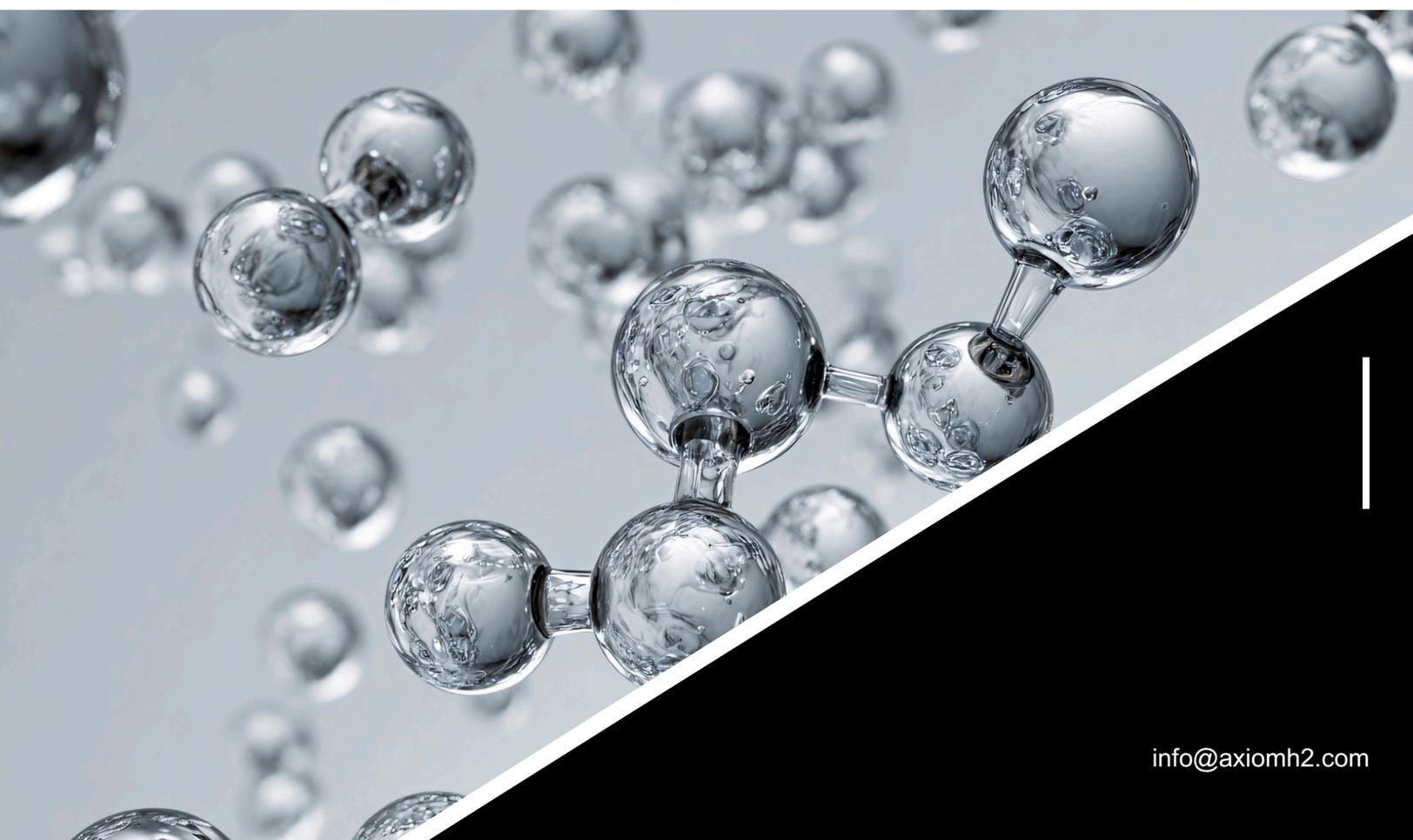




A X I O M H 2

**Axiom H2 - Molecular hydrogen therapy**  
Literature Review  
JAN 2026



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## 2. Introduction

Molecular hydrogen ( $H_2$ ) was long considered a biologically inert molecule with no functional relevance in the human body. This paradigm was challenged after experimental evidence demonstrated that  $H_2$  selectively reacts with highly cytotoxic reactive oxygen species, such as the hydroxyl radical ( $\bullet OH$ ) and peroxynitrite ( $ONOO^-$ ), acting as a preventive and therapeutic antioxidant. These findings established the foundation of a new research field known as *hydrogen medicine*, positioning molecular hydrogen as a bioactive molecule with significant clinical potential (Ohsawa et al., 2007; Ohta, 2014).

One of the main advantages of molecular hydrogen lies in its physicochemical properties. As the smallest molecule in nature,  $H_2$  rapidly diffuses across cell membranes and readily reaches subcellular compartments, including mitochondria and nuclei. Importantly, its antioxidant action is mild and selective, meaning it does not disrupt essential metabolic redox reactions or physiological reactive oxygen species signaling pathways. Consequently, molecular hydrogen exhibits a highly favorable safety profile, with minimal or no reported adverse effects (Ohta, 2014).

Several administration routes for  $H_2$  have been investigated, including inhalation of hydrogen gas, ingestion of hydrogen-rich water, intravenous or intraperitoneal injection of hydrogen-dissolved saline, as well as topical applications and hydrogen baths. Hydrogen gas inhalation represents a simple and rapidly acting therapeutic approach, particularly suitable for acute oxidative stress conditions, without inducing significant hemodynamic changes such as increased blood pressure. In contrast, hydrogen-rich water offers a portable, easy-to-administer, and safe method for regular  $H_2$  intake, facilitating both clinical and preventive applications (Ohsawa et al., 2007; Ohta, 2014).

From a mechanistic perspective, the biological effects of molecular hydrogen are not limited to the direct scavenging of potent oxidants. Evidence indicates that  $H_2$  also exerts indirect effects by modulating gene expression related to inflammation, apoptosis, and energy metabolism. Through these mechanisms, molecular hydrogen demonstrates anti-inflammatory and antiapoptotic properties while stimulating cellular energy metabolism, thereby contributing to the maintenance of cellular homeostasis (Ohta, 2014).

Oxidative stress plays a central role in the pathophysiology of numerous lifestyle-related chronic diseases, including diabetes mellitus, obesity, atherosclerosis, heart failure, and neurodegenerative disorders such as Alzheimer's and Parkinson's diseases. Experimental and clinical studies have shown that both



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inhalation of low concentrations (1–2%) of hydrogen gas and consumption of hydrogen-rich water effectively protect organs such as the brain, heart, liver, kidneys, and intestine against oxidative damage. Furthermore, molecular hydrogen has been shown to improve energy metabolism and regulate metabolic factors, including hepatic fibroblast growth factor 21 (FGF21), resulting in beneficial effects in obesity and diabetes models (Kamimura et al., 2011).

Unlike conventional pharmacological agents, which typically act on specific molecular targets, molecular hydrogen appears to exert pleiotropic and systemic effects. Its high therapeutic efficacy combined with an excellent safety profile supports the growing scientific and clinical interest in H<sub>2</sub> as a promising preventive and therapeutic agent for a wide range of diseases associated with oxidative stress and chronic inflammation.

### **3. Data acquisition and study selection**

Potentially eligible publications on molecular hydrogen–based therapies were identified through a systematic search of PubMed, conducted without time restrictions and using the “clinical trial” filter. The search strategy was: "molecular hydrogen"[Title/Abstract] OR "hydrogen gas"[Title/Abstract] OR "hydrogen-rich water"[Title/Abstract] OR "hydrogen water"[Title/Abstract] OR "H2 therapy"[Title/Abstract] OR "hydrogen inhalation"[Title/Abstract] OR "hydrogen therapy"[Title/Abstract].

Only clinical studies evaluating the health effects of these modalities were included. Publications were limited to articles published in English, Portuguese, Spanish, Italian, French, and German. The literature search was completed in December 2025.

## 4. Results

### 4.1. Number of publications retrieved for Molecular Hydrogen Therapy

The purpose of this literature review is to provide an updated summary of published clinical studies on this field.

**Table 1.** Search results

Keywords used	
("molecular hydrogen"[Title/Abstract] OR "hydrogen gas"[Title/Abstract] OR "hydrogen-rich water"[Title/Abstract] OR "hydrogen water"[Title/Abstract] OR "H2 therapy"[Title/Abstract] OR "hydrogen inhalation"[Title/Abstract] OR "hydrogen therapy"[Title/Abstract])	
Total retrieved	77
After duplicate exclusion	76
Included in this review	47

A total of 47 studies were identified and categorized according to their method of administration.

### 4.2. Summary of the retrieved publications on Hydrogen-rich Water

A total of 21 studies were found. More details are presented in Table 2.

1. **Kajiyama et al., 2008 [n= 30; males and females; mean age 58.6 ± 4.7 years]**, the aim of the study was to investigate the effects of hydrogen-rich water (HRW) intake on lipid and glycemic metabolism in patients with type 2 diabetes mellitus (T2DM) or impaired glucose tolerance (IGT). The intervention consisted of consuming 900 mL/day of HRW or placebo water for 8 weeks in a crossover design with a 12-week washout period. The results showed significant reductions in modified low-density lipoprotein cholesterol (LDL), small dense LDL, and urinary 8-isoprostanes, as well as trends toward decreased oxidized LDL and free fatty acids, and increased plasma adiponectin and extracellular superoxide dismutase; in 4 of 6 IGT patients, the oral glucose tolerance test (OGTT) normalized. The authors concluded that HRW supplementation may exert beneficial effects on oxidative stress, lipid metabolism, and insulin sensitivity, potentially contributing to the prevention of T2DM.

2. **Yoritaka et al., 2013 [n= 17; males and females; mean age 60.1 ± 10.6/ 65.2 ± 8.5 years]**, the aim of the study was to evaluate the efficacy of hydrogen water (HW) intake in Japanese patients with Parkinson's disease receiving levodopa. The intervention consisted of daily consumption of 1,000 mL of HW or pseudo-water (placebo) for 48 weeks. The results showed improvement in total Unified Parkinson's Disease Rating Scale (UPDRS) scores in the HW group, whereas scores worsened in the placebo group, with a statistically significant between-group difference ( $P < 0.05$ ). The authors concluded that HW intake was safe and well tolerated and was associated with a significant improvement in total UPDRS scores in patients with Parkinson's disease.
3. **Matsumoto et al., 2013 [n= 30; males and females; mean age 65.2 ± 7.9 / 64.5 ± 4.5 years]**, the aim of the study was to investigate the efficacy of hydrogen-rich water (HRW) in the treatment of patients with interstitial cystitis/painful bladder syndrome (IC/PBS). The intervention consisted of HRW or placebo water intake for 8 weeks in a randomized 2:1 design, with symptom assessment using the Interstitial Cystitis Symptom Index (ICSI), Interstitial Cystitis Problem Index (ICPI), Parsons Pelvic Pain and Urgency/Frequency Scale, visual analog scale (VAS) for bladder pain, and a 3-day voiding diary. The results showed a significant reduction in bladder pain in both groups, with no significant differences between HRW and placebo in overall outcomes, although 11% of patients receiving HRW exhibited marked improvement in bladder pain. The authors concluded that the findings do not support the use of HRW supplementation for the treatment of IC/PBS.
4. **Xia et al., 2013 [n= 60; males and females; mean age 36.8 ± 15.2/ 35.3 ± 11.1 years]**, the aim of the study was to investigate the effects of hydrogen-rich water (HRW) on oxidative stress, liver function, and hepatitis B virus (HBV) DNA levels in patients with chronic hepatitis B (CHB). The intervention consisted of routine treatment alone or routine treatment combined with oral intake of hydrogen-distilled water (HDW; 1200–1800 mL/day) for 6 consecutive weeks in a randomized design, with healthy individuals serving as controls. The results showed that oxidative stress remained unchanged in the routine-treatment group but was significantly reduced in the hydrogen-treated group; liver function and HBV DNA levels decreased after both treatments, with no significant between-group differences after intervention. The authors concluded that HRW significantly attenuates oxidative stress in patients with CHB, while longer-term studies are required to confirm its effects on liver function and HBV DNA levels.
5. **Tan et al., 2014 [n= 32; males and females; mean age 23 ± 3 years]**, the aim of the study was to investigate the impact of hydrogen-rich water (HRW) intake on fatigue and dyspnea in patients with long COVID. The intervention consisted of daily consumption of HRW or placebo water (PW) for 14 consecutive days in a randomized design. The results showed that HRW significantly reduced Fatigue Severity Scale (FSS) scores and improved performance in the Six-Minute Walk Test (6MWT), the 30-Second Chair Stand Test (30s-CST), and the Pittsburgh Sleep Quality Index (PSQI), with no significant effects on the Modified Medical Research Council Dyspnea Scale (mMRC) or the Depression, Anxiety and Stress Scale (DASS-21). The authors concluded that HRW may be an effective strategy to alleviate fatigue and improve functional capacity and sleep quality in patients with long COVID, although it does not significantly improve dyspnea.

6. **Sakai et al., 2014 [n= 34; males and females; mean age 37.7 ± 7.60 years]**, the objective of the study was to evaluate the influence of the hydroxyl radical on endothelial function and to investigate whether molecular hydrogen (H<sub>2</sub>), a gaseous antioxidant, can modulate vascular function. The intervention consisted of ingestion of molecular hydrogen-rich water (H<sub>2</sub>) (7 ppm; 3.5 mg of H<sub>2</sub> in 500 mL), compared with placebo, with assessment of flow-mediated dilation (FMD) of the brachial artery (BA). The results showed that FMD significantly increased in the H<sub>2</sub> group (6.80% ± 1.96% to 7.64% ± 1.68%) and decreased in the placebo group (8.07% ± 2.41% to 6.87% ± 2.94%), with a significant improvement in the change ratio relative to baseline in the H<sub>2</sub> group (p < 0.05). The authors concluded that H<sub>2</sub> may protect the vascular system against reactive oxygen species (ROS), such as the hydroxyl radical, by preserving nitric oxide-mediated vasomotor responses.
7. **Da Ponte et al., 2018 [n= 8; males; mean age 41 ± 7 years]**, the aim of the study was to investigate the effect of two weeks of hydrogen-rich water (HRW) ingestion on repeated sprint performance and acid-base balance during prolonged intermittent cycling exercise. The intervention consisted of daily consumption of 2 L of HRW (pH 9.8; oxidation-reduction potential, ORP -180 mV; free hydrogen 450 ppb) or placebo water (PLA; pH 7.6; ORP +230 mV; free hydrogen 0 ppb), using a randomized, counterbalanced design over 2-week periods. The results showed that peak power output (PPO) declined significantly in the final sprints in the PLA group, while remaining unchanged in the HRW group; no between-group differences were observed for mean power, fatigue index (FI), time to peak power, or total work, and both conditions exhibited increased lactate and progressive reductions in pH and bicarbonate (HCO<sub>3</sub><sup>-</sup>). The authors concluded that two weeks of HRW intake may help maintain PPO during repeated sprints to exhaustion in prolonged intermittent exercise.
8. **Korovljev et al., 2019 [n= 12; males and females; mean age 56.2 ± 10.0 years]**, the objective of this study was to analyze the effects of hydrogen-rich water (HRW) ingestion for 28 days on hepatic fat deposition, body composition, and laboratory biochemical profiles in overweight patients with mild to moderate non-alcoholic fatty liver disease (NAFLD). The intervention consisted of daily intake of 1 L of HRW or placebo water for 28 days in overweight outpatients (body mass index, BMI: 37.7 ± 5.3 kg/m<sup>2</sup>). The results showed that HRW significantly reduced hepatic fat accumulation assessed by dual-echo magnetic resonance imaging, with liver fat content decreasing from 284.0 ± 118.1 mM to 256.5 ± 108.3 mM after 28 days, along with a 10.0% reduction in serum aspartate aminotransferase (AST) levels, while no significant changes were observed in body weight or body composition. The authors concluded that, although preliminary, these findings suggest HRW as a potential adjunctive therapy for mild to moderate NAFLD, warranting further clinical trials to establish the safety and efficacy of molecular hydrogen.
9. **Botek et al., 2019 [n= 12; males and females; mean age 27.1 ± 4.9 years]**, the objective of this study was to evaluate physiological and perceptual responses to an incremental exercise protocol following acute ingestion of hydrogen-rich water (HRW). The intervention consisted of consuming 600 mL of HRW or placebo within 30 minutes before exercise, which included a 10-minute warm-up at 1.0 W·kg<sup>-1</sup> followed by 8-minute

stages at 2.0, 3.0, and 4.0 W·kg<sup>-1</sup>, with assessment of cardiorespiratory variables, blood lactate, and rating of perceived exertion (RPE). The results showed significantly lower blood lactate levels with HRW compared with placebo at 3.0 and 4.0 W·kg<sup>-1</sup>, as well as lower ventilatory equivalent for oxygen and RPE at the highest exercise intensity. The authors concluded that acute pre-exercise supplementation with HRW reduced blood lactate at higher exercise intensities, improved exercise-induced perceived exertion, and enhanced ventilatory efficiency.

10. **Sim et al., 2020 [n= 38; males and females; mean age 32.9 ± 10.9/ 29.6 ± 8.1 years]**, the aim of the study was to investigate the effects of hydrogen water (HW) consumption on oxidative stress and immune functions in healthy adults. The intervention consisted of consuming 1.5 L/day of HW or pure water (PW) for 4 weeks. The results showed no overall differences between groups in changes in serum biological antioxidant potential (BAP), reactive oxygen species–derived products, or 8-oxo-2'-deoxyguanosine; however, in participants aged ≥ 30 years, BAP increased more in the HW group. In addition, peripheral blood mononuclear cell (PBMC) apoptosis was lower, CD14<sup>+</sup> cell frequency decreased, and RNA sequencing (RNA-seq) revealed distinct transcriptomic profiles, with reduced inflammatory networks and nuclear factor kappa B (NF-κB) signaling in the HW group. The authors concluded that HW enhances antioxidant capacity and attenuates inflammatory responses in healthy adults.
11. **Ooi et al., 2020 [n= 14; males; mean age 34 ± 4 years]**, the objective of this study was to investigate the effects of hydrogen-rich water (H<sub>2</sub> water) ingestion on physiological responses and performance during an incremental treadmill test in endurance-trained runners. The intervention consisted of ingesting two 290 mL doses of H<sub>2</sub> water or placebo, with the first dose administered before six 4-minute bouts of submaximal running and the second before a maximal incremental run to exhaustion, while expired gases, heart rate (HR), rating of perceived exertion (RPE), and blood gas indices were assessed. The results showed no significant differences between H<sub>2</sub> water and placebo in cardiorespiratory responses, RPE, or blood gas parameters across submaximal intensities (34% to 91% of maximal oxygen uptake, VO<sub>2</sub>max), nor in time to exhaustion, VO<sub>2</sub>max, maximal HR, or RPE during the maximal test. The authors concluded that acute ingestion of H<sub>2</sub> water at the tested doses was not ergogenic and did not modulate buffering capacity or endurance exercise performance in trained athletes.
12. **Hori et al., 2020 [n= 29; males and females; mean age 19.9 ± 0.4/ 20.3 ± 0.4/ 20.4 ± 1.5 years]**, the objective of this study was to investigate whether acute or continuous ingestion of hydrogen-rich water (HRW) for two weeks increases aerobic capacity during incremental exercise in healthy individuals. The intervention consisted of incremental cycling tests to assess maximal oxygen uptake (VO<sub>2</sub>max) and maximal workload before and after a single 500 mL dose of HRW or after continuous supplementation for two weeks (total of 5 L; 500 mL consumed on 10 occasions). The results showed that single HRW ingestion did not significantly affect VO<sub>2</sub>max, maximal workload, blood lactate, oxidative stress markers, or antioxidant activity; in contrast, continuous HRW intake for two weeks significantly increased VO<sub>2</sub>max and tended to increase maximal workload, without changes in lactate levels, oxidative stress, or antioxidant responses. The authors concluded that continuous HRW supplementation may enhance aerobic capacity,

- suggesting a potential contribution to improved aerobic exercise performance and physical health.
13. **Ishibashi et al., 2020 [n= 68; males and females; mean age 37.3 ± 10.7 years]**, the objective of this study was to investigate the effect of molecular hydrogen (H<sub>2</sub>) on reactive hyperemia assessed by the reactive hyperemia index (RHI), measured using peripheral arterial tonometry (PAT), in healthy individuals. The intervention consisted of ingestion of high-concentration H<sub>2</sub> water (7 ppm; 3.5 mg of H<sub>2</sub> in 500 mL) or placebo water containing molecular nitrogen (N<sub>2</sub>), with assessment of the natural logarithm of the reactive hyperemia index (Ln\_RHI) at baseline, 1 h and 24 h after the first intake, and after 14 days of daily consumption, in a randomized trial including 68 volunteers and analyzed using a mixed-effects model for repeated measures. The results showed that the H<sub>2</sub> group exhibited significantly greater improvements in Ln\_RHI compared with placebo, with increases of 22.2% at 24 h and 25.4% after two weeks of daily intake ( $p < 0.05$ ). The authors concluded that continuous consumption of high-concentration H<sub>2</sub> water improves endothelial function of peripheral arteries and arterioles, suggesting a beneficial contribution to cardiovascular health.
  14. **Zanini et al., 2021 [n= 40; males and females; mean age 76.0 ± 5.6 years]**, the aim of the study was to investigate the effects of hydrogen-rich water (HRW) intake over 6 months on molecular and phenotypic aging biomarkers in adults aged 70 years or older. The intervention consisted of daily consumption of 0.5 L of HRW (15 ppm hydrogen) or a control beverage (0 ppm hydrogen) in a randomized parallel-group design. The results showed a significant treatment-by-time interaction for telomere length, with an increase in the HRW group and a decrease in the control group, as well as a greater increase in Tet methylcytosine dioxygenase 2 (TET2) expression in the HRW group; increases in choline, N-acetylaspartate (NAA), and creatine in specific brain regions and improved chair-stand test performance were also observed, with no significant differences in other outcomes. The authors concluded that HRW may act as a potential anti-aging agent, being associated with telomere preservation, epigenetic modulation, and functional improvements in older adults.
  15. **Hong et al., 2021 [n= 18; males and females; mean age 67.53 ± 8.83 years]**, the objective of this study was to determine the safety and efficacy of photobiomodulation (PBM) combined with molecular hydrogen (H<sub>2</sub>) in patients with Parkinson's disease (PD). The intervention consisted of daily PBM + H<sub>2</sub> therapy for two weeks in patients with PD at Hoehn and Yahr stages II–III, with monitoring of adverse events and clinical assessment using the Unified Parkinson's Disease Rating Scale (UPDRS). The results showed that UPDRS scores decreased significantly from the first week of treatment and remained reduced until the end of therapy, with no adverse events reported; one week after discontinuation, scores slightly increased but remained significantly improved compared with baseline. The authors concluded that this proof-of-concept study demonstrates that combined PBM + H<sub>2</sub> therapy is safe and reduces disease severity, supporting the need for larger-scale clinical trials.
  16. **Valenta et al., 2022 [n= 24; males; mean age 17.5 ± 1.8 years]**, the objective of this study was to investigate the effects of acute hydrogen-rich water (HRW) ingestion before exercise on time to exhaustion at maximal aerobic speed (MAS) in trained track-and-

field runners. The intervention consisted of ingesting a total of 1,260 mL of HRW or placebo, divided into four doses administered 120, 60, 30, and 10 minutes before exercise, followed by a running protocol including warm-up, transition, and running at individual MAS until exhaustion, with assessment of time to exhaustion, cardiorespiratory variables, and post-exercise blood lactate. The results showed that HRW had no significant effects compared with placebo on time to exhaustion, blood lactate concentration, maximal heart rate, or oxygen uptake, and no potential moderating variables were significantly correlated with performance. The authors concluded that acute pre-exercise HRW ingestion does not exert an ergogenic effect on running performance to exhaustion at MAS in trained runners.

17. **Botek et al., 2022a [n= 16; males; mean age 18.8 ± 1.2 years]**, the objective of this study was to evaluate the effect of pre-exercise hydrogen-rich water (HRW) ingestion on repeated sprint performance, blood lactate levels, and rating of perceived exertion (RPE) in professional soccer players. The intervention consisted of ingesting HRW or placebo before completing a repeated sprint protocol of 15 × 30 m sprints on an indoor track, interspersed with 20 s recovery, using a crossover design with a one-week washout period; sprint times were recorded at 15 m and 30 m, RPE was assessed after each sprint, and post-exercise blood lactate was measured after the final sprint. The results showed significantly improved sprint performance with HRW compared with placebo, with faster 15 m sprint times in the 14th and 15th sprints (3.4% and 2.7%, respectively) and faster 30 m sprint time in the final sprint (1.9%), while blood lactate concentrations and RPE did not differ between conditions. The authors concluded that pre-exercise HRW supplementation is associated with enhanced fatigue resistance, particularly during the later stages of repeated sprint exercise.
18. **Botek et al., 2022b [n= 12; males; mean age 18.8 ± 1.2 years]**, the objective of this study was to evaluate the effects of acute ingestion of 1,260 mL of hydrogen-rich water (HRW) on physiological, perceptual, and performance responses during resistance training and after 24 hours of recovery in men. The intervention consisted of consuming HRW or placebo before a resistance training protocol including half-squat, knee flexion and extension at 70% of one-repetition maximum (1RM) for three sets of 10 repetitions, and lunges at 30% of body mass for three sets of 20 repetitions, with assessment of set duration, blood lactate, and rating of perceived exertion (RPE), as well as creatine kinase, delayed-onset muscle soreness assessed by the visual analog scale (VAS), countermovement jump, and heart rate variability during recovery. The results showed that lunges were performed faster with HRW, blood lactate levels were significantly lower during and immediately after exercise, and VAS pain scores were significantly reduced 24 hours into recovery compared with placebo. The authors concluded that acute intermittent hydration with HRW improves muscle function, reduces lactate responses, and alleviates delayed-onset muscle soreness following resistance training.
19. **Najmanová et al., 2023 [n= 24; males and females; mean age 23 ± 3 years]**, the aim of the study was to evaluate the intraocular pressure (IOP) response to acute ingestion of hydrogen-rich water (HRW) compared with hydrogen-free water (placebo), as well as to monitor central corneal thickness (CCT) in healthy individuals. The intervention consisted of acute ingestion of 1260 mL of HRW or placebo over 15 minutes in a

randomized crossover design, with IOP and CCT measured for up to 75 minutes. The results showed a significant increase in IOP after both HRW and placebo, with no difference in mean IOP between groups; however, clinically relevant IOP increases were more frequent after HRW (58%) than placebo (25%), while CCT remained unchanged. The authors concluded that acute HRW ingestion may induce clinically relevant IOP increases in healthy individuals, suggesting potential risk that warrants further investigation in high-risk populations such as glaucoma and ocular hypertension.

20. **Aker et al., 2024 [n= 65; females; mean age 20.60 ± 1.129 years]**, the objective of this study was to investigate the effect of hydrogen-rich water (HRW) ingestion on the severity of premenstrual syndrome (PMS) symptoms and quality of life in affected women. The intervention consisted of a block-randomized controlled trial in which the intervention group consumed 1,500–2,000 mL of HRW daily, while the control group consumed placebo water, from day 16 of the menstrual cycle until day 2 of the subsequent cycle, for three consecutive cycles, with assessments using the Premenstrual Syndrome Scale (PMSS) and the World Health Organization Quality of Life Questionnaire – Brief version (WHOQOL-BREF). The results showed that the HRW group had significantly lower PMSS scores at both follow-ups ( $p < 0.05$ ), as well as significantly higher scores in the Physical Health and Psychological domains of the WHOQOL-BREF at the first follow-up ( $p < 0.05$ ), with a significant group  $\times$  time interaction for PMSS ( $F = 10.54$ ;  $p < 0.001$ ). The authors concluded that HRW consumption reduces the severity of premenstrual symptoms and improves quality of life, particularly in the physical and psychological domains.
21. **Todorovic et al., 2025 [n= 36; males and females; mean age 42.1 ± 13.2 years]**, the aim of the study was to evaluate the effects of molecular hydrogen ( $H_2$ ) supplementation on appetite, body composition, sleep quality, obesity-specific quality of life, and related biomarkers in obese men and women. The intervention consisted of daily consumption of 1.0 L of hydrogen-rich water (HRW; 15 mg  $H_2$ ) or control water (0 mg  $H_2$ ) for eight weeks in a randomized design. The results showed that HRW significantly reduced food cravings, improved subjective sleep quality, decreased total cholesterol and low-density lipoprotein cholesterol (LDL), and increased plasma glucagon-like peptide-1 (GLP-1) levels, with no serious adverse events reported. The authors concluded that HRW may serve as a safe and effective dietary strategy to regulate appetite and obesity-related metabolic parameters.

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### 4.3 Summary of the publications retrieved on Hydrotherapy with Hydrogen-enriched Water

A total of 1 study were found. More details are presented in Table 3.

1. **Javorac et al., 2021 [n= 18; males; mean age 23.7 ± 4.0 years]**, the objective of the study was to evaluate the effects of an experimental intensive hydrotherapy protocol using hydrogen-rich water (HRW) on recovery following acute ankle sprain (AAS) in male athletes, compared with the conventional RICE protocol (Rest, Ice, Compression, and Elevation). The intervention consisted of six 30-minute ankle baths with HRW administered every 4 hours during the first 24 hours after injury, while the control group followed the standard RICE protocol. The results showed that the HRW protocol was equivalent to RICE in reducing ankle edema, restoring range of motion, and improving single-leg balance with eyes open and closed, with no statistically significant differences between groups. The authors concluded that hydrogen-rich water hydrotherapy represents an effective and non-inferior alternative to RICE for the management of acute ankle sprain, although further studies are required to confirm its efficacy in other soft tissue injuries.

#### 4.4 Summary of the publications retrieved on Summary of the retrieved publications on Hydrogen Inhalation

A total of 17 studies were found. More details are presented in Table 4.

1. **Tamasawa et al., 2015 [n= 16; males and females; mean age 52.17 ± 15.4 years]**, the objective of the study was to investigate the effects of a single dose of acarbose, an  $\alpha$ -glucosidase inhibitor, on postprandial hydrogen gas ( $H_2$ ) production in expired air and on interleukin-1 beta (IL-1 $\beta$ ) mRNA expression in peripheral blood of Japanese patients with type 2 diabetes mellitus (T2DM). The intervention consisted of administering acarbose immediately before a test meal, comparing one day without acarbose and one day with acarbose, using continuous glucose monitoring (CGM), measurement of expired  $H_2$ , and assessment of IL-1 $\beta$  mRNA expression. The results showed that neither  $H_2$  production nor IL-1 $\beta$  mRNA levels differed significantly between days with and without acarbose; however, individual increases in total  $H_2$  production were inversely associated with changes in peripheral blood IL-1 $\beta$  mRNA expression. The authors concluded that increased endogenous hydrogen gas production following a single dose of acarbose may be associated with reduced IL-1 $\beta$  expression, suggesting a potential hydrogen-mediated anti-inflammatory effect in patients with T2DM.
2. **Tamura et al., 2016 [n= 5; males and females; mean age 65 ± 15 years]**, the objective of the study was to evaluate the feasibility and safety of hydrogen gas inhalation (HI) in patients with post-cardiac arrest syndrome (PCAS) following out-of-hospital cardiac arrest with return of spontaneous circulation (ROSC). The intervention consisted of intermittent hypoxia (IH) combined with targeted temperature management (TTM) during post-resuscitation intensive care. The results showed that no adverse effects attributable to IH were observed, and four patients survived for 90 days with favorable neurological outcomes. The authors concluded that IH combined with TTM is a feasible therapeutic approach for patients with PCAS.
3. **Ono et al., 2017 [n= 50; males and females; mean age 76.0/ 73.3 years]**, the objective of the study was to evaluate the safety and efficacy of molecular hydrogen ( $H_2$ ) inhalation in patients with acute cerebral infarction of mild to moderate severity, as assessed by the National Institutes of Health Stroke Scale (NIHSS; scores 2–6). The intervention consisted of inhalation of 3%  $H_2$  gas twice daily for 1 hour over 7 days, compared with conventional intravenous therapy, within a therapeutic window of 6 to 24 hours after stroke onset. The results showed no significant adverse effects, improvement in oxygen saturation, reduced relative signal intensity on magnetic resonance imaging (MRI), improvement in NIHSS scores, and enhanced functional outcomes assessed by the Barthel Index. The authors concluded that  $H_2$  inhalation is safe and effective in acute cerebral infarction and may have potential for broad clinical application.
4. **Katsumata et al., 2017 [n= 20; males and females; mean age 50.7 ± 8.6/ 60.0 ± 11.4 years]**, the objective of the study was to evaluate the feasibility, safety, and potential effects of intermittent hypoxia with molecular hydrogen (HI;  $H_2$ ) during percutaneous

coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI). The intervention consisted of inhalation of a gas mixture containing 1.3% H<sub>2</sub> with 26% oxygen in the HI group, compared with 26% oxygen alone in the control group, administered during PCI. The results showed no serious adverse events related to HI and no significant difference in the myocardial salvage index assessed by cardiac magnetic resonance imaging 7 days after PCI; however, at 6-month follow-up, the HI group showed numerically greater improvements in left ventricular (LV) remodeling surrogate outcomes, including LV stroke volume index and LV ejection fraction. The authors concluded that HI during PCI is feasible and safe and may promote reverse LV remodeling after STEMI, although larger-scale clinical trials are required to establish efficacy.

5. **Shibayama et al., 2020 [n= 8; males; mean age 20.9 ± 0.3 years]**, the objective of the study was to examine the impact of acute inhalation of hydrogen-rich gas (HG; molecular hydrogen, H<sub>2</sub>) on oxidative stress, muscle damage, and physical performance during the recovery period following exhaustive exercise. The intervention consisted of inhalation of HG (maximum inspired fractions of 21.57% oxygen and 4.08% H<sub>2</sub>) or placebo gas (ambient air at 400 m above sea level) for 60 minutes during recovery after an oxidative stress-inducing exercise protocol, including 30 minutes of treadmill running at 75% of maximal oxygen uptake (VO<sub>2</sub>max) and squat jumps (5 sets × 10 repetitions), in physically active volunteers. The results showed that HG inhalation attenuated the increase in urinary excretion of 8-hydroxydeoxyguanosine (8-OHdG), a marker of DNA oxidation, and reduced the decline in countermovement jump performance, while other performance variables, blood oxidative stress markers, and muscle damage indices did not differ between HG and placebo; additionally, increases in 8-OHdG were negatively correlated with jump performance. The authors concluded that HG inhalation during post-exercise recovery may enhance physical performance by reducing systemic oxidative damage.
6. **Chen et al., 2020a [n= 20; females and males; from 41 to 80 years of age]**, the objective of the study was to evaluate immunosenescence in patients with advanced non-small cell lung cancer (NSCLC) and to investigate the potential of molecular hydrogen (H<sub>2</sub>) inhalation as an immune reconstitution strategy. The intervention consisted of daily inhalation for two weeks of a gas mixture containing 66.7% hydrogen (H<sub>2</sub>) and 33.3% oxygen (O<sub>2</sub>), delivered at a flow rate of 3 L/min for 4 hours per day, without concomitant standard anticancer therapy. The results showed that, prior to treatment, patients exhibited marked immunosenescence, characterized by increased exhausted and senescent cytotoxic T cells and cytotoxic Vδ1 gamma delta T cells, along with reduced functional helper and cytotoxic T cells, T helper 1 (Th1) cells, natural killer (NK) cells, natural killer T (NKT) cells, and Vδ2 gamma delta T cells; following two weeks of H<sub>2</sub> inhalation, elevated subsets returned to normal levels and reduced subsets increased significantly. The authors concluded that immunosenescence in advanced NSCLC involves nearly all lymphocyte subsets and that two weeks of hydrogen inhalation can significantly improve most immunological indices.
7. **Chen et al., 2020b n= 20; females and males; from 41 to 80 years of age]**, the objective of the study was to evaluate whether molecular hydrogen (H<sub>2</sub>) inhalation could

- alleviate pulmonary symptoms, reduce adverse events associated with chemotherapy, targeted therapy, and immunotherapy, and influence tumor progression in patients with advanced non–small cell lung cancer (NSCLC). The intervention consisted of H<sub>2</sub> inhalation for 4–5 hours per day for up to 5 months, administered either as monotherapy in patients who refused pharmacological treatment or combined with chemotherapy, targeted therapy, or immunotherapy according to tumor mutation status and drug sensitivity, and compared with a control group receiving no active treatment. The results showed that, during the first 5 months, symptom prevalence progressively increased in the control group but gradually decreased in the H<sub>2</sub>-only and H<sub>2</sub>-combination groups; furthermore, after 16 months of follow-up, progression-free survival was lower in the control group and higher in the H<sub>2</sub>-treated groups, particularly in those receiving combined therapies, with most drug-related adverse events being reduced or even resolved. The authors concluded that H<sub>2</sub> inhalation may help control tumor progression and alleviate adverse effects of anticancer therapies in patients with advanced NSCLC.
8. **Yoritaka et al., 2021 [n= 20; females and males; mean age 66.4 ± 10.3/ 65.9 ± 9.4 years]**, the objective of the study was to evaluate the efficacy of molecular hydrogen (H<sub>2</sub>) inhalation in Japanese patients with Parkinson's disease (PD) receiving levodopa, given the involvement of oxidative stress in disease progression. The intervention consisted of inhalation of 6.5 vol% (±0.1) hydrogen gas mixed with air at a flow rate of 2 L/min, administered twice daily for 1 hour over 16 weeks, compared with placebo air inhalation. The results showed no significant difference in the change in total Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) scores from baseline to week 16 between the hydrogen and placebo groups, with no adverse events reported, although adherence to the inhalation protocol declined in older participants, those receiving higher daily doses of levodopa, and those with higher emotional scores on the Parkinson's Disease Questionnaire-39 (PDQ-39). The authors concluded that molecular hydrogen inhalation was safe but did not demonstrate clinical benefit in patients with PD in this pilot study.
  9. **Tao et al., 2022 [n= 43; females and males; mean age 53.4 ± 8.2/ 54.3 ± 7.8 years]**, the objective of the study was to investigate the effects of molecular hydrogen/oxygen (H<sub>2</sub>/O<sub>2</sub>) inhalation in individuals with nonalcoholic fatty liver disease (NAFLD) and to explore the underlying mechanisms, with a focus on hepatocyte autophagy. The intervention consisted of H<sub>2</sub>/O<sub>2</sub> inhalation for 13 weeks in patients with NAFLD, combined with preclinical experiments in methionine- and choline-deficient (MCD) mouse models of nonalcoholic steatohepatitis (NASH) and in AML-12 hepatocyte cells. The results showed improvements in serum lipid levels and liver enzymes, along with significant reductions in hepatic fat content assessed by ultrasonography and computed tomography in moderate to severe cases; in animal and cellular models, H<sub>2</sub>/O<sub>2</sub> reduced inflammation, improved liver histology, inhibited lipid accumulation, and enhanced autophagy, effects that were partially blocked by chloroquine and 3-methyladenine (3-MA). The authors concluded that H<sub>2</sub>/O<sub>2</sub> inhalation alleviates NASH in patients with moderate to severe NAFLD, likely through activation of hepatic autophagy.
  10. **Botek et al., 2022c [n= 50; females and males; mean age 53.4 ± 8.2/ 54.3 ± 7.8 years]**, the objective of this study was to evaluate the effects of molecular hydrogen (H<sub>2</sub>)

inhalation on respiratory status and physical fitness in patients with acute-phase COVID-19. The intervention consisted of H<sub>2</sub> or placebo inhalation, twice daily for 60 minutes over 14 days, in symptomatic men and women recruited 21–33 days after a positive polymerase chain reaction (PCR) test, assessed using the 6-minute walk test (6MWT) and pulmonary function tests, including forced vital capacity (FVC) and forced expiratory volume in one second (FEV1). The results showed that H<sub>2</sub> therapy significantly increased 6MWT distance by 64 ± 39 m, FVC by 0.19 ± 0.24 L, and FEV1 by 0.11 ± 0.28 L compared with placebo ( $p \leq 0.025$ ). In conclusion, H<sub>2</sub> inhalation provided clinically meaningful benefits by improving physical and respiratory function in patients with acute COVID-19 and may represent a safe and effective strategy to accelerate early functional recovery in the post-COVID-19 period.

11. **Eda et al., 2022 [n= 8; females and males; mean age 25.6 ± 3.3 years]**, the objective of this study was to examine the effects of molecular hydrogen (H<sub>2</sub>) produced by the intestinal microbiota on physical conditioning and the prevention of exercise-induced damage. Participants ingested an H<sub>2</sub>-producing dairy beverage, which stimulated bacterial intestinal hydrogen production, or a placebo, 4 hours before performing continuous intense exercise at 75% of maximal oxygen uptake for 60 minutes. Blood biomarkers, respiratory variables, and oxidative stress indicators were assessed before, during, and after exercise. The results showed that general and lower-limb muscle soreness scores the morning after exercise were significantly higher during the placebo condition but not following consumption of the H<sub>2</sub>-producing beverage. Urinary concentrations and production rates of 8-hydroxy-2'-deoxyguanosine (8-OHdG), a marker of oxidative DNA damage, increased significantly with placebo intake, whereas no changes were observed with the test beverage. Post-exercise blood lactate levels were lower following consumption of the H<sub>2</sub>-producing beverage. A negative correlation was observed between changes in 8-OHdG and the area under the curve (AUC) of expired H<sub>2</sub> concentrations, along with a significant 1.3-fold increase in lipid oxidation AUC compared with placebo. In conclusion, activation of intestinal bacterial H<sub>2</sub> production through the intake of a specific beverage may represent a novel strategy to reduce oxidative stress, enhance recovery, and improve physical conditioning in athletes frequently exposed to high-intensity exercise.
12. **Deryugina et al., 2023 [n= 24; females and males; mean age 57.1 ± 6.3/ 62.3 ± 5.5 years]**, the objective of this study was to investigate the potential of molecular hydrogen (H<sub>2</sub>) as a component of anesthesia in cardiac surgery with cardiopulmonary bypass (CPB), by evaluating red blood cell (RBC) functional status and indicators of cardiac functional activity. The intervention consisted of administering H<sub>2</sub> at a concentration of 1.5–2.0% via face mask integrated into the ventilator breathing circuit, starting immediately after tracheal intubation and maintained throughout the surgical procedure, in patients undergoing elective valvular surgery with CPB, compared with a control group without H<sub>2</sub>. The results showed increased electrophoretic mobility and metabolic activity of RBCs, reduced platelet aggregation, and a more pronounced reduction in oxidative stress in the H<sub>2</sub>-treated group, particularly 24 hours after surgery, as well as statistically significant differences in myocardial contractile function on postoperative days 1 and 3. The authors concluded that H<sub>2</sub> inhalation improves red blood cell functional status and

contributes to a more favorable immediate postoperative course, demonstrating the cytoprotective properties of molecular hydrogen.

13. **Tamura et al., 2024 [n= 72; females and males]**, the objective of this study was to investigate the combined effect of molecular hydrogen inhalation and targeted temperature management (TTM) on clinical outcomes after cardiogenic out-of-hospital cardiac arrest. The intervention consisted of administering a hydrogen–oxygen gas mixture compared with pure oxygen in patients enrolled in the HYBRID II study, who underwent TTM with target temperatures of 32–34 °C (TTM32–TTM34) or 35–36 °C (TTM35–TTM36), according to institutional protocols. The results showed that under the TTM32–TTM34 regimen, the proportion of favorable neurological outcomes at 90 days was significantly higher in the hydrogen group than in the control group (68% vs. 38%; relative risk: 1.81; 95% confidence interval: 1.05–3.66;  $p < 0.05$ ), and the combination of hydrogen inhalation and TTM32–TTM34 was independently associated with good neurological outcomes (adjusted odds ratio: 16.10; 95% confidence interval: 1.88–138.17;  $p = 0.01$ ). However, this combined therapy did not significantly improve 90-day survival compared with TTM32–TTM34 alone. In conclusion, the combination of hydrogen inhalation and TTM32–TTM34 was associated with improved neurological outcomes after cardiogenic out-of-hospital cardiac arrest, suggesting that hydrogen inhalation is a promising therapeutic strategy to reduce post-cardiac arrest brain injury.
14. **Chitapanarux et al., 2024 [n= 10; females and males; from 43 to 68 years of age]**, the objective of this study was to investigate the feasibility and safety of molecular hydrogen gas ( $H_2$ ) inhalation during concurrent chemoradiotherapy (CRT) in patients with locally advanced head and neck cancer (LAHNC). The intervention consisted of concurrent chemoradiotherapy (CCRT), including intensity-modulated radiotherapy (IMRT) delivered in 33 fractions and weekly chemotherapy, combined with daily  $H_2$  inhalation via nasal cannula or mask for 1 hour, administered 1–2 hours before IMRT. The results showed that all patients completed 33  $H_2$  inhalation sessions, with stable vital signs, no  $H_2$ -related adverse events, and acute toxicities consistent with CCRT, including grade 3 leukopenia in 20% and grade 2 radiation dermatitis and pharyngitis in 30% of patients. The authors concluded that  $H_2$  gas inhalation combined with CCRT is feasible and safe in patients with locally advanced head and neck cancer.
15. **Zhao et al., 2024 [n= 12; males; from mean age  $23 \pm 2.65$  years]**, the objective of this study was to determine the effects of molecular hydrogen ( $H_2$ ) inhalation on plasma levels of nitric oxide (NO) and its synthetic precursors in professional athletes. The intervention consisted of a three-week crossover trial conducted in male professional rugby players, including one week of  $H_2$  inhalation, one week of placebo, and one intervening week of low-intensity training as a washout period, with interventions performed prior to daily high-intensity physical training sessions. The results showed that plasma levels of NO, L-arginine, and tetrahydrobiopterin were significantly higher after exercise and remained elevated after 24 hours of recovery during the  $H_2$  inhalation week, while levels of 8-hydroxydeoxyguanosine and interleukin-6 were lower compared with placebo, alongside a significant increase in total antioxidant capacity. The authors concluded that  $H_2$  inhalation helps preserve NO signaling and attenuates exercise-induced oxidative stress and inflammation in professional athletes.

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16. **Salomez et al., 2024 [n= 12; females and males; from mean age 58.42 ± 10.84 years]**, the objective of this study was to evaluate the safety and tolerability of molecular dihydrogen (H<sub>2</sub>) inhalation as an adjunctive treatment in hospitalized patients with coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The intervention consisted of a phase I, open-label, prospective, single-center, single ascending-dose clinical trial using a 3 + 3 design, in which patients inhaled a gas mixture containing H<sub>2</sub> (3.6%) and nitrogen (N<sub>2</sub>, 96.4%) for three different exposure durations: 1 day, 3 days, or 6 days. The results showed that the maximum tolerated duration was at least 3 days, with excellent tolerability, no relevant adverse events, and clinical improvement observed in all enrolled patients. The authors concluded that H<sub>2</sub> inhalation is safe in hospitalized COVID-19 patients, representing the first phase I clinical trial to establish the safety of this approach and supporting further investigation in larger controlled clinical trials.
  17. **Grepl et al., 2025 [n= 12; females; from mean age 22.1 ± 1.6 years]**, the objective of this study was to evaluate the effects of 60 minutes of molecular hydrogen (H<sub>2</sub>) inhalation on respiratory gas analysis parameters in physically active women. The intervention consisted of a randomized, double-blind, placebo-controlled crossover study in which participants inhaled H<sub>2</sub> or ambient air via nasal cannula (300 mL/min) for 60 minutes at rest, with metabolic responses assessed by indirect calorimetry. The results showed that, compared with placebo, H<sub>2</sub> inhalation significantly reduced the respiratory exchange ratio (RER) and ventilation across all analyzed intervals, and changes in RER were negatively correlated with body fat percentage from 30 minutes onward. The authors concluded that 60 minutes of H<sub>2</sub> inhalation at rest significantly increases fat oxidation, particularly in individuals with higher body fat percentages.

## 4.5 Summary of the publications retrieved on Intravenous Infusion of Hydrogen-enriched Solution

A total of 3 studies were found. More details are presented in Table 5.

1. **Terawaki et al., 2014 [n= 8; males and females; mean age 58 ± 16 years]**, the objective of this study was to evaluate whether molecular hydrogen (H<sub>2</sub>) can attenuate the increase in oxidative stress (OS) induced during hemodialysis (HD) sessions in patients undergoing regular treatment. The intervention consisted of a crossover clinical trial in which participants underwent two HD sessions using standard dialysis solution and hydrogen-enriched solution (H<sub>2</sub>-HD; ~50 ppb H<sub>2</sub>), with blood samples collected at the inlet and outlet of the dialyzer to assess glutathione, hydrogen peroxide, and albumin redox state. The results showed that although both HD modalities reduced glutathione levels and increased hydrogen peroxide, the proportion of reversibly oxidized albumin was significantly lower after H<sub>2</sub>-HD, indicating reduced intradialyzer oxidative stress. The authors concluded that the use of hydrogen-enriched dialysis solutions may attenuate oxidative stress during hemodialysis.
2. **Takeuchi et al., 2021 [n= 37; females; mean age 57.1 ± 9.4/ 60.8 ± 9.3/ 60.8 ± 11.6 years]**, the objective of the study was to evaluate the efficacy of intracisternal magnesium sulfate (MgSO<sub>4</sub>) infusion, alone or combined with intravenous molecular hydrogen (H<sub>2</sub>) therapy, in patients with poor-grade subarachnoid hemorrhage (SAH). The intervention consisted of randomizing patients with severe SAH into magnesium plus hydrogen (Mg+H<sub>2</sub>), magnesium alone (Mg), and control groups; the Mg and Mg+H<sub>2</sub> groups received intracisternal MgSO<sub>4</sub> infusion (2.5 mmol/L) at 20 mL/h for 14 days, and the Mg+H<sub>2</sub> group additionally received intravenous hydrogen-rich solution for the same period. The results showed that the Mg+H<sub>2</sub> group exhibited lower serum and cerebrospinal fluid levels of neuron-specific enolase (NSE), a reduced incidence of cerebral vasospasm (CV) and delayed cerebral ischemia (DCI), and higher Barthel Index scores at 12 months. The authors concluded that intracisternal magnesium sulfate reduces CV and DCI and that its combination with intravenous hydrogen therapy provides additional neuroprotective effects and improved functional recovery.
3. **Ishibashi et al., 2014 [n= 24; females; mean age 68.2 ± 12.6/ 62.4 ± 18.4 years]**, the objective of the study was to demonstrate the safety and efficacy of intravenous infusion of hydrogen-enriched saline solution (H<sub>2</sub>-saline) for the treatment of rheumatoid arthritis (RA). The intervention consisted of randomizing 24 patients with RA to receive 500 mL of H<sub>2</sub>-saline containing 1 ppm of molecular hydrogen or placebo (saline), administered intravenously (IV) daily for 5 days, with assessment of the Disease Activity Score in 28 joints (DAS28) and the biomarkers tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), matrix metalloproteinase-3 (MMP-3), and urinary 8-hydroxydeoxyguanosine (8-OHdG). The results showed that the H<sub>2</sub> group exhibited a significant reduction in DAS28 immediately after infusion and at 4 weeks, along with decreases in IL-6, MMP-3, and 8-OHdG levels, with no significant changes in TNF-α, whereas no clinical improvement

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was observed in the placebo group. The authors concluded that intravenous H<sub>2</sub>-saline infusion safely and effectively reduces rheumatoid arthritis disease activity.

#### 4.6 Summary of the publications retrieved on Molecular Hydrogen Capsules/Tablets

A total of 3 studies were found. More details are presented in Table 6.

1. **Korovljev et al., 2018 [n= 7; females; mean age 56.4 ± 12.6 years]**, the objective of this study was to evaluate the effects of molecular hydrogen (H<sub>2</sub>) intervention on body composition, hormonal status, and mitochondrial function in overweight middle-aged women. The intervention consisted of oral administration of hydrogen-generating minerals, providing approximately 6 parts per million (ppm) of H<sub>2</sub> per day, or placebo, in capsule form for 4 weeks. The results showed that, although no significant differences were observed in body weight, body mass index (BMI), or body circumferences, the H<sub>2</sub> group exhibited a significant reduction in body fat percentage and arm fat index compared with placebo, along with decreased serum triglyceride levels and reduced fasting insulin levels. The authors concluded that oral administration of H<sub>2</sub> via hydrogen-generating minerals may be a beneficial strategy for improving body composition and insulin resistance in overweight women.
2. **Ostojic et al., 2014 [n= 36; males; mean age 23.1 ± 2.3 years]**, the objective of this study was to examine the effects of two-week molecular hydrogen (H<sub>2</sub>) administration on biochemical markers of inflammation and functional recovery in professional male athletes following acute soft tissue injury. The intervention consisted of comparing a control group receiving standard soft tissue injury treatment with two experimental groups: one receiving oral hydrogen-rich tablets (2 g/day) and another receiving combined oral hydrogen supplementation (2 g/day) plus topical hydrogen-rich compresses applied six times daily for 20 minutes, with assessments at baseline and at 7 and 14 days. The results showed that combined oral and topical hydrogen administration led to a greater reduction in plasma viscosity and a faster recovery of joint range of motion, for both flexion and extension, compared with the control group (p < 0.05). The authors concluded that adding molecular hydrogen to conventional treatment protocols may be a potentially effective strategy for managing acute soft tissue injuries in professional athletes.
3. **Lu et al., 2024 [n= 30; males and females; mean age 64.86 ± 12.77 years]**, the objective of this study was to evaluate the impact of supplementation with oral solid hydrogen-generating compounds (CHSOs) in individuals with chronic inflammation. The intervention consisted of an initial in vitro comparison of the oxidation–reduction potential (ORP) of CHSO solutions with hydrogen-rich water (HRW) and calcium hydride–treated water (CaH<sub>2</sub>), followed by a clinical study in which stable outpatients with chronic diseases were randomized to receive low-, medium-, or high-dose CHSOs for four weeks, with assessment of primary outcomes — erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) — and secondary outcomes — Taiwan Brief Fatigue Inventory (BFI-T), Diabetes Control Scale (CSSD70), and Disease Activity Score 28 (DAS28). The results showed that CHSOs induced a prolonged reduction in ORP for up



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to 60 minutes in vitro and enabled regulated hydrogen release over 24 hours, along with a significant dose-dependent reduction in ESR over four weeks, a downward trend in CRP levels, a significant decrease in DAS28, and improvements in fatigue and metabolic control scores. The authors concluded that CHSO supplementation may exert antioxidant and anti-inflammatory effects in individuals with chronic inflammation, although further clinical studies are required to explore their therapeutic potential.

## 4.7 Summary of the publications retrieved on Hydrogen-rich Calcium Powder

A total of 2 studies were found. More details are presented in Table 7.

1. **Alharbi et al., 2021 [n= 18; males; mean age 21 ± 1 years]**, the objective of the study was to investigate the effects of molecular hydrogen (H<sub>2</sub>) supplementation on acid–base balance, pulmonary gas exchange responses, and local muscle oxygenation during incremental exercise. The intervention consisted of administering hydrogen-rich calcium powder (HCP; 1500 mg/day, containing 2.544 µg/day of H<sub>2</sub>) or hydrogen-depleted placebo for three consecutive days to healthy trained individuals, followed by incremental cycle ergometer exercise with assessment of pulmonary ventilation ( $\dot{V}E$ ), carbon dioxide production ( $\dot{V}CO_2$ ), oxygen uptake ( $\dot{V}O_2$ ), pH, bicarbonate (HCO<sub>3</sub><sup>-</sup>), partial pressure of carbon dioxide (PCO<sub>2</sub>), and muscle deoxygenation (deoxy[Hb + Mb]) in the vastus lateralis (VL) and rectus femoris (RF). The results showed that the HCP group exhibited lower resting  $\dot{V}E$  and  $\dot{V}CO_2$ , higher HCO<sub>3</sub><sup>-</sup> and PCO<sub>2</sub> concentrations, reduced pH during exercise, lower  $\dot{V}E$  without changes in  $\dot{V}CO_2$  or  $\dot{V}O_2$ , and increased deoxy[Hb + Mb] in the RF but not in the VL. The authors concluded that HCP supplementation induces hypoventilation associated with reduced pH and a regional imbalance between oxygen delivery and utilization in the RF during incremental exercise, likely related to inherent metabolic and vascular differences between muscle groups.
2. **Alharbi et al., 2022 [n= 10; males; mean age 20 ± 1 years]**, the objective of the study was to examine the effects of a single dose of molecular hydrogen (H<sub>2</sub>) supplementation on acid–base balance, local muscle deoxygenation, high-intensity interval training (HIIT) performance, and recovery. The intervention consisted of administering hydrogen-rich calcium powder (HCP; 1500 mg, containing 2.544 µg of H<sub>2</sub>) or a low-hydrogen placebo in a randomized, double-blind, crossover design, one hour before six bouts of maximal cycling, with assessment of pH, partial pressure of carbon dioxide (PCO<sub>2</sub>), bicarbonate (HCO<sub>3</sub><sup>-</sup>), muscle deoxygenation (deoxy[Hb + Mb]), and tissue oxygen saturation (StO<sub>2</sub>) in the vastus lateralis (VL) and rectus femoris (RF). The results showed that the HCP group exhibited higher resting PCO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup> levels, greater peak power output in the first HIIT bout, significantly increased deoxy[Hb + Mb], greater oxygen extraction in the VL, and increased microvascular volume in the RF, with no differences in heart rate, as well as improved blood flow and muscle reoxygenation during recovery. The authors concluded that acute HCP supplementation may exert ergogenic effects and enhance performance during anaerobic HIIT exercise.

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## 5. Conclusions

In general, molecular hydrogen–based interventions demonstrate consistent evidence of potential benefits related to the reduction of oxidative stress, modulation of inflammatory responses, improvement of metabolic regulation, and enhancement of tissue protection across multiple organ systems. Clinical studies involving hydrogen inhalation, hydrogen-rich water, and hydrogen-dissolved saline report favorable effects on parameters such as oxidative stress biomarkers, inflammatory mediators, endothelial function, metabolic efficiency, and functional outcomes, particularly when interventions are applied repeatedly over days or weeks.

Evidence from studies using hydrogen gas inhalation indicates improvements in tissue oxygenation, endothelial responsiveness, nitric oxide–mediated vasodilation, and protection against ischemia–reperfusion injury, with additional benefits observed in neurological recovery, cardiovascular function, respiratory performance, and post-exercise recovery. Similarly, interventions involving hydrogen-rich water or orally administered hydrogen-generating compounds suggest beneficial effects on glucose and lipid metabolism, mitochondrial function, and systemic redox balance, supporting a role for molecular hydrogen in metabolic and lifestyle-related conditions.

From a mechanistic standpoint, the findings collectively reinforce the biological plausibility that molecular hydrogen exerts both direct and indirect effects on cellular homeostasis. Beyond selectively neutralizing highly reactive oxygen species, H<sub>2</sub> appears to modulate gene expression pathways associated with inflammation, apoptosis, autophagy, and energy metabolism, thereby influencing hemodynamic, metabolic, and immunological responses relevant to symptom relief and functional recovery.

Despite these promising observations, it is important to acknowledge that the available evidence remains heterogeneous with respect to study design, population characteristics, dosing strategies, and modes of administration. Well-designed, adequately powered clinical trials are required to establish optimal administration parameters and to confirm, in a robust and reproducible manner, the therapeutic effects of molecular hydrogen across different clinical indications and technological configurations.

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## 6. References

Aker MN, Gönenç İM, Çalışıcı D, Bulut M, Alwazeer D, LeBaron TW. The effect of hydrogen-rich water consumption on premenstrual symptoms and quality of life: a randomized controlled trial. *BMC Womens Health*. 2024;24(1):197. Published 2024 Mar 26. doi:10.1186/s12905-024-03029-8

Alharbi AAD, Ebine N, Nakae S, Hojo T, Fukuoka Y. Application of Molecular Hydrogen as an Antioxidant in Responses to Ventilatory and Ergogenic Adjustments during Incremental Exercise in Humans. *Nutrients*. 2021;13(2):459. Published 2021 Jan 30. doi:10.3390/nu13020459

Alharbi AAD, Iwamoto N, Ebine N, Nakae S, Hojo T, Fukuoka Y. The Acute Effects of a Single Dose of Molecular Hydrogen Supplements on Responses to Ergogenic Adjustments during High-Intensity Intermittent Exercise in Humans. *Nutrients*. 2022;14(19):3974. Published 2022 Sep 24. doi:10.3390/nu14193974

Botek M, Khanna D, Krejčí J, et al. Molecular Hydrogen Mitigates Performance Decrement during Repeated Sprints in Professional Soccer Players. *Nutrients*. 2022a;14(3):508. Published 2022 Jan 25. doi:10.3390/nu14030508

Botek M, Krejčí J, McKune A, Valenta M, Sládečková B. Hydrogen Rich Water Consumption Positively Affects Muscle Performance, Lactate Response, and Alleviates Delayed Onset of Muscle Soreness After Resistance Training. *J Strength Cond Res*. 2022b;36(10):2792-2799. doi:10.1519/JSC.0000000000003979

Botek M, Krejčí J, McKune AJ, Sládečková B, Naumovski N. Hydrogen Rich Water Improved Ventilatory, Perceptual and Lactate Responses to Exercise. *Int J Sports Med*. 2019;40(14):879-885. doi:10.1055/a-0991-0268

Botek M, Krejčí J, Valenta M, et al. Molecular Hydrogen Positively Affects Physical and Respiratory Function in Acute Post-COVID-19 Patients: A New Perspective in Rehabilitation. *Int J Environ Res Public Health*. 2022c;19(4):1992. Published 2022 Feb 10. doi:10.3390/ijerph19041992

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Chen JB, Kong XF, Mu F, Lu TY, Lu YY, Xu KC. Hydrogen therapy can be used to control tumor progression and alleviate the adverse events of medications in patients with advanced non-small cell lung cancer. *Med Gas Res.* 2020b;10(2):75-80. doi:10.4103/2045-9912.285560

Chen JB, Kong XF, Qian W, et al. Two weeks of hydrogen inhalation can significantly reverse adaptive and innate immune system senescence patients with advanced non-small cell lung cancer: a self-controlled study. *Med Gas Res.* 2020a;10(4):149-154. doi:10.4103/2045-9912.304221

Chitapanarux I, Onchan W, Chakrabandhu S, et al. Pilot Feasibility and Safety Study of Hydrogen Gas Inhalation in Locally Advanced Head and Neck Cancer Patients. *Onco Targets Ther.* 2024;17:863-870. Published 2024 Oct 29. doi:10.2147/OTT.S478613

Da Ponte A, Giovanelli N, Nigris D, Lazzer S. Effects of hydrogen rich water on prolonged intermittent exercise. *J Sports Med Phys Fitness.* 2018;58(5):612-621. doi:10.23736/S0022-4707.17.06883-9

Deryugina AV, Danilova DA, Brichkin YD, et al. Molecular hydrogen exposure improves functional state of red blood cells in the early postoperative period: a randomized clinical study. *Med Gas Res.* 2023;13(2):59-66. doi:10.4103/2045-9912.356473

Eda N, Tsuno S, Nakamura N, Sone R, Akama T, Matsumoto M. Effects of Intestinal Bacterial Hydrogen Gas Production on Muscle Recovery following Intense Exercise in Adult Men: A Pilot Study. *Nutrients.* 2022;14(22):4875. Published 2022 Nov 18. doi:10.3390/nu14224875

Grepl P, Botek M, Krejčí J, McKune A. Molecular hydrogen inhalation modulates resting metabolism in healthy females: findings from a randomized, double-blind, placebo-controlled crossover study. *Med Gas Res.* 2025;15(3):367-373. doi:10.4103/mgr.MEDGASRES-D-24-00085

Hong CT, Hu CJ, Lin HY, Wu D. Effects of concomitant use of hydrogen water and photobiomodulation on Parkinson disease: A pilot study. *Medicine (Baltimore).* 2021;100(4):e24191. doi:10.1097/MD.00000000000024191

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Hori A, Sobue S, Kurokawa R, Hirano SI, Ichihara M, Hotta N. Two-week continuous supplementation of hydrogenrich water increases peak oxygen uptake during an incremental cycling exercise test in healthy humans: a randomized, single-blinded, placebo-controlled study. *Med Gas Res.* 2020;10(4):163-169. doi:10.4103/2045-9912.304223

Ishibashi T, Kawamoto K, Matsuno K, Ishihara G, Baba T, Komori N. Peripheral endothelial function can be improved by daily consumption of water containing over 7 ppm of dissolved hydrogen: A randomized controlled trial. *PLoS One.* 2020;15(5):e0233484. Published 2020 May 29. doi:10.1371/journal.pone.0233484

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. doi:10.1016/j.intimp.2014.06.001

Javorac D, Stajer V, Ratgeber L, et al. Hydrotherapy with hydrogen-rich water compared with RICE protocol following acute ankle sprain in professional athletes: a randomized non-inferiority pilot trial. *Res Sports Med.* 2021;29(6):517-525. doi:10.1080/15438627.2020.1868468

Kajiyama S, Hasegawa G, Asano M, et al. Supplementation of hydrogen-rich water improves lipid and glucose metabolism in patients with type 2 diabetes or impaired glucose tolerance. *Nutr Res.* 2008;28(3):137-143. doi:10.1016/j.nutres.2008.01.008

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. doi:10.1038/oby.2011.6

Katsumata Y, Sano F, Abe T, et al. The Effects of Hydrogen Gas Inhalation on Adverse Left Ventricular Remodeling After Percutaneous Coronary Intervention for ST-Elevated Myocardial Infarction - First Pilot Study in Humans. *Circ J.* 2017;81(7):940-947. doi:10.1253/circj.CJ-17-0105

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Korovljev D, Stajer V, Ostojic J, LeBaron TW, Ostojic SM. Hydrogen-rich water reduces liver fat accumulation and improves liver enzyme profiles in patients with non-alcoholic fatty liver disease: a randomized controlled pilot trial. *Clin Res Hepatol Gastroenterol*. 2019;43(6):688-693. doi:10.1016/j.clinre.2019.03.008

Korovljev D, Trivic T, Drid P, Ostojic SM. Molecular hydrogen affects body composition, metabolic profiles, and mitochondrial function in middle-aged overweight women. *Ir J Med Sci*. 2018;187(1):85-89. doi:10.1007/s11845-017-1638-4

Lu KC, Shen MC, Wang RL, et al. Using oral molecular hydrogen supplements to combat microinflammation in humans: a pilot observational study. *Int J Med Sci*. 2024;21(12):2390-2401. Published 2024 Sep 9. doi:10.7150/ijms.101114

Matsumoto S, Ueda T, Kakizaki H. Effect of supplementation with hydrogen-rich water in patients with interstitial cystitis/painful bladder syndrome. *Urology*. 2013;81(2):226-230. doi:10.1016/j.urology.2012.10.026

Najmanová E, Manethová H, Botek M, Pluháček F. EFFECT OF ACUTE HYDROGEN-RICH WATER INTAKE ON INTRAOCULAR PRESSURE IN HEALTHY SUBJECTS. VLIV RYCHLÉHO PŘÍJMU VODÍKEM SYCENÉ VODY NA NITROOČNÍ TLAK U ZDRAVÝCH OSOB. *Cesk Slov Oftalmol*. 2023;79(4):180-184. doi:10.31348/2023/23

Ohsawa I, Ishikawa M, Takahashi K, et al. Hydrogen acts as a therapeutic antioxidant by selectively reducing cytotoxic oxygen radicals. *Nat Med*. 2007;13(6):688-694. doi:10.1038/nm1577

Ohta S. Molecular hydrogen as a preventive and therapeutic medical gas: initiation, development and potential of hydrogen medicine. *Pharmacol Ther*. 2014;144(1):1-11. doi:10.1016/j.pharmthera.2014.04.006

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. doi:10.1016/j.jstrokecerebrovasdis.2017.06.012

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Ooi CH, Ng SK, Omar EA. Acute ingestion of hydrogen-rich water does not improve incremental treadmill running performance in endurance-trained athletes. *Appl Physiol Nutr Metab.* 2020;45(5):513-519. doi:10.1139/apnm-2019-0553

Ostojic SM, Vukomanovic B, Calleja-Gonzalez J, Hoffman JR. Effectiveness of oral and topical hydrogen for sports-related soft tissue injuries. *Postgrad Med.* 2014;126(5):187-195. doi:10.3810/pgm.2014.09.2813

Sakai T, Sato B, Hara K, et al. Consumption of water containing over 3.5 mg of dissolved hydrogen could improve vascular endothelial function. *Vasc Health Risk Manag.* 2014;10:591-597. Published 2014 Oct 17. doi:10.2147/VHRM.S68844

Salomez-Ihl C, Giai J, Barbado M, et al. H2 inhalation therapy in patients with moderate COVID-19 (H2COVID): a prospective ascending-dose phase I clinical trial. *Antimicrob Agents Chemother.* 2024;68(8):e0057324. doi:10.1128/aac.00573-24

Shibayama Y, Dobashi S, Arisawa T, Fukuoka T, Koyama K. Impact of hydrogen-rich gas mixture inhalation through nasal cannula during post-exercise recovery period on subsequent oxidative stress, muscle damage, and exercise performances in men. *Med Gas Res.* 2020;10(4):155-162. doi:10.4103/2045-9912.304222

Sim M, Kim CS, Shon WJ, Lee YK, Choi EY, Shin DM. Hydrogen-rich water reduces inflammatory responses and prevents apoptosis of peripheral blood cells in healthy adults: a randomized, double-blind, controlled trial. *Sci Rep.* 2020;10(1):12130. Published 2020 Jul 22. doi:10.1038/s41598-020-68930-2

Takeuchi S, Kumagai K, Toyooka T, Otani N, Wada K, Mori K. Intravenous Hydrogen Therapy With Intracisternal Magnesium Sulfate Infusion in Severe Aneurysmal Subarachnoid Hemorrhage. *Stroke.* 2021;52(1):20-27. doi:10.1161/STROKEAHA.120.031260

Tamasawa A, Mochizuki K, Hariya N, et al. Hydrogen gas production is associated with reduced interleukin-1 $\beta$  mRNA in peripheral blood after a single dose of acarbose in Japanese type 2 diabetic patients. *Eur J Pharmacol.* 2015;762:96-101. doi:10.1016/j.ejphar.2015.04.051

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Tamura T, Hayashida K, Sano M, et al. Feasibility and Safety of Hydrogen Gas Inhalation for Post-Cardiac Arrest Syndrome - First-in-Human Pilot Study. *Circ J.* 2016;80(8):1870-1873. doi:10.1253/circj.CJ-16-0127

Tamura T, Narumiya H, Homma K, Suzuki M; Efficacy of Inhaled Hydrogen on Neurologic Outcome Following Brain Ischemia During PostCardiac Arrest Care (HYBRID II) Study Group. Combination of Hydrogen Inhalation and Hypothermic Temperature Control After Out-of-Hospital Cardiac Arrest: A Post hoc Analysis of the Efficacy of Inhaled Hydrogen on Neurologic Outcome Following Brain Ischemia During PostCardiac Arrest Care II Trial. *Crit Care Med.* 2024;52(10):1567-1576. doi:10.1097/CCM.0000000000006395

Tan Y, Xie Y, Dong G, et al. The Effect of 14-Day Consumption of Hydrogen-Rich Water Alleviates Fatigue but Does Not Ameliorate Dyspnea in Long-COVID Patients: A Pilot, Single-Blind, and Randomized, Controlled Trial. *Nutrients.* 2024;16(10):1529. Published 2024 May 19. doi:10.3390/nu16101529

Tao G, Zhang G, Chen W, et al. A randomized, placebo-controlled clinical trial of hydrogen/oxygen inhalation for non-alcoholic fatty liver disease. *J Cell Mol Med.* 2022;26(14):4113-4123. doi:10.1111/jcmm.17456

Terawaki H, Zhu WJ, Matsuyama Y, et al. Effect of a hydrogen (H<sub>2</sub>)-enriched solution on the albumin redox of hemodialysis patients. *Hemodial Int.* 2014;18(2):459-466. doi:10.1111/hdi.12112

Todorovic N, Baltic S, Nedeljkovic D, et al. The Effects of 8-Week Hydrogen-Rich Water Consumption on Appetite, Body Composition, Sleep Quality, and Circulating Glucagon-like Peptide-1 in Obese Men and Women (HYDRAPPET): A Randomized Controlled Trial. *Medicina (Kaunas).* 2025;61(7):1299. Published 2025 Jul 18. doi:10.3390/medicina61071299

Valenta M, Botek M, Krejčí J, et al. Acute pre-exercise hydrogen rich water intake does not improve running performance at maximal aerobic speed in trained track and field runners: A randomized, double-blind, placebo-controlled crossover study. *PLoS One.* 2022;17(12):e0279307. Published 2022 Dec 20. doi:10.1371/journal.pone.0279307

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Xia C, Liu W, Zeng D, Zhu L, Sun X, Sun X. Effect of hydrogen-rich water on oxidative stress, liver function, and viral load in patients with chronic hepatitis B. *Clin Transl Sci.* 2013;6(5):372-375. doi:10.1111/cts.12076

Yoritaka A, Kobayashi Y, Hayashi T, Saiki S, Hattori N. Randomized double-blind placebo-controlled trial of hydrogen inhalation for Parkinson's disease: a pilot study. *Neurol Sci.* 2021;42(11):4767-4770. doi:10.1007/s10072-021-05489-4

Yoritaka A, Takanashi M, Hirayama M, Nakahara T, Ohta S, Hattori N. Pilot study of H<sub>2</sub> therapy in Parkinson's disease: a randomized double-blind placebo-controlled trial. *Mov Disord.* 2013;28(6):836-839. doi:10.1002/mds.25375

Zanini D, Todorovic N, Korovljev D, et al. 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. *Exp Gerontol.* 2021;155:111574. doi:10.1016/j.exger.2021.111574

Zhao Y, Li C, Zhou S, Xu Z, Huang X, Wen L. Hydrogen gas inhalation prior to high-intensity training reduces attenuation of nitric oxide bioavailability in male rugby players. *PeerJ.* 2024;12:e18503. Published 2024 Dec 16. doi:10.7717/peerj.18503

Table 2. More details from the studies retrieved Hydrogen-rich Water.

Author/Year	Title	Country	Study type	Characteristics	N	Condition	Conclusion
Kajiyama et al., 2008	Supplementation of hydrogen-rich water improves lipid and glucose metabolism in patients with type 2 diabetes or impaired glucose tolerance	Japan	Randomized, double-blind, placebo-controlled, crossover study	Patients consumed 900 mL/day of hydrogen-rich pure water for 8 weeks, followed by a 12-week washout period. The water showed pH 6.7, high dissolved hydrogen (1.2 mg/L), low dissolved oxygen (0.8 mg/L), low electrical conductivity, and an extremely negative redox potential (-600 mV).	30	Type 2 diabetes or impaired glucose tolerance	The results suggest that supplementation with hydrogen-rich water may have a beneficial role in prevention of T2DM and insulin resistance.
Yoritaka et al., 2013	Pilot study of H <sub>2</sub> therapy in Parkinson's disease: a randomized double-blind placebo-controlled trial	Japan	Randomized double-blind placebo-controlled trial	Participants ingested 1,000 mL/day of hydrogen-rich water for 48 weeks, prepared by dissolving H <sub>2</sub> at a concentration of 0.8 mM.	17	PD	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.
Matsumoto et al., 2013	Effect of supplementation with hydrogen-rich water in patients with interstitial cystitis/painful bladder syndrome	Japan	Prospective, randomized, double-blind, placebo-controlled clinical trial	Participants received hydrogen-rich water for 8 weeks, consuming 3 packs of 200 mL of water daily.	30	IC/PBS	The results of the present study do not support the use of supplementation with hydrogen-rich water for treating patients with IC/PBS.
Xia et al., 2013	Effect of Hydrogen-Rich Water on Oxidative Stress, Liver Function, and Viral Load in Patients with Chronic Hepatitis B	China	Clinical study	HRW was administered orally for 6 consecutive weeks, with a total daily intake of 1,200–1,800 mL. Intake was divided into three daily doses (8–9 a.m.; 2–3 p.m.; 6–7 p.m.). The final hydrogen concentration ranged from 0.55 to 0.65 mM.	60	CHB	HRW significantly attenuates oxidative stress in CHB patients.

Tan et al., 2014	The Effect of 14-Day Consumption of Hydrogen-Rich Water Alleviates Fatigue but Does Not Ameliorate Dyspnea in Long-COVID Patients: A Pilot, Single-Blind, and Randomized, Controlled Trial.	China	Pilot, Single-Blind, and Randomized, Controlled Trial	Participants consumed 500 mL of hydrogen-rich water twice daily, in the morning and evening, drinking the HRW immediately after preparation (within 10 minutes). The water had 1600 ppb of H <sub>2</sub> , pH 7.6, ORP -590 mV, and a temperature of 22 °C.	32	Long-COVID	This study demonstrates that HRW might be an effective strategy for alleviating fatigue and improving cardiorespiratory endurance, musculoskeletal function, and sleep quality. Still, it does not ameliorate dyspnea among Long-COVID patients.
Sakai et al., 2014	Consumption of water containing over 3.5 mg of dissolved hydrogen could improve vascular endothelial function	Japan	Pilot study	Participants ingested high-concentration H <sub>2</sub> water, containing 7 ppm of H <sub>2</sub> (equivalent to 3.5 mg of H <sub>2</sub> in 500 mL of water).	34	Vascular endothelial function	H <sub>2</sub> may protect the vasculature from shear stress-derived detrimental ROS, such as the hydroxyl radical, by maintaining the nitric oxide-mediated vasomotor response.
Da Ponte et al., 2018	Effects of hydrogen rich water on prolonged intermittent exercise	Italy	Cross over single-blind protocol	Participants consumed 2 liters of hydrogen-rich water daily (pH 9.8; ORP -180 mV; 450 ppb free hydrogen) for 4 weeks.	8	Prolonged intermittent exercise	Two weeks of HRW intake may help to maintain PPO in repetitive sprints to exhaustion over 30 minutes.
Korovljev et al., 2019	Hydrogen-rich water reduces liver fat accumulation and improves liver enzyme profiles in patients with non-alcoholic fatty liver disease: a randomized controlled pilot trial	Serbia	Randomized controlled pilot trial	They received 1 liter per day of HRW for 28 days.	12	NAFLD	The results of this trial perhaps nominate HRW as an adjuvant treatment for mild-to-moderate NAFLD.
Botek et al., 2019	Hydrogen Rich Water Improved Ventilatory, Perceptual and Lactate Responses to Exercise	Czech Republic/ Australia/ South Africa	Randomized, double blinded placebo-controlled	Administration of 600 mL of HRW in the 30 minutes preceding exercise (H <sub>2</sub> concentration: 0.5 ppm).	12	Physiological responses	Acute pre-exercise supplementation with HRW reduced blood lactate at higher exercise intensities, improved exercise-induced perception of effort, and ventilatory efficiency.

			cross over study				
Sim et al., 2020	Hydrogen-rich water reduces inflammatory responses and prevents apoptosis of peripheral blood cells in healthy adults: a randomized, double-blind, controlled trial.	Korea	Randomized, double-blind, controlled trial	Participants consumed 1.5 L/day of HW for 4 weeks. The hydrogen concentration was $0,753 \pm 0,012$ mg/L. Each participant received three 500-mL bottles per day and was instructed to drink each bottle within one hour after opening to minimize the loss of dissolved H <sub>2</sub> .	38	Inflammatory responses	HW increases antioxidant capacity thereby reducing inflammatory responses in healthy adults.
Ooi et al., 2020	Acute ingestion of hydrogen-rich water does not improve incremental treadmill running performance in endurance-trained athletes	Malaysia	Double-blind crossover design	They ingested two 290 mL doses of hydrogen-enriched water.	14	Endurance-trained athletes	Acute ingestion of H <sub>2</sub> -water does not seem to be ergogenic for endurance performance. A small dose of H <sub>2</sub> -water does not modulate buffering capacity during intense endurance exercise in athletes.
Hori et al., 2020	Two-week continuous supplementation of hydrogenrich water increases peak oxygen uptake during an incremental cycling exercise test in healthy humans: a randomized, single-blinded, placebo-controlled study	Japan	Randomized, single-blinded, placebo-controlled study	Participants underwent either a single intake of HW (500 mL) or two-week supplementation (500 mL/day, totaling 5 L). In Experiment 1, participants ingested 500 mL during a single laboratory visit; in Experiment 2, 500 mL was consumed on 10 days. The measured H <sub>2</sub> concentrations were $4.3 \pm 0.9$ ppm (Experiment 1) and $5.9 \pm 0.2$ ppm (Experiment 2).	29	Oxygen uptake	The continuous supplementation of HW potentially augments the aerobic capacity, implying that continuous supplementation of H <sub>2</sub> might help improve aerobic exercise performance and physical health.
Ishibashi et al., 2020	Peripheral endothelial function can be improved by daily consumption of water containing over 7 ppm of dissolved hydrogen: A	Japan	Randomized controlled trial	Participants received high-concentration H <sub>2</sub> water, containing 7 ppm of H <sub>2</sub> (equivalent to 3.5 mg of H <sub>2</sub> in 500 mL of water).	68	Reactive hyperemia-PAT	Daily consumption of high H <sub>2</sub> water improved the endothelial function of the arteries or arterioles assessed by the PAT test. The results suggest that the continuous consumption of high H <sub>2</sub> water contributes to improved cardiovascular health.

	randomized controlled trial						
Zanini et al., 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.	Serbia	Randomized controlled pilot trial	Participants consumed 0.5 L/day of hydrogen-rich water (HRW), containing 15 ppm of H <sub>2</sub> , over a 6-month intervention period.	40	Aging	This simple biomedical gas could be recognized as a possible anti-aging agent that tackles several hallmarks of aging, including loss of function and telomere length shortening.
Hong et al., 2021	Effects of concomitant use of hydrogen water and photobiomodulation on Parkinson disease	Taiwan	Clinical study	PBM + H <sub>2</sub> for 2 weeks. Intake of hydrogen-rich water (200 mL per can) with a dissolved hydrogen concentration of 2.5 ppm.	18	PD	The study demonstrated that PBM+H <sub>2</sub> therapy is safe and reduces disease severity.
Valenta et al., 2022	Acute pre-exercise hydrogen rich water intake does not improve running performance at maximal aerobic speed in trained track and field runners: A randomized, double-blind, placebo-controlled crossover study	Czech Republic/ South Africa/ Australia	Randomized, double-blind, placebo-controlled crossover study	Participants ingested 1.260 mL of water, divided into four doses: 420 mL at 120 min, 420 mL at 60 min, 210 mL at 30 min, and 210 mL at 10 min before exercise, with an H <sub>2</sub> concentration of 0.9 ppm.	24	Running performance	Pre-exercise administration of 1260 ml of HRW showed no ergogenic effect on running performance to exhaustion at maximal aerobic speed in trained track and field runners.
Botek et al., 2022a	Molecular Hydrogen Mitigates Performance Decrement during Repeated Sprints in Professional Soccer Players	Czech Republic/ USA/ Australia/ South Africa	Randomized, double blinded, placebo controlled, crossover study	A total volume of 1.260 mL of HRW was administered in four doses: 420 mL at 120 min, 420 mL at 60 min, and 210 mL at 15 and 5 min before repeated sprints. The total absolute H <sub>2</sub> dose administered was 756 μmol per participant.	16	Repeated sprint performance	Pre-exercise HRW supplementation is associated with an increased ability to reduce fatigue, especially during the later stages of repeated sprint exercise.



Botek et al., 2022b	Hydrogen Rich Water Consumption Positively Affects Muscle Performance, Lactate Response, and Alleviates Delayed Onset of Muscle Soreness After Resistance Training	Czech Republic/ Australia/ South Africa	Randomized, double-blinded placebo-controlled cross-over study	A total volume of 1.260 mL of HRW was administered in five doses: 210 mL at 30 min and 1 min before training, 210 mL mid-exercise, 210 mL immediately after exercise, and 420 mL 30 minutes after recovery. The H <sub>2</sub> concentration was 0.9 ppm.	12	Physiological responses	An acute intermittent HRW hydration improved muscle function, reduced the lactate response, and alleviated delayed onset of muscle soreness.
Najmanová et al., 2023	Effect of Acute Hydrogen-Rich Water Intake on Intraocular Pressure in Healthy Subjects	ns	Prospective, randomized and double-blind, with crossover design	A total volume of 1260 mL of HRW was administered over 15 min in three doses.	24	Intraocular Pressure	The rapid intake of 1260 ml of both HRW and hydrogen-free water causes a statistically significant increase in IOP compared to the baseline in healthy individuals.
Aker et al., 2024	The effect of hydrogen-rich water consumption on premenstrual symptoms and quality of life: a randomized controlled trial	Turkey	Randomized controlled trial	Participants consumed 1500 to 2000 mL of HRW daily, starting on day 16 of the menstrual cycle until day 2 of the subsequent cycle, for three consecutive menstrual cycles.	65	PMS	The consumption of HRW reduces the severity of premenstrual symptoms and improves individuals' quality of life in physical and psychological domains.
Todorovic et al., 2025	The Effects of 8-Week Hydrogen-Rich Water Consumption on Appetite, Body Composition, Sleep Quality, and Circulating Glucagon-like Peptide-1 in Obese Men and Women (HYDRAPPET): A Randomized Controlled Trial	Serbia	Randomized Controlled Trial	Participants consumed 1.0 L/day of hydrogen-rich water (15 mg of H <sub>2</sub> ) for eight weeks.	36	Obesity	These findings suggest that hydrogen-rich water may serve as a safe and effective dietary strategy to address appetite regulation and related metabolic indices in individuals with obesity.



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T2DM - type 2 diabetes mellitus; PD - Parkinson's disease; UPDRS - Unified Parkinson's Disease Rating Scale; IC/PBS - interstitial cystitis/painful bladder syndrome; CHB - chronic hepatitis B; HRW - hydrogen water; ROS - reactive oxygen species; PPO - peak power output; NAFLD - non-alcoholic fatty liver disease; PAT - peripheral arterial tonometry; PBM - photobiomodulation

Table 3. More details from the studies retrieved Hydrotherapy with Hydrogen-enriched Water

Author/Year	Title	Country	Study type	Characteristics	N	Condition	Conclusion
Javorac et al., 2021	Hydrotherapy with hydrogen-rich water compared with RICE protocol following acute ankle sprain in professional athletes: a randomized non-inferiority pilot trial	Serbia	Randomized non-inferiority pilot trial	The hydrogen group received six 30-minute ankle baths with HRW during the first 24 hours after injury. Hydrotherapy was administered every 4 hours, using a whirlpool with a hydrogen concentration of approximately 8 ppm.	18	AAS	This non-inferiority pilot trial supports the use of HRW as an effective choice in AAS management.

AAS - acute ankle sprain; HRW - hydrogen water.

Table 4. More details from the studies retrieved Hydrogen Inhalation

Author/Year	Title	Country	Study type	Characteristics	N	Condition	Conclusion
Tamasawa et al., 2015	Hydrogen gas production is associated with reduced interleukin-1 $\beta$ mRNA in peripheral blood after a single dose of acarbose in Japanese type 2 diabetic patients	Japan	Clinical study	Gaseous hydrogen was administered for 60, 120, 180, and 300 minutes.	16	Type 2 diabetic	The results suggest that an increase in hydrogen gas production is inversely associated with a reduction of the peripheral blood IL-1 $\beta$ mRNA level after a single dose of acarbose in Japanese type 2 diabetic patients.
Tamura et al., 2016	Feasibility and Safety of Hydrogen Gas Inhalation for Post-Cardiac Arrest Syndrome - First-in-Human Pilot Study	Japan	First-in-Human Pilot Study	Patients underwent HI with 2% H <sub>2</sub> in oxygen, initiated via a ventilator upon ICU admission and continued for 18 hours.	5	PCAS	HI in combination with TTM is a feasible therapy for patients with PCAS.
Ono et al., 2017	Hydrogen Gas Inhalation Treatment in Acute Cerebral Infarction: A Randomized Controlled Clinical Study on Safety and Neuroprotection	Japan	Randomized Controlled Clinical Study on Safety and Neuroprotection	The treated group inhaled 3% hydrogen gas (H <sub>2</sub> ) via a conventional non-rebreathing face mask for 1 hour, twice daily, over a 7-day period.	50	Acute Cerebral Infarction	H <sub>2</sub> treatment was safe and effective in patients with acute cerebral infarction. These results suggested a potential for widespread and general application of H <sub>2</sub> gas.
Katsumata et al., 2017	The Effects of Hydrogen Gas Inhalation on Adverse Left Ventricular Remodeling After Percutaneous	Japan	First Pilot Study in Humans	The HI intervention used a gas mixture containing 1.3% H <sub>2</sub> and 26% oxygen.	20	AMI	HI during PCI is feasible and safe and may also promote LV reverse remodeling at 6 months after STEMI.

	Coronary Intervention for ST-Elevated Myocardial Infarction - First Pilot Study in Humans						
Shibayama et al., 2020	Impact of hydrogen-rich gas mixture inhalation through nasal cannula during post-exercise recovery period on subsequent oxidative stress, muscle damage, and exercise performances in men	Japan	Two-trial, double-blind, crossover, repeated measures study	Participants inhaled hydrogen gas, with estimated inspired fractions of up to 21.57% oxygen and 4.08% hydrogen.	8	Post-exercise recovery	These findings suggested that HG inhalation during post-exercise recovery period might improve exercise performance via reducing systemic oxidative damage.
Chen et al., 2020a	Two weeks of hydrogen inhalation can significantly reverse adaptive and innate immune system senescence patients with advanced non-small cell lung cancer: a self-controlled study	China	Self-controlled study	Participants inhaled a gas mixture of hydrogen (66.7%) and oxygen (33.3%) via nasal cannula or mask, at a flow rate of 3 L/min, for 4 hours per day over 2 weeks.	20	Immune system senescence	The study provides initial evidence that two weeks of hydrogen inhalation can significantly reverse senescence in both the adaptive and innate immune systems.
Chen et al., 2020b	Hydrogen therapy can be used to control tumor progression and alleviate the adverse events of medications in patients with advanced non-small cell lung cancer	China	Clinical study	Patients inhaled H <sub>2</sub> for 4–5 hours per day for 5 months, with treatment discontinued in case of cancer recurrence. H <sub>2</sub> was generated using a hydrogen–oxygen nebulizer delivering 66.7% H <sub>2</sub> and 33.3% oxygen, with a maximum gas flow of 3 L/min.	20	Lung cancer	Treatment with H <sub>2</sub> inhalation may enable control of tumor growth and reduce the prevalence of drug-associated adverse events.

Yoritaka et al., 2021	Randomized double-blind placebo-controlled trial of hydrogen inhalation for Parkinson's disease: a pilot study	Japan	Randomized double-blind placebo-controlled trial	Participants inhaled hydrogen gas at $6.5 \pm 0.1\%$ (v/v), delivered at 2 L/min of mixed air, twice daily, for 1 hour, over 16 weeks.	20	PD	Inhalation of molecular hydrogen gas was safe, but did not show any beneficial effects in patients with PD.
Tao et al., 2022	A randomized, placebo-controlled clinical trial of hydrogen/oxygen inhalation for non-alcoholic fatty liver disease	China	Randomized, placebo-controlled clinical trial	The hydrogen/oxygen group inhaled a gas mixture of 66% hydrogen and 33% oxygen at a flow rate of 3 L/min for 1 hour per day over 13 weeks.	43	NAFLD	Hydrogen inhalation alleviated NAFLD in moderate–severe patients. This protective effect of hydrogen was possibly by activating hepatic autophagy.
Botek et al., 2022c	Molecular Hydrogen Positively Affects Physical and Respiratory Function in Acute Post-COVID-19 Patients: A New Perspective in Rehabilitation	Czech Republic/ Australia	Randomized, single-blind, placebo-controlled study	H <sub>2</sub> inhalation: 2 daily sessions of 60 minutes for 14 days, at a flow rate of 300 mL/min.	50	COVID-19	H <sub>2</sub> inhalation may represent a safe, effective approach for accelerating early function restoration in post-COVID-19 patients.
Eda et al., 2022	Effects of Intestinal Bacterial Hydrogen Gas Production on Muscle Recovery following Intense Exercise in Adult Men: A Pilot Study		Double-blind, randomized, crossover study	Participants ingested H <sub>2</sub> -producing milk, which stimulated intestinal bacterial hydrogen production. The milk was prepared by adding galactooligosaccharide (2 g), maltitol (2 g), and glucomannan (0.2 g) to cow's milk.	8	Muscle Recovery	Activating intestinal bacterial H <sub>2</sub> production by consuming a specific beverage may be a new strategy for promoting recovery and conditioning in athletes frequently performing intense exercises.
Deryugina et al., 2023	Molecular hydrogen exposure improves functional state of red blood cells in the early postoperative period: a randomized clinical study	Russian Federation	Randomized clinical study	Participants received H <sub>2</sub> at a concentration of 1.5–2.0% via face mask, using the ventilator breathing circuit together with anesthesia, immediately after tracheal intubation and throughout the surgical procedure.	24	Red blood cells	H <sub>2</sub> inhalation leads to improvement of functional state of red blood cells, which is accompanied by a more favorable course of the early postoperative period.

Tamura et al., 2024	Combination of Hydrogen Inhalation and Hypothermic Temperature Control After Out-of-Hospital Cardiac Arrest: A Post hoc Analysis of the Efficacy of Inhaled Hydrogen on Neurologic Outcome Following Brain Ischemia During PostCardiac Arrest Care II Trial	Japan	Clinical study	Therapeutic hypothermia was applied using two target temperature ranges: 32–34 °C (HT32–HT34) or 35–36 °C (HT35–HT36).	72	PCABI	Hydrogen inhalation is a promising treatment option for reducing PCABI when combined with TTM32–TTM34.
Chitapanarux et al., 2024	Pilot Feasibility and Safety Study of Hydrogen Gas Inhalation in Locally Advanced Head and Neck Cancer Patients	Japan	Pilot prospective study	Patients inhaled hydrogen gas via cannula or mask for 1 hour per day, 1–2 hours before IMRT, completing 33 inhalation sessions.	10	LAHNC	H2 gas inhalation combined with CCRT is feasible and safe for patients with LAHNC.
Zhao et al., 2024	Hydrogen gas inhalation prior to high-intensity training reduces attenuation of nitric oxide bioavailability in male rugby players	China/ Australia	Randomized, placebo-controlled, double-blind, crossover trial	Participants completed 1 week of H <sub>2</sub> supplementation. During the first training week, each group received the assigned supplement (H <sub>2</sub> or placebo) for 20 min, starting 1 hour before each training session. The seventh day was a rest day, with no training and no H <sub>2</sub> administration. The gas mixture contained 66.7% H <sub>2</sub> and 33.3% oxygen.	22	NO	The results suggest that H <sub>2</sub> inhalation helps to maintain NO signaling after exercise and to alleviate inflammation and oxidative stress induced by high-intensity exercise training in professional athletes.
Salomez et al., 2024	H <sub>2</sub> inhalation therapy in patients with moderate COVID-19 (H <sub>2</sub> COVID): a prospective	France	Open-label, prospective, monocentric, single ascending-dose study	A fixed flow of 1 L/min of a medical-grade gas mixture containing 3.6% H <sub>2</sub> and 96.4% N <sub>2</sub> was administered, combined with oxygen (O <sub>2</sub> ) supplied from a wall outlet. Using a 3+3 design, the study evaluated three exposure	12	COVID-19	Every patient showed clinical improvement and excellent tolerance to H <sub>2</sub> therapy.

	ascending-dose phase I clinical trial			durations: 1 day (D1), 3 days (D2), and 6 days (D3).			
Grepl et al., 2025	Molecular hydrogen inhalation modulates resting metabolism in healthy females: findings from a randomized, double-blind, placebo-controlled crossover study	Czech Republic	Randomized, double-blind, placebo-controlled crossover study	Participants underwent molecular hydrogen inhalation for 60 min via nasal cannula, at a flow rate of 300 mL/min. The gas mixture consisted of 99.8% molecular hydrogen, 0.12% nitrogen, 0.055% oxygen, and < 0.002% carbon dioxide.	20	Resting metabolism	60 minutes of resting molecular hydrogen inhalation significantly increased resting fat oxidation, as evidenced by decreased respiratory exchange ratio, particularly in individuals with higher body fat percentages.

PCAS - post-cardiac arrest syndrome; HI - hydrogen gas inhalation; TTM - targeted temperature management; PCI - percutaneous coronary intervention; LV - left ventricular; STEMI - ST-segment elevation myocardial infarction; AMI - acute myocardial infarction; HG - hydrogen-rich gas; PD - Parkinson's disease; NAFLD - non-alcoholic fatty liver disease; PCABI - post-cardiac arrest brain injury; LAHNC - locally advanced head and neck cancer; NO - nitric oxide.

Table 5. More details from the studies retrieved Intravenous Infusion of Hydrogen-enriched Solution

Author/Year	Title	Country	Study type	Characteristics	N	Condition	Conclusion
Ishibashi et al., 2014	Therapeutic efficacy of infused molecular hydrogen in saline on rheumatoid arthritis: a randomized, double-blind, placebo-controlled pilot study	Japan	Randomized, double-blind, placebo-controlled pilot study	A 1 ppm hydrogen-rich saline solution (H <sub>2</sub> -saline) was administered at 500 mL per day via intravenous drip infusion (IV), before breakfast, for 5 days.	24	RA	Drop infusion of H <sub>2</sub> safely and effectively reduced RA disease activity.
Terawaki et al., 2014	Effect of a hydrogen (H <sub>2</sub> )-enriched solution on the albumin redox of hemodialysis patients	Japan	Cross-over study	Two hydrogen-enriched sessions were performed, with a mean H <sub>2</sub> concentration of 50 ppb (H <sub>2</sub> -HD).	8	HD	The application of H <sub>2</sub> -enriched solutions could ameliorate OS during HD.
Takeuchi et al., 2021	Intravenous Hydrogen Therapy With Intracisternal Magnesium Sulfate Infusion in Severe Aneurysmal Subarachnoid Hemorrhage	Japan	Randomized, double-blind, placebo-controlled trial	Participants received intravenous infusion of hydrogen-rich solution for 14 days. The H <sub>2</sub> concentration in the infusion bag reached saturation (>1.0 ppm) due to diffusion through the bag wall. The intravenous solution (200 mL) was administered at 200 mL/h, twice daily, for 14 days.	37	Severe Aneurysmal Subarachnoid Hemorrhage	Intracisternal magnesium sulfate infusion combined with intravenous hydrogen therapy decreases serum malondialdehyde and neuron-specific enolase and improves Barthel index, indicating hydrogen has additional effects.

rheumatoid arthritis; HD – hemodialysis; OS - oxidative stress.

Table 6. More details from the studies retrieved Molecular Hydrogen Capsules/Tablets

Author/Year	Title	Country	Study type	Characteristics	N	Condition	Conclusion
Korovljevic et al., 2018	Molecular hydrogen affects body composition, metabolic profiles, and mitochondrial function in middle-aged overweight women	Serbia	Double blind, placebo-controlled, crossover pilot trial	Participants received hydrogen-generating minerals, administered orally in capsule form, providing ~6 ppm of H <sub>2</sub> per day for 4 weeks.	7	Obesity	Orally administered H <sub>2</sub> as a blend of hydrogen-generating minerals might be a beneficial agent in the management of body composition and insulin resistance in obesity.
Ostojic et al., 2014	Effectiveness of oral and topical hydrogen for sports-related soft tissue injuries	Serbia	Randomly assigned trials in a single-blind design	Group 2: administration of oral hydrogen-rich tablets (2 g/day). Group 3: oral hydrogen-rich tablets (2 g/day) combined with topical hydrogen-rich compresses, applied 6 times per day for 20 min.	36	Sports-related soft tissue injuries	The preliminary results support the hypothesis that the addition of hydrogen to traditional treatment protocols is potentially effective in the treatment of soft tissue injuries in male professional athletes.
Lu et al., 2024	Using oral molecular hydrogen supplements to combat microinflammation in humans: a pilot observational study	Taiwan	Clinical study	Each capsule contained 0.17 mg of hydrogen-rich coral calcium, equivalent to $7.5 \times 10^{16}$ molecules of H <sub>2</sub> per capsule. The protocol lasted 4 weeks with three dosing levels: Low dose: 1 capsule/day, fasting (28 capsules); Medium dose: 3 capsules/day, fasting (84 capsules); High dose: 6 capsules/day (3 in the morning and 3 in the evening; 168 capsules).	30	Microinflammation	CHSOs supplementation may exert anti-inflammatory and antioxidant effects on individuals with chronic inflammation. However, further clinical studies could be investigated to explore the potential therapeutic effects of CHSOs.

RA - rheumatoid arthritis; HD – hemodialysis; OS - oxidative stress; CHSOs - oral solid hydrogen-generating compounds.

Table 7. More details from the studies retrieved Hydrogen-rich Calcium Powder.

Author/Year	Title	Country	Study type	Characteristics	N	Condition	Conclusion
Alharbi et al., 2021	Application of Molecular Hydrogen as an Antioxidant in Responses to Ventilatory and Ergogenic Adjustments during Incremental Exercise in Humans	Japan	Randomized, double-blind, crossover design	Participants received HCP at a dose of 1,500 mg/day, providing 2.544 µg/day of H <sub>2</sub> , for 3 consecutive days.	18	Responses during incremental exercise	H <sub>2</sub> -rich calcium powder supplementation, which increased the potential for antioxidant-dependent slightly lower pH at rest, resulted in significantly lower V <sup>E</sup> and pH status during the incremental exercise compared to placebo.
Alharbi et al., 2022	The Acute Effects of a Single Dose of Molecular Hydrogen Supplements on Responses to Ergogenic Adjustments during High-Intensity Intermittent Exercise in Humans	Japan	Randomized, double-blind, crossover design	Participants received HCP (1.500 mg, containing 2.544 µg of H <sub>2</sub> ) or a low-H <sub>2</sub> placebo (.,500 mg), administered 1 hour before exercise.	10	Responses Ergogenic	The HCP supplement might exert ergogenic effects on high-intensity exercise and prove advantageous for improving anaerobic HIIT exercise performance.

HCP - hydrogen-rich calcium powder supplements; HIIT - high-intensity interval training.