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Abstract: ***Background and Aims***: Preliminary studies indicate that dihydrogen (H_2) may affect molecular pathways involved in appetite regulation; however, its role in influencing patient-reported appetite outcomes in individuals with obesity remains uncertain. This randomized, placebo-controlled, double-blind trial aimed to evaluate the effects of H_2 supplementation on appetite, body composition, sleep quality, obesity-specific quality of life, and related biomarkers in obese men and women. ***Methods and Results:*** The study included 36 participants (24 females; age 42.1 ± 13.2 years, BMI 30.8 ± 4.2 kg/m^2) randomized to receive either 1.0 L of hydrogen-rich water (15 mg of H_2) or 1.0 L of control water (0 mg of H_2) daily for eight weeks. Results demonstrated that hydrogen-rich water significantly mitigated cravings ($P = 0.05$), improved subjective sleep quality ($P = 0.05$), reduced total cholesterol ($P = 0.02$) and LDL cholesterol ($P = 0.04$), and increased plasma glucagon-like peptide-1 levels ($P = 0.05$) compared to the control. No severe adverse effects were reported throughout the trial. ***Conclusions***: 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. The study is registered at ClinicalTrials.gov (NCT06722326).

Keywords*:* dihydrogen; cravings; cholesterol; sleep; supplementation; GLP-1

Introduction

Molecular hydrogen (H_2, dihydrogen) has emerged as an innovative biomedical agent with significant therapeutic potential across various domains of human health. Among these, dihydrogen shows particular promise for metabolic conditions. Recent studies have demonstrated the benefits of molecular hydrogen in individuals with metabolic syndrome (Nakao et al., 2010; Song et al., 2013; LeBaron et al., 2020), type 2 diabetes (Kajiyama et al., 2008; Asada et al., 2020), non-alcoholic fatty liver disease (Korovljev et al., 2019; Kura et al., 2022; Sumbalová et al., 2023), hyperuricemia (Wu et al., 2024), and obesity (Korovljev et al., 2018; Korovljev et al., 2023b). In these conditions, dihydrogen likely acts as a hormetic and signaling agent. It may also help suppress endoplasmic reticulum stress, activate autophagy, upregulate mitochondrial function, and regulate gut microbiota (for a detailed review, see Xie et al., 2023). Preliminary findings suggest that dihydrogen might also influence the cerebral regulation of energy homeostasis, potentially impacting both orexigenic and anorexigenic

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signaling (Ostojic, 2021). Our research group recently demonstrated that dihydrogen can modulate the glutamate-GABA-glutamine cycle, a critical pathway underlying appetite suppression and weight-loss effects (Korovljev et al., 2023a). However, the effects of dihydrogen on other key neurotransmitters involved in appetite regulation, such as glucagon-like peptide-1 (GLP-1), and on appetite measures in obese individuals, remain unknown. Thus, the primary aim of this randomized controlled trial was to evaluate the effects of dihydrogen supplementation on body composition indices, appetite, obesity-specific quality of life, and circulating GLP-1 levels in obese men and women. We hypothesized that dihydrogen would upregulate GLP-1 levels, reduce appetite, and promote weight loss within this population.

Methods

Participants

The present trial employed a parallel-group, randomized, placebo-controlled, double-blind design, with an allocation ratio of 1:1 between the experimental group (hydrogen-rich water) and the control group (placebo). Eligibility criteria for participant inclusion required individuals to be aged 18-65 years, classified as obese (body fat > 30% for women, and >25% for men), and sedentary, defined as engaging in less than 150 minutes of moderate physical activity per week. Exclusion criteria included the presence of any major chronic diseases or acute injuries at the time of recruitment, dietary supplement use within four weeks prior to study initiation, use of obesity-related pharmaceutical within eight weeks prior to study initiation, refusal to consent to randomization, and concurrent participation in other trials. All eligible participants provided informed consent, and ethical approval was obtained from the local IRB at the University of Novi Sad (#50-06-18/2024-1). The study adhered to the principles of the Declaration of Helsinki (7th revision). Data collection took place at the Applied Bioenergetics Lab at the University of Novi Sad between April and December 2024. The baseline characteristics of study participants are presented in Table 1. The study is registered at ClinicalTrials.gov (NCT06722326).

Table 1. Baseline characteristics of study participants (n = 36).

	Mean ± SD	**Min - Max**
Age (years)	42.1 ± 13.2	20 – 62
Female (%)	66.7	-
Weight (kg)	89.2 ± 17.6	61.6 – 141.1
Body mass index (kg/m²)	30.8 ± 4.2	24.0 – 42.1
Waist circumference (cm)	94.7 ± 11.6	74.0 – 122.5
Body fat percentage (%)	34.4 ± 7.0	25.0 – 47.5
Blood glucose (mmol/L)	5.47 ± 0.60	4.61 – 7.39
Total cholesterol (mmol/l)	5.33 ± 1.01	3.58 – 7.20
LDL-cholesterol (mmol/L)	3.26 ± 0.90	1.87 – 5.44
HDL-cholesterol (mmol/L)	1.46 ± 0.44	0.86 – 2.85
Triglycerides (mmol/L)	1.51 ± 1.43	0.59 – 8.67

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Interventions

Participants in the experimental group received hydrogen-rich water at a daily dosage of 1.0 L, while the control group (placebo) received an equal amount of tap water. Both interventions were administered three times daily (morning, early afternoon, and before dinner; 333 mL per serving), with a dihydrogen concentration of 5 mg per serving in the experimental drink (totaling 15 mg of H_2 per day) and 0 mg per serving in the control drink. The appearance, texture, and sensory characteristics of both drinks were identical. The interventions were provided by Natural Wellness Now Health Products Inc. (Maple Ridge, BC, Canada). The intervention period lasted eight weeks, during which participants were asked to refrain from using any other nutritional supplements or weight management interventions, including diet modifications, exercise, anti-obesity medications, behavioral therapy, or bariatric surgery.

Outcomes

The study's predetermined primary and secondary outcomes included appetite assessments, body composition indices, obesity-related quality of life, sleep quality components, biochemical markers, and the prevalence and severity of side effects. The primary endpoint was the change in appetite (total cravings score) from baseline to the follow-up (see below). All measures were assessed at baseline (pre-administration) and at the 8-week follow-up (post-administration). Laboratory assessments were conducted between 08:00 and 12:00 following an overnight fast. Participants were instructed to abstain from physical exercise for 12 hours and to avoid alcohol, coffee, tea, fizzy drinks, or energy drinks for 24 hours before measurements. Anthropometric measurements included height (Seca 210, Hamburg, Germany) and weight (Omron BF508, Tokyo, Japan), with body mass index (BMI) calculated as weight in kilograms divided by the square of height in meters. Waist circumference was measured with an anthropometric tape (Gulic CHP, Ann Arbor, MI, USA). Body composition was assessed using a multifrequency bioelectrical impedance analyzer (BioScan 920, Maltron International Ltd, Rayleigh, Essex, UK), recording parameters such as fat and fat-free mass, muscle mass, total and compartmental body water (intracellular and extracellular), protein mass, mineral mass, total body calcium, and glycogen mass. Appetite was assessed using the Food Cravings Questionnaire (FCQ) (Meule, 2020), a validated tool designed to measure five key dimensions of appetite: (1) an intense desire to eat, (2) the anticipation of positive reinforcement from eating, (3) the expectation of relief from negative emotional states through eating, (4) a lack of control over eating behaviors, and (5) cravings as a physiological state, such as hunger. Respondents rated items on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree), with higher scores reflecting greater intensity of food cravings. The Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire (Kolotkin et al., 2019), a validated 31-item self-report tool, assessed obesity-specific quality of life across five domains: physical function, self-esteem, sexual life, public distress, and work, with scores ranging from 0 to 100 (higher scores indicating better quality of life). Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989), covering seven subcategories (subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep medication, and daytime dysfunction), where higher scores indicate more significant sleep disturbances. Fasting blood samples were collected at each lab visit for biochemical analyses. Glucose, total cholesterol, triglycerides, and lipoprotein levels were determined by standard enzymatic methods using an automated analyzer (Hitachi, Tokyo, Japan). Serum levels of short-chain fatty acids (SCFA)—acetic acid, propionic acid, and butyric acid—were measured by a sensitive gas chromatography tandem mass spectroscopy method with modifications (Yao et al., 2022). Plasma GLP-1 levels were assessed with a commercial ELISA kit (Elabscience, Houston, TX). Molecular hydrogen levels in breath were measured using an electrochemical fuel cell microprocessor (LactoFAN2, Fischer Analysen Instrumente GmbH, Leipzig, Germany). Participants were also asked to report any side effects (*e.g.*, stomach upset, bloating, constipation, diarrhea, nausea, vomiting) experienced due to either intervention throughout the study using an open-ended questionnaire. No modifications to trial outcomes were made after the study began.

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Statistical analyses

The minimum sample size (n = 24) was determined by power analysis using G*Power 3.1 (Heinrich-Heine-Universität Düsseldorf), with an effect size of 0.30 (indicating a small effect), an alpha level of 0.05, and a power of 0.80, based on the anticipated change in appetite (total cravings score) from baseline to the 8-week follow-up. This calculation assumed two groups with two measurement points for study outcomes. To allow for potential attrition, the sample size was increased to 36 participants. To maintain balanced participant characteristics across groups, a stratified randomization model was applied, creating separate blocks based on gender (male and female). Data normality was assessed using the Shapiro-Wilk test, and variance homogeneity was examined with Bartlett's test. Within-group differences over time were compared using t-tests for normally distributed data and the Wilcoxon Signed-Ranks Test for non-normally distributed data. For data with a normal distribution and homogeneous variances, interaction effects (time *vs.* intervention) were analyzed with a mixed model ANOVA. In cases of non-homogeneous variances, comparisons were conducted using the Friedman test. Effect sizes for within-group comparisons were calculated using Cohen's d, while interaction effects were assessed using partial eta squared (η_p^2). Statistical significance was set at $P \leq 0.05$. Missing data were excluded from the analyses. All statistical analyses were conducted using SPSS version 24.0 for Mac (IBM SPSS Statistics, Chicago, IL).

Results

A total of 35 participants (n = 35; 23 females) were randomly assigned to the intervention or control group, received the allocated supplementation, and were included in the primary outcome analysis. Of these, 18 participants (12 females) were in the experimental group, and 17 participants (11 females) were in the control group. The flow of participants through each stage of the randomized trial is depicted in Figure 1.

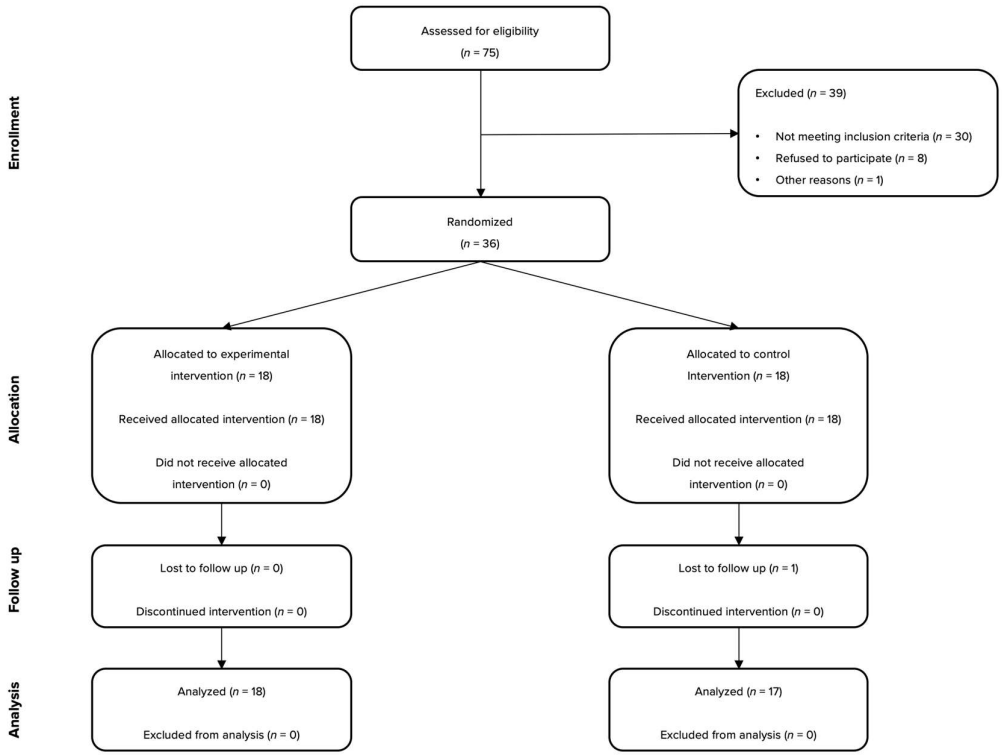

Figure 1. Participants flow during the study.

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Changes in primary and secondary outcomes over the course of the trial are presented in Table 2 (appetite assessments), Table 3 (body composition indices), Table 4 (obesity-related quality of life), Table 5 (sleep quality components), and Table 6 (biochemical markers).

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Table 2. Food appetite domains in the experimental group (HRW) and control group (CON) at baseline and after 8 weeks. Values are expressed as mean ± SD.

	Group	Baseline	Follow-up	Delta	95% CI	p †	Cohen d	p ‡	η_p^2
Intense desire to eat									
Total	HRW	12.9 ± 4.4	11.2 ± 4.5	1.8 ± 3.0	0.3 – 3.3	0.01	0.38	0.30	0.07
	CON	12.2 ± 3.4	11.5 ± 2.9	0.6 ± 3.4	-1.1 – 2.4	0.22	0.22		
Female	HRW	13.7 ± 4.3	11.5 ± 4.0	2.2 ± 2.7	0.5 – 3.9	0.01	0.53	0.26	0.12
	CON	11.4 ± 3.9	11.2 ± 3.1	0.2 ± 4.1	-2.6 – 3.0	0.44	0.06		
Male	HRW	11.3 ± 4.5	10.3 ± 5.9	1.0 ± 3.5	-2.7 – 4.7	0.26	0.19	0.70	0.03
	CON	13.7 ± 1.6	12.2 ± 2.5	1.5 ± 1.4	0.0 – 3.0	0.02	0.72		
Anticipation of positive reinforcement from eating									
Total	HRW	11.8 ± 4.0	10.6 ± 4.4	1.2 ± 2.7	-0.1 – 2.5	0.04	0.28	0.64	0.01
	CON	11.3 ± 3.2	10.6 ± 2.4	0.6 ± 2.5	-0.7 – 1.9	0.15	0.25		
Female	HRW	12.4 ± 3.8	11.5 ± 4.3	0.9 ± 3.1	-1.1 – 2.9	0.16	0.22	0.53	0.04
	CON	10.1 ± 3.0	10.2 ± 2.6	-0.1 ± 2.4	-1.7 – 1.5	0.45	0.04		
Male	HRW	10.7 ± 4.3	8.8 ± 4.4	1.8 ± 1.8	-0.1 – 3.7	0.03	0.44	0.88	0.01
	CON	13.5 ± 2.5	11.5 ± 1.8	2.0 ± 2.3	-0.4 – 4.4	0.04	0.92		
Expectation of relief from negative emotional states through eating									
Total	HRW	11.1 ± 4.4	10.0 ± 3.5	1.1 ± 2.1	0.1 – 2.1	0.02	0.28	0.16	0.12
	CON	9.5 ± 2.8	9.6 ± 2.8	-0.1 ± 2.5	-1.4 – 1.2	0.46	0.04		
Female	HRW	11.6 ± 4.1	10.4 ± 3.4	1.2 ± 2.4	-0.3 – 2.7	0.06	0.32	0.19	0.17
	CON	9.7 ± 2.9	10.2 ± 2.7	-0.5 ± 3.0	-2.5 – 1.5	0.31	0.18		
Male	HRW	10.3 ± 5.2	9.3 ± 3.9	1.0 ± 1.7	-0.8 – 2.8	0.10	0.22	0.66	0.04
	CON	9.2 ± 2.9	8.5 ± 3.0	0.7 ± 1.4	-0.8 – 2.2	0.14	0.24		
Lack of control over eating behaviors									
Total	HRW	10.5 ± 4.1	9.6 ± 4.1	0.9 ± 2.8	-0.5 – 2.3	0.09	0.22	0.41	0.04
	CON	10.0 ± 2.7	9.8 ± 2.7	0.2 ± 2.2	-0.9 – 1.3	0.38	0.07		
Female	HRW	11.3 ± 3.8	10.1 ± 3.7	1.2 + 3.1	-0.8 – 3.2	0.11	0.32	0.17	0.18
	CON	9.8 ± 3.1	10.0 ± 3.1	-0.2 ± 1.9	-1.5 – 1.1	0.38	0.07		
Male	HRW	9.0 ± 4.6	8.5 ± 4.9	0.5 ± 2.4	-2.0 – 3.0	0.32	0.11	0.82	0.01

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	CON	10.3 ± 2.1	9.5 ± 2.1	0.8 ± 2.9	-2.2 – 3.8	0.25	0.38		
				Cravings as a physiological state					
Total	HRW	11.8 ± 2.9	9.5 ± 4.3	2.3 ± 3.3	0.7 – 3.9	< 0.01	0.63		
								0.05	0.22
	CON	10.4 ± 3.6	10.5 ± 2.6	-0.1 ± 3.2	-1.7 – 1.5	0.47	0.03		
Female	HRW	11.7 ± 3.0	9.2 ± 3.7	2.5 ± 3.3	0.4 – 4.6	0.01	0.74		
								0.05	0.33
	CON	10.4 ± 3.8	10.9 ± 2.8	-0.5 ± 3.7	-3.0 – 2.0	0.32	0.15		
Male	HRW	11.8 ± 3.1	10.0 ± 5.6	1.8 ± 3.6	-2.0 – 5.6	0.13	0.40		
								0.47	0.11
	CON	10.5 ± 3.5	9.7 ± 2.3	0.8 ± 1.8	-1.1 – 2.7	0.16	0.27		
				Total score					
Total	HRW	58.2 ± 17.1	50.8 ± 18.9	7.4 ± 5.6	4.6 – 10.2	< 0.01	0.41		
								0.05	0.21
	CON	53.3 ± 12.7	52.0 ± 11.0	1.3 ± 10.0	-3.8 – 6.4	0.29	0.11		
Female	HRW	60.7 ± 16.0	52.7 ± 17.1	8.0 ± 4.5	5.1 – 10.9	< 0.01	0.48		
								0.03	0.41
	CON	51.3 ± 14.1	52.4 ± 11.8	-1.1 ± 11.0	-8.5 – 6.3	0.37	0.09		
Male	HRW	53.1 ± 19.6	46.9 ± 23.5	6.2 ± 7.8	-2.0 – 14.4	0.06	0.29		
								0.89	0.01
	CON	57.1 ± 9.6	51.3 ± 10.1	5.8 ± 6.4	-0.9 – 12.5	0.04	0.59		

Abbreviations. HRW, hydrogen-rich water; CON, control water. Cross (†) indicates statistical significance for within-group comparison versus baseline leves. Double dagger (‡) indicates statistical significance for interaction effect (time *vs.* treatment).

Hydrogen-rich water consumption significantly reduced all dimensions of appetite after eight weeks compared to baseline values in the overall sample, except for the dimension related to a lack of control over eating behaviors. No significant differences were observed in the placebo group when comparing pre- and post-intervention measurements across the entire sample. A significant interaction effect (time × treatment) was observed for cravings as a physiological state ($P = 0.05$) and total scores for cravings ($P = 0.05$), with hydrogen-rich water demonstrating greater efficacy than placebo in mitigating these specific appetite dimensions in the overall sample. The effect sizes for these interactions exceeded the threshold for large effects ($\eta_p^2 > 0.14$). Gender-specific analyses yielded comparable findings for the female subsample, showing significant interaction effects (with large effect sizes) for cravings as a physiological state and total scores ($P < 0.05$).

Table 3. Body size and body composition in the experimental group (HRW) and control group (CON) at baseline and after 8 weeks. Values are expressed as mean ± SD.

	Group	Baseline	Follow-up	Delta	95% CI	p †	Cohen d	p ‡	η_p^2
				Weight (kg)					
Total	HRW	90.0 ± 19.3	89.4 ± 19.0	0.6 ± 2.0	-0.4 – 1.6	0.26	0.03		
								0.41	0.04
	CON	88.3 ± 16.5	88.2 ± 17.1	0.0 ± 1.3	-0.7 – 0.7	0.46	0.01		

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Female	HRW	81.7 ± 13.5	81.8 ± 13.2	-0.2 ± 1.4	-1.1 – 0.7	0.36	0.01	0.77	0.01
	CON	79.8 ± 13.6	79.7 ± 13.9	0.1 ± 1.5	-0.9 – 1.1	0.44	0.01		
Male	HRW	106.7 ± 19.1	104.7 ± 20.6	2.0 ± 2.4	-0.5 – 4.5	0.05	0.10	0.07	0.52
	CON	103.9 ± 9.2	103.9 ± 9.4	0.0 ± 0.7	-0.7 – 0.7	0.44	0.00		
Body mass index (kg/m²)									
Total	HRW	30.9 ± 4.3	30.9 ± 4.4	0.0 ± 0.8	-0.4 – 0.4	0.49	0.01	0.34	0.06
	CON	30.4 ± 4.5	30.2 ± 3.9	0.2 ± 1.1	-0.4 – 0.8	0.21	0.05		
Female	HRW	30.4 ± 3.8	30.5 ± 3.8	-0.1 ± 0.7	-0.5 – 0.3	0.26	0.03	0.44	0.06
	CON	29.5 ± 5.3	29.1 ± 4.3	0.3 ± 1.3	-0.6 – 1.2	0.22	0.08		
Male	HRW	32.0 ± 5.2	31.7 ± 5.7	0.3 ± 1.1	-0.9 – 1.5	0.27	0.06	0.54	0.08
	CON	32.1 ± 2.2	32.0 ± 2.3	0.0 ± 0.4	-0.4 – 0.4	0.41	0.04		
Waist circumference (cm)									
Total	HRW	96.0 ± 12.5	96.0 ± 12.7	0.0 ± 3.0	-1.5 – 1.5	0.49	0.01	0.82	0.01
	CON	93.4 ± 11.2	93.3 ± 11.6	0.1 ± 2.4	-1.1 – 1.3	0.46	0.06		
Female	HRW	91.2 ± 10.9	91.5 ± 11.2	-0.3 ± 2.3	-1.8 – 1.2	0.35	0.03	0.82	0.01
	CON	88.6 ± 9.7	88.8 ± 9.3	-0.2 ± 2.0	-1.5 – 1.1	0.39	0.02		
Male	HRW	105.4 ± 10.2	105.0 ± 11.5	0.5 ± 4.4	-4.1 – 5.1	0.41	0.04	0.99	0.00
	CON	102.0 ± 9.2	101.5 ± 11.5	0.5 ± 3.2	-2.9 – 3.9	0.36	0.05		
Fat mass (%)									
Total	HRW	35.0 ± 6.9	34.6 ± 8.6	0.4 ± 3.5	-1.3 – 2.1	0.31	0.05	0.53	0.03
	CON	33.2 ± 7.2	33.4 ± 6.8	-0.2 ± 2.3	-1.4 – 1.0	0.40	0.02		
Female	HRW	38.1 ± 4.4	38.2 ± 6.3	0.0 ± 3.7	-2.4 – 2.4	0.48	0.02	0.46	0.06
	CON	36.8 ± 5.2	36.7 ± 4.8	0.1 ± 2.1	-1.3 – 1.5	0.45	0.02		
Male	HRW	28.8 ± 7.0	27.5 ± 8.6	1.3 ± 3.0	-1.8 – 4.4	0.17	0.17	0.23	0.27
	CON	26.7 ± 5.1	27.2 ± 5.7	-0.6 ± 2.9	-3.6 – 2.4	0.33	0.09		
Fat free mass (kg)									
Total	HRW	60.0 ± 13.5	59.8 ± 13.3	0.2 ± 2.9	-1.2 – 1.6	0.38	0.02	0.74	0.01
	CON	59.2 ± 14.3	58.9 ± 14.1	0.3 ± 2.4	-0.9 – 1.5	0.30	0.02		
Female	HRW	52.5 ± 8.6	53.2 ± 7.4	0.2 ± 3.3	-1.9 – 2.3	0.40	0.09	0.50	0.05

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	CON	49.8 ± 6.0	49.8 ± 6.3	0.0 ± 1.5	-1.0 – 1.0	0.46	0.00		
Male	HRW	75.0 ± 7.2	74.9 ± 8.7	0.1 ± 2.3	-2.3 – 2.5	0.44	0.01		
								0.60	0.06
	CON	76.3 ± 6.5	75.4 ± 6.6	0.9 ± 3.6	-2.9 – 4.7	0.27	0.14		
				Muscle mass (kg)					
Total	HRW	26.8 ± 8.2	26.7 ± 8.2	0.1 ± 1.1	-0.4 – 0.6	0.41	0.10		
								0.70	0.01
	CON	27.2 ± 8.4	27.1 ± 8.2	0.1 ± 1.0	-0.4 – 0.6	0.30	0.01		
Female	HRW	21.5 ± 2.9	21.5 ± 2.1	0.0 ± 1.3	-0.8 – 0.8	0.46	0.00		
								0.51	0.05
	CON	21.5 ± 2.6	21.6 ± 2.8	-0.1 ± 0.5	-0.4 – 0.2	0.32	0.04		
Male	HRW	37.3 ± 3.7	37.2 ± 4.3	0.1 ± 0.8	-0.7 – 0.9	0.39	0.03		
								0.52	0.09
	CON	37.7 ± 3.1	37.2 ± 3.3	0.5 ± 1.5	-1.2 – 2.1	0.23	0.16		
				Total body water (L)					
Total	HRW	45.6 ± 10.3	45.3 ± 9.4	0.3 ± 3.6	-1.5 – 2.1	0.36	0.03		
								0.97	0.01
	CON	45.7 ± 10.6	45.4 ± 10.5	0.3 ± 2.7	-1.1 – 1.7	0.36	0.02		
Female	HRW	40.3 ± 7.6	39.8 ± 4.3	0.6 ± 4.2	-2.1 – 3.1	0.32	0.08		
								0.59	0.03
	CON	38.9 ± 5.5	39.0 ± 6.0	-0.1 ± 1.5	-1.1 – 0.9	0.39	0.02		
Male	HRW	56.1 ± 5.9	56.3 ± 6.6	-0.2 ± 2.2	-2.5 – 2.1	0.41	0.03		
								0.58	0.07
	CON	58.0 ± 5.0	57.1 ± 5.0	0.5 ± 3.6	-3.3 – 4.3	0.38	0.18		
				Intracellular water (L)					
Total	HRW	25.3 ± 6.5	25.3 ± 6.2	0.1 ± 2.2	-1.0 – 1.2	0.45	0.01		
								0.78	0.01
	CON	25.3 ± 6.9	25.5 ± 6.7	-0.2 ± 2.5	-1.5 – 1.1	0.38	0.03		
Female	HRW	21.7 ± 4.3	21.5 ± 2.5	0.3 ± 2.5	-1.3 – 1.9	0.35	0.06		
								0.69	0.02
	CON	20.7 ± 3.1	21.4 ± 3.6	-0.7 ± 2.0	-2.0 – 0.6	0.15	0.21		
Male	HRW	32.5 ± 3.2	32.9 ± 3.7	-0.4 ± 1.4	-1.9 – 1.1	0.28	0.11		
								0.52	0.09
	CON	33.9 ± 3.1	33.2 ± 3.2	0.7 ± 3.2	-2.7 – 4.1	0.31	0.22		
				Extracellular water (L)					
Total	HRW	20.3 ± 3.9	20.0 ± 3.3	0.2 ± 1.5	-0.5 – 0.9	0.25	0.07		
								0.98	0.01
	CON	20.1 ± 3.7	20.0 ± 3.7	0.1 ± 0.9	-0.4 – 0.6	0.28	0.04		
Female	HRW	18.6 ± 3.3	18.3 ± 1.9	0.3 ± 1.7	-0.8 – 1.4	0.28	0.11		
								0.61	0.03
	CON	17.9 ± 2.3	17.8 ± 2.5	0.1 ± 0.8	-0.4 – 0.6	0.38	0.04		

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Male	HRW	23.5 ± 2.8	23.4 ± 3.0	0.1 ± 1.2	-1.2 – 1.4	0.39	0.03	0.87	0.01
	CON	24.2 ± 2.0	23.9 ± 1.9	0.2 ± 1.2	-1.1 – 1.5	0.33	0.15		
Protein mass (L)									
Total	HRW	9.4 ± 3.8	9.5 ± 3.5	-0.1 ± 0.8	-0.5 – 0.3	0.28	0.03	0.33	0.06
	CON	9.8 ± 3.5	9.7 ± 3.4	0.2 ± 1.0	-0.3 – 0.7	0.27	0.04		
Female	HRW	7.0 ± 1.5	7.3 ± 1.0	-0.3 ± 0.8	-0.8 – 0.2	0.12	0.24	0.50	0.05
	CON	7.7 ± 1.9	7.5 ± 1.7	0.2 ± 1.1	-0.5 – 0.9	0.30	0.11		
Male	HRW	14.0 ± 2.1	13.8 ± 2.7	0.3 ± 0.7	-0.4 – 1.0	0.19	0.08	0.77	0.02
	CON	13.6 ± 1.8	13.5 ± 1.7	0.1 ± 0.6	-0.5 – 0.7	0.38	0.06		
Mineral mass (L)									
Total	HRW	3.6 ± 1.2	3.6 ± 1.1	-0.1 ± 0.3	-0.2 – 0.0	0.26	0.04	0.32	0.06
	CON	3.7 ± 1.1	3.7 ± 1.0	0.1 ± 0.4	-0.1 – 0.3	0.28	0.05		
Female	HRW	2.9 ± 0.6	3.0 ± 0.4	-0.1 ± 0.3	-0.3 – 0.1	0.12	0.20	0.37	0.08
	CON	3.2 ± 0.8	3.1 ± 0.7	0.1 ± 0.5	-0.2 – 0.4	0.28	0.13		
Male	HRW	4.9 ± 0.8	4.8 ± 1.0	0.1 ± 0.2	-0.1 – 0.3	0.19	0.11	0.50	0.10
	CON	4.8 ± 0.6	4.8 ± 0.6	0.0 ± 0.2	-0.2 – 0.2	0.48	0.00		
Total body calcium (kg)									
Total	HRW	1.2 ± 0.3	1.2 ± 0.3	0.0 ± 0.1	0.0 – 0.0	0.39	0.01	0.94	0.01
	CON	1.2 ± 0.3	1.2 ± 0.3	0.0 ± 0.5	-0.3 – 0.3	0.38	0.01		
Female	HRW	1.0 ± 0.1	1.0 ± 0.1	0.0 ± 0.1	-0.1 – 0.1	0.37	0.00	0.72	0.01
	CON	1.0 ± 0.1	1.0 ± 0.1	0.0 ± 0.3	-0.2 – 0.2	0.27	0.00		
Male	HRW	1.6 ± 0.2	1.6 ± 0.2	0.0 ± 0.1	-0.1 – 0.1	0.47	0.00	0.53	0.08
	CON	1.6 ± 0.1	1.6 ± 0.2	0.0 ± 0.1	-0.1 – 0.1	0.27	0.00		
Glycogen mass (kg)									
Total	HRW	531 ± 126	530 ± 123	1.3 ± 25.9	-11.6 – 14.2	0.41	0.01	0.60	0.02
	CON	538 ± 129	534 ± 128	3.7 ± 21.6	-7.4 – 14.8	0.24	0.03		
Female	HRW	456 ± 64	455 ± 45	1.3 ± 28.8	-17.0 – 19.6	0.44	0.02	0.39	0.07
	CON	454 ± 52	453 ± 58	1.0 ± 13.7	-8.2 – 10.2	0.41	0.02		
Male	HRW	682 ± 66	680 ± 79	1.3 ± 21.1	-20.8 – 23.4	0.44	0.03	0.60	0.06

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CON	694 ± 59	685 ± 60	8.7 ± 32.7	-25.6 – 43.0	0.27	0.15

Abbreviations. HRW, hydrogen-rich water; CON, control water. Cross (†) indicates statistical significance for within-group comparison versus baseline leves. Double dagger (‡) indicates statistical significance for interaction effect (time *vs.* treatment).

Hydrogen-rich water consumption resulted in a significant reduction in body weight among the male subsample (mean change: −2.0 ± 2.4 kg; $P = 0.05$) after 8 weeks compared to baseline values. No significant changes were observed for other body size or body composition indices in the overall sample or within gender-specific subsamples during the pre-post assessment period. No significant interaction effect was observed between interventions for body size or composition indices throughout the trial. However, a notable trend ($P = 0.07$) suggested that hydrogen-rich water may outperform placebo in reducing body weight among men.

Table 4. Obesity-related quality of life in the experimental group (HRW) and control group (CON) at the baseline and after 8 weeks. Values are expressed as mean ± SD.

	Group	Baseline	Follow-up	Delta	95% CI	p †	Cohen d	p ‡	η_p^2
Physical function (score)									
Total	HRW	70.2 ± 16.2	77.2 ± 14.3	-7.0 ± 13.0	-13.5 – -0.5	0.02	0.46	0.30	0.07
	CON	79.4 ± 24.0	82.5 ± 25.9	-3.1 ± 9.2	-7.8 – 1.6	0.09	0.12		
Female	HRW	68.9 ± 17.5	78.3 ± 15.6	-9.4 ± 12.2	-17.2 – -1.6	0.01	0.57	0.42	0.07
	CON	75.4 ± 28.0	80.8 ± 28.9	-5.4 ± 8.6	-11.2 – 0.4	0.03	0.19		
Male	HRW	72.7 ± 14.2	75.0 ± 12.2	-2.3 ± 14.3	-17.3 – 12.7	0.36	0.17	0.61	0.06
	CON	86.7 ± 14.0	85.6 ± 21.5	1.1 ± 9.5	-8.9 – 11.1	0.39	0.06		
Self-esteem (score)									
Total	HRW	68.7 ± 28.4	72.8 ± 22.5	-4.1 ± 10.3	-9.2 – 1.0	0.05	0.16	0.67	0.01
	CON	67.0 ± 27.4	72.5 ± 27.5	-5.5 ± 8.8	-10.0 – -1.0	0.01	0.20		
Female	HRW	62.5 ± 31.7	69.6 ± 26.4	-7.1 ± 10.1	-13.5 – -0.7	0.02	0.24	0.14	0.05
	CON	64.0 ± 31.2	67.9 ± 32.2	-3.9 ± 8.7	-9.7 – 1.9	0.08	0.12		
Male	HRW	81.0 ± 15.8	79.1 ± 11.3	1.9 ± 8.6	-7.1 – 10.9	0.31	0.14	< 0.01	0.87
	CON	72.6 ± 20.9	81.0 ± 14.9	-8.3 ± 8.9	-17,6 – 1.0	0.04	0.46		
Sexual life (score)									
Total	HRW	78.8 ± 21.7	84.0 ± 19.3	-5.2 ± 12.0	-11.2 – 0.8	0.04	0.25	0.51	0.03
	CON	88.6 ± 26.3	91.5 ± 24.7	-2.9 ± 14.2	-10.2 – 4.4	0.20	0.11		
Female	HRW	74.5 ± 22.2	81.8 ± 21.4	-7.3 ± 13.8	-16.1 – 1.5	0.05	0.34	0.34	0.03
	CON	82.4 ± 31.5	86.9 ± 30.2	-4.5 ± 17.7	-16.4 – 7.4	0.21	0.15		

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Male	HRW	87.5 ± 19.4	88.5 ± 15.0	-1.0 ± 6.1	-7.4 – 5.4	0.35	0.06	0.69	0.03
	CON	100.0 ± 0.0	100.0 ± 0.0	0.0 ± 0.0	0.0 – 0.0	0.99	0.00		
Public distress (score)									
Total	HRW	95.3 ± 7.8	95.6 ± 9.8	-0.3 ± 4.0	-2.3 – 1.7	0.39	0.03	0.99	0.01
	CON	92.1 ± 22.5	92.4 ± 24.0	-0.3 ± 4.5	-2.1 – 1.5	0.40	0.01		
Female	HRW	95.0 ± 9.0	95.0 ± 11.9	0.0 ± 4.8	-3.0 – 3.0	0.50	0.00	0.99	0.02
	CON	89.1 ± 28.2	89.5 ± 29.8	-0.5 ± 5.2	-4.0 – 3.0	0.39	0.01		
Male	HRW	95.8 ± 4.9	96.7 ± 4.1	-0.8 ± 2.0	-2.9 – 1.3	0.18	0.20	0.61	0.06
	CON	97.5 ± 6.1	97.5 ± 4.2	0.0 ± 3.2	-3.4 – 3.4	0.50	0.00		
Work (score)									
Total	HRW	94.4 ± 9.3	91.3 ± 10.9	3.1 ± 11.0	-2.4 – 8.6	0.12	0.31	0.18	0.11
	CON	91.5 ± 24.8	91.9 ± 24.1	-0.4 ± 4.6	-2.8 – 2.0	0.36	0.02		
Female	HRW	97.9 ± 4.1	90.6 ± 11.5	7.3 ± 9.5	1.3 – 13.3	0.01	0.85	0.57	0.37
	CON	88.1 ± 31.1	89.2 ± 29.9	-1.1 ± 3.8	-3.7 – 1.5	0.17	0.04		
Male	HRW	87.5 ± 13.1	92.7 ± 7.3	-5.2 ± 9.2	-14.9 – 4.5	0.11	0.49	0.18	0.33
	CON	97.9 ± 3.2	97.0 ± 5.1	1.0 ± 6.0	-5.3 – 7.3	0.35	0.21		
Total scores (score)									
Total	HRW	80.9 ± 13.1	84.1 ± 12.5	-3.2 ± 5.4	-5.9 – -0.5	0.01	0.25	0.69	0.01
	CON	83.7 ± 22.9	86.2 ± 23.2	-2.4 ± 5.2	-5.1 – 0.3	0.04	0.11		
Female	HRW	78.9 ± 14.1	82.9 ± 14.3	-4.1 ± 5.8	-7.8 – -0.4	0.02	0.28	0.66	0.02
	CON	79.8 ± 28.0	82.9 ± 28.4	-3.1 ± 6.3	-7.2 – 1.1	0.07	0.11		
Male	HRW	84.9 ± 10.7	86.4 ± 8.5	-1.5 ± 4.6	-6.3 – 3.3	0.23	0.16	0.88	0.01
	CON	91.0 ± 6.7	92.2 ± 6.5	-1.2 ± 2.3	-3.6 – 1.2	0.12	0.18		

Abbreviations. HRW, hydrogen-rich water; CON, control water. Cross (†) indicates statistical significance for within-group comparison versus baseline leves. Double dagger (‡) indicates statistical significance for interaction effect (time *vs.* treatment).

Hydrogen-rich water consumption significantly improved physical function, self-esteem, sexual life, and total scores for obesity-related quality of life after eight weeks compared to baseline values in the overall sample. The placebo intervention similarly improved self-esteem and cumulative scores in pre-post comparisons within the total sample. Still, no significant interaction effects were observed across the total sample. Subgroup analysis revealed significant improvements across nearly all indices (excluding public distress) following hydrogen-rich water intake, and in physical function and work performance following placebo intake in females, with no significant interaction effects

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observed between interventions in this group. In males, no significant changes were detected during the trial except for a self-esteem interaction effect ($P < 0.01$), where placebo demonstrated greater efficacy than hydrogen-rich water in enhancing this variable.

Table 5. Sleep quality indices in the experimental group (HRW) and control group (CON) at the baseline and after 8 weeks. Values are expressed as mean ± SD.

	Group	Baseline	Follow-up	Delta	95% CI	p †	Cohen d	p ‡	η_p^2
Subjective sleep quality									
Total	HRW	1.7 ± 0.8	0.7 ± 0.7	1.0 ± 0.8	0.6 – 1.4	< 0.01	1.33	0.05	0.21
	CON	1.8 ± 0.9	1.2 ± 0.7	0.6 ± 0.8	0.2 – 1.0	< 0.01	0.74		
Female	HRW	1.8 ± 0.7	0.6 ± 0.7	1.3 ± 0.9	0.7 – 1.9	< 0.01	1.71	0.14	0.21
	CON	1.7 ± 0.8	1.0 ± 0.6	0.7 ± 0.6	0.3 – 1.1	< 0.01	0.99		
Male	HRW	1.5 ± 0.8	1.0 ± 0.6	0.5 ± 0.5	0.0 – 1.0	0.04	0.71	0.61	0.06
	CON	1.8 ± 1.2	1.5 ± 0.5	0.3 ± 1.0	-0.7 – 1.3	0.23	0.45		
Sleep latency									
Total	HRW	1.6 ± 1.4	0.9 ± 1.3	0.7 ± 1.6	-0.1 – 1.5	0.05	0.52	0.91	0.00
	CON	1.5 ± 1.3	0.7 ± 0.9	0.8 ± 1.1	0.2 – 1.4	0.01	0.72		
Female	HRW	1.9 ± 1.5	0.8 ± 1.3	1.1 ± 1.6	0.1 – 2.1	0.02	0.78	0.64	0.02
	CON	1.3 ± 0.8	0.5 ± 0.7	0.7 ± 0.8	0.2 – 1.2	0.01	1.06		
Male	HRW	1.0 ± 1.1	1.3 ± 1.0	-0.3 ± 1.4	-1.9 – 1.3	0.29	0.29	0.34	0.18
	CON	1.8 ± 1.8	1.0 ± 1.3	0.8 ± 1.7	-1.0 – 2.6	0.14	0.51		
Sleep duration									
Total	HRW	0.8 ± 0.8	0.8 ± 0.6	-0.1 ± 0.9	-0.5 – 0.3	0.40	0.00	0.07	0.20
	CON	1.1 ± 1.2	0.8 ± 0.9	0.4 ± 0.7	0.0 – 0.8	0.03	0.28		
Female	HRW	0.9 ± 0.9	0.7 ± 0.7	0.3 ± 1.0	-0.3 – 0.9	0.19	0.25	0.52	0.04
	CON	1.2 ± 1.1	0.6 ± 0.5	0.5 ± 0.8	0.0 – 1.0	0.03	0.70		
Male	HRW	0.5 ± 0.5	1.2 ± 0.4	-0.7 ± 0.5	-1.2 – -0.2	0.01	1.54	0.07	0.60
	CON	0.8 ± 1.3	1.0 ± 1.4	0.2 ± 0.5	-0.3 – 0.7	0.99	0.15		
Sleep efficiency									
Total	HRW	0.1 ± 0.2	0.1 ± 0.3	-0.1 ± 0.5	-0.3 – 0.1	0.29	0.00	0.77	0.01
	CON	0.4 ± 0.8	0.5 ± 0.8	-0.1 ± 0.6	-0.4 – 0.2	0.22	0.13		

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Female	HRW	0.1 ± 0.3	0.2 ± 0.4	0.1 ± 0.5	-0.2 – 0.4	0.29	0.28	0.99	0.00
	CON	0.2 ± 0.3	0.2 ± 0.4	0.0 ± 0.6	-0.4 – 0.4	0.50	0.00		
Male	HRW	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 – 0.0	0.99	0.00	0.18	0.40
	CON	0.7 ± 1.2	1.2 ± 1.1	-0.3 ± 0.5	-0.8 – 0.2	0.09	0.43		
Sleep disturbance									
Total	HRW	1.2 ± 0.5	0.9 ± 0.5	0.2 ± 0.5	0.0 – 0.4	0.05	0.60	0.54	0.02
	CON	1.3 ± 0.8	1.2 ± 0.6	0.1 ± 0.5	-0.2 – 0.4	0.17	0.14		
Female	HRW	1.3 ± 0.5	1.1 ± 0.5	0.3 ± 0.6	-0.1 – 0.7	0.10	0.40	0.19	0.16
	CON	1.3 ± 0.7	1.3 ± 0.6	0.0 ± 0.4	-0.3 – 0.3	0.50	0.00		
Male	HRW	0.8 ± 0.4	0.7 ± 0.5	0.2 ± 0.4	-0.2 – 0.6	0.18	0.22	0.61	0.06
	CON	1.3 ± 1.0	1.0 ± 0.6	0.3 ± 0.5	-0.2 – 0.8	0.09	0.36		
Use of sleep medication									
Total	HRW	0.2 ± 0.7	0.5 ± 1.0	-0.3 ± 0.8	-0.7 – 0.1	0.07	0.35	0.24	0.09
	CON	0.4 ± 1.0	0.4 ± 0.9	0.0 ± 0.6	-0.3 – 0.3	0.50	0.00		
Female	HRW	0.3 ± 0.9	0.6 ± 1.0	-0.3 ± 0.7	-0.7 – 0.1	0.05	0.32	0.05	0.33
	CON	0.4 ± 1.0	0.3 ± 0.9	0.1 ± 0.3	-0.1 – 0.3	0.17	0.11		
Male	HRW	0.2 ± 0.4	0.2 ± 0.4	0.0 ± 0.0	0.0 – 0.0	0.99	0.00	0.70	0.03
	CON	0.5 ± 1.2	0.7 ± 1.0	-0.2 ± 1.0	-1.2 – 0.8	0.35	0.18		
Daytime dysfunction									
Total	HRW	1.4 ± 0.7	0.8 ± 0.5	0.6 ± 0.9	0.2 – 1.0	0.01	0.99	0.71	0.01
	CON	1.1 ± 1.1	0.6 ± 0.9	0.5 ± 0.9	0.1 – 0.9	0.02	0.50		
Female	HRW	1.4 ± 0.8	0.8 ± 0.6	0.6 ± 0.9	0.0 – 1.2	0.02	0.85	0.84	0.00
	CON	1.0 ± 1.1	0.5 ± 0.9	0.5 ± 1.1	-0.2 – 1.2	0.11	0.50		
Male	HRW	1.3 ± 0.5	0.7 ± 0.5	0.7 ± 1.0	-0.3 – 1.7	0.09	1.20	0.99	0.00
	CON	1.3 ± 1.2	0.7 ± 0.8	0.7 ± 0.5	0.2 – 1.2	0.01	0.59		
Total score									
Total	HRW	6.9 ± 2.5	4.8 ± 2.2	2.2 ± 3.3	0.6 – 3.8	0.01	0.89	0.92	0.00
	CON	7.5 ± 4.9	5.2 ± 4.1	2.2 ± 2.5	0.9 – 3.5	< 0.01	0.51		
Female	HRW	7.8 ± 2.6	4.8 ± 2.6	3.0 ± 3.7	0.6 – 5.4	0.01	1.15	0.77	0.01

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	CON	7.0 ± 3.2	4.5 ± 3.1	2.5 ± 2.1	1.1 – 3.9	< 0.01	0.79		
Male	HRW	5.3 ± 1.2	4.8 ± 1.3	0.5 ± 1.6	-1.2 – 2.2	0.24	0.40		
								0.51	0.09
	CON	8.3 ± 7.3	6.7 ± 5.6	1.7 ± 3.3	-1.8 – 5.2	0.14	0.25		

Abbreviations. HRW, hydrogen-rich water; CON, control water. Cross (†) indicates statistical significance for within-group comparison versus baseline leves. Double dagger (‡) indicates statistical significance for interaction effect (time *vs.* treatment).

Hydrogen-rich water consumption significantly enhanced subjective sleep quality, sleep latency, sleep disturbance, daytime dysfunction, and total sleep scores post-intervention compared to baseline values in the overall sample. Similarly, the placebo intervention improved subjective sleep quality, sleep latency, sleep duration, daytime dysfunction, and total sleep scores in pre-post comparisons. Notably, a significant interaction effect was observed for subjective sleep quality (P = 0.05), with hydrogen-rich water demonstrating superior improvements compared to placebo across the overall sample. Subgroup analysis identified several domain-specific improvements in sleep following either intervention in pre-post comparisons, with a significant interaction effect (P = 0.05) observed for the use of sleep medication in the female subsample.

Table 6. Biochemical markers in the experimental group (HRW) and control group (CON) at the baseline and after 8 weeks. Values are expressed as mean ± SD.

	Group	Baseline	Follow-up	Delta	95% CI	p †	Cohen d	p ‡	η_p^2
				GLP-1 (pg/mL)					
Total	HRW	69.3 ± 50.7	86.2 ± 65.4	-16.9 ± 40.1	-36.8 – 3.0	0.05	0.29		
								0.05	0.20
	CON	80.6 ± 70.5	78.1 ± 51.2	2.4 ± 37.0	-16.6 – 21.4	0.40	0.04		
Female	HRW	60.9 ± 47.3	88.5 ± 70.7	-27.6 ± 43.2	-55.0 – -0.2	0.02	0.36		
								0.09	0.25
	CON	70.2 ± 75.6	74.2 ± 61.2	-4.0 ± 30.4	-16.4 – 24.4	0.34	0.21		
Male	HRW	86.6 ± 56.7	81.4 ± 59.7	5.2 ± 22.2	-18.1 – 28.5	0.30	0.09		
								0.58	0.07
	CON	99.6 ± 61.7	85.4 ± 28.5	14.1 ± 47.8	-36.1 – 64.3	0.25	0.29		
				Acetic acid (μg/mL)					
Total	HRW	3.35 ± 1.01	3.03 ± 0.85	0.32 ± 1.05	-0.31 – 0.95	0.11	0.34		
								0.95	< 0.01
	CON	3.11 ± 0.72	2.76 ± 0.64	0.35 ± 0.90	-0.09 – 0.79	0.06	0.52		
Female	HRW	3.12 ± 0.76	2.73 ± 0.52	0.39 ± 0.92	-0.16 – 0.94	0.09	0.60		
								0.65	0.02
	CON	3.10 ± 0.52	2.87 ± 0.47	0.23 ± 0.70	-0.21 – 0.67	0.16	0.46		
Male	HRW	3.81 ± 1.34	3.63 ± 1.11	0.18 ± 1.35	-1.30 – 1.76	0.38	0.14		
								0.43	0.13
	CON	3.14 ± 1.06	2.55 ± 0.90	0.59 ± 1.23		0.15	0.60		
				Propionic acid (μg/mL)					
Total	HRW	0.37 ± 0.20	0.23 ± 0.05	0.14 ± 0.20	0.04 – 0.24	0.01	0.91	0.30	0.07

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	CON	0.31 ± 0.07	0.22 ± 0.05	0.09 ± 0.09	0.05 – 0.13	< 0.01	1.51		
Female	HRW	0.30 ± 0.09	0.23 ± 0.05	0.07 ± 0.11	0.01 – 0.13	0.02	0.99	0.89	< 0.01
	CON	0.31 ± 0.06	0.23 ± 0.03	0.08 ± 0.08	0.04 – 0.12	< 0.01	1.64		
Male	HRW	0.50 ± 0.31	0.24 ± 0.03	0.26 ± 0.30	-0.02 – 0.54	0.04	1.20	0.20	0.31
	CON	0.32 ± 0.09	0.21 ± 0.07	0.11 ± 0.11	0.01 – 0.21	0.03	1.35		
Butyric acid (μg/mL)									
Total	HRW	1.52 ± 0.49	1.03 ± 0.29	0.49 ± 0.48	0.22 – 0.76	< 0.01	1.96	0.72	0.01
	CON	1.42 ± 0.45	0.97 ± 0.26	0.45 ± 0.56	0.19 – 0.71	< 0.01	1.22		
Female	HRW	1.45 ± 0.26	1.10 ± 0.30	0.35 ± 0.29	0.11 – 0.59	< 0.01	1.60	0.91	< 0.01
	CON	1.39 ± 0.31	1.00 ± 0.27	0.39 ± 0.42	0.13 – 0.65	0.01	1.36		
Male	HRW	1.66 ± 0.79	0.90 ± 0.23	0.75 ± 0.69	0.01 – 1.51	0.02	2.79	0.58	0.07
	CON	1.48 ± 0.67	0.93 ± 0.25	0.55 ± 0.81	-0.10 – 1.20	0.08	1.09		
Breath hydrogen (ppm)									
Total	HRW	34 ± 29	28 ± 30	6 ± 45	-16 – 28	0.28	0.21	0.76	0.01
	CON	29 ± 31	26 ± 26	3 ± 42	-19 – 25	0.38	0.10		
Female	HRW	36 ± 32	23 ± 18	14 ± 41	-12 – 40	0.14	0.52	0.26	0.13
	CON	21 ± 24	27 ± 32	6 ± 38	-20 – 32	0.31	0.21		
Male	HRW	30 ± 24	39 ± 45	9 ± 52	-46 – 64	0.35	0.24	0.47	0.11
	CON	44 ± 38	24 ± 15	20 ± 47	-29 - 69	0.18	0.67		
Glucose (mmol/L)									
Total	HRW	5.60 ± 0.56	5.63 ± 0.66	-0.03 ± 0.42	-0.24 – 0.18	0.39	0.05	0.87	< 0.01
	CON	5.38 ± 0.66	5.46 ± 0.96	-0.09 ± 0.47	-0.33 – 0.15	0.23	0.10		
Female	HRW	5.60 ± 0.63	5.64 ± 0.77	-0.05 ± 0.50	-0.37 – 0.27	0.38	0.07	0.43	0.07
	CON	5.28 ± 0.81	5.50 ± 1.16	-0.22 ± 0.49	-0.55 – 0.11	0.08	0.22		
Male	HRW	5.60 ± 0.43	5.60 ± 0.39	0.00 ± 0.24	-0.25 – 0.25	0.49	0.01	0.39	0.15
	CON	5.55 ± 0.25	5.40 ± 0.46	0.16 ± 0.34	-0.20 – 0.52	0.16	0.42		
Total cholesterol (mmol/L)									
Total	HRW	5.63 ± 1.14	5.31 ± 1.13	0.32 ± 0.44	0.10 – 0.54	< 0.01	0.28	0.02	0.31
	CON	5.05 ± 0.79	5.16 ± 0.86	-0.11 ± 0.55	-0.39 – 0.17	0.20	0.14		

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Female	HRW	5.49 ± 1.23	5.27 ± 1.20	0.21 ± 0.46	-0.08 – 0.50	0.07	0.18	0.04	0.35
	CON	5.08 ± 0.69	5.37 ± 0.73	-0.29 ± 0.56	-0.67 – 0.09	0.06	0.40		
Male	HRW	5.91 ± 0.96	5.39 ± 1.06	0.52 ± 0.37	0.13 – 0.91	0.01	0.51	0.16	0.35
	CON	5.00 ± 0.99	4.79 ± 1.03	0.21 ± 0.38	-0.19 – 0.61	0.12	0.20		
LDL cholesterol (mmol/L)									
Total	HRW	3.45 ± 1.06	3.16 ± 1.03	0.28 ± 0.53	0.02 – 0.54	0.02	0.28	0.04	0.24
	CON	3.08 ± 0.73	3.15 ± 0.61	-0.07 ± 0.48	-0.32 – 0.18	0.29	0.10		
Female	HRW	3.21 ± 0.99	3.02 ± 0.98	0.20 ± 0.52	-0.13 – 0.53	0.11	0.20	0.08	0.30
	CON	3.02 ± 0.69	3.26 ± 0.56	-0.21 ± 0.47	-0.53 – 0.11	0.08	0.38		
Male	HRW	4.04 ± 1.11	3.45 ± 1.17	0.49 ± 0.57	-0.11 – 1.09	0.06	0.52	0.30	0.26
	CON	3.18 ± 0.85	2.96 ± 0.71	0.22 ± 0.32	-0.12 – 0.56	0.08	0.28		
HDL cholesterol (mmol/L)									
Total	HRW	1.57 ± 0.52	1.51 ± 0.52	0.07 ± 0.15	0.00 – 0.14	0.04	0.13	0.30	0.07
	CON	1.34 ± 0.31	1.32 ± 0.34	0.02 ± 0.14	-0.05 – 0.09	0.29	0.06		
Female	HRW	1.74 ± 0.56	1.65 ± 0.57	0.09 ± 0.14	0.00 – 0.18	0.02	0.16	0.30	0.11
	CON	1.40 ± 0.36	1.39 ± 0.39	0.00 ± 0.16	-0.11 – 0.11	0.46	0.01		
Male	HRW	1.24 ± 0.07	1.22 ± 0.20	0.02 ± 0.18	-01.7 – 0.21	0.41	0.12	0.68	0.04
	CON	1.24 ± 0.19	1.19 ± 0.17	0.05 ± 0.13	-0.09 – 0.19	0.21	0.26		
Triglycerides (mmol/L)									
Total	HRW	1.41 ± 0.85	1.43 ± 0.63	-0.02 ± 0.67	-0.35 – 0.31	0.46	0.02	0.46	0.04
	CON	1.63 ± 1.95	1.92 ± 2.58	-0.28 ± 0.76	-0.67– 0.11	0.07	0.12		
Female	HRW	1.17 ± 0.20	1.35 ± 0.62	-0.18 ± 0.51	-0.50 – 0.14	0.12	0.39	0.43	0.06
	CON	1.83 ± 2.46	2.19 ± 3.19	-0.37 ± 0.91	-0.98 – 0.24	0.11	0.13		
Male	HRW	1.90 ± 1.40	1.59 ± 0.67	0.31 ± 0.87	-0.60 – 1.22	0.21	0.28	0.13	0.40
	CON	1.28 ± 0.45	1.41 ± 0.61	-0.13 ± 0.34	-0.49 – 0.23	0.20	0.24		

Abbreviations. HRW, hydrogen-rich water; CON, control water; GLP-1, glucagon-like peptide-1. Cross (†) indicates statistical significance for within-group comparison versus baseline leves. Double dagger (‡) indicates statistical significance for interaction effect (time *vs.* treatment).

The consumption of hydrogen-rich water significantly increased serum GLP-1 levels in both the entire sample and the female subsample after 8 weeks compared to baseline. In contrast, no significant changes in serum GLP-1 levels were observed in the placebo group during the pre-post assessment period. A significant interaction effect was identified for serum GLP-1 levels in the entire

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sample (P = 0.05), indicating that hydrogen-rich water was more effective than placebo in increasing serum GLP-1 levels, with a large effect size for the interaction (η_p^2 = 0.20).

The consumption of hydrogen-rich water had no effect on serum acetic acid levels but significantly reduced serum propionic acid and butyric acid concentrations in the overall sample and within both gender subgroups after 8 weeks, compared to baseline. Similarly, the placebo intervention led to reductions in circulating propionic acid and butyric acid in pre-post comparisons. No significant interaction effects between the interventions were observed for any of the three serum SCFAs throughout the trial.

Drinking hydrogen-rich water significantly reduced total cholesterol, LDL cholesterol, and HDL cholesterol levels after eight weeks of administration compared to baseline values, while no significant changes were observed in the placebo group during pre-post comparisons across the overall sample. A significant interaction effect was detected for total cholesterol (P = 0.02) and LDL cholesterol (P = 0.04), with hydrogen-rich water showing superior reductions in these parameters compared to placebo. Subgroup analysis revealed notable improvements in lipid profiles following hydrogen-rich water consumption, with a significant interaction effect observed for total cholesterol in the female subsample (P = 0.04). The effect sizes for above interactions were considered large (η_p^2 > 0.14).

Finally, no participants reported any severe adverse effects that impeded their participation in the trial; one participant was lost to follow-up. Among those in the experimental group, one female participant (aged 50) noted more frequent bowel movements after the intervention, while another female participant (aged 51) reported a reduction in dizziness frequently experienced prior to the study. In the control group, one female participant (aged 25) indicated an improvement in work performance during daily activities. Adherence to the intervention was high, averaging 98.3 ± 2.4% in the experimental group and 97.1 ± 2.9% in the control group (P = 0.18), based on the number of unused bottles.

Discussion

Our trial is among the first to evaluate the effects of hydrogen-rich water on appetite-related indicators and associated outcomes in individuals with obesity. The findings revealed that hydrogen-rich water, administered over an eight-week period, was superior to placebo in reducing food cravings, lowering serum total and LDL cholesterol levels, and upregulating GLP-1 levels in our cohort of obese participants. These effects were particularly pronounced in women, with hydrogen-rich water demonstrating large effect sizes for these outcomes. Additionally, hydrogen-rich water outperformed placebo in improving subjective sleep quality. No adverse effects were reported, and no major differences in body composition or obesity-related quality of life measures were observed between interventions during the study period. These results suggest that hydrogen-rich water is a safe and potentially effective dietary intervention for reducing appetite and improving lipid profiles in adults with obesity. Further research is warranted to explore these effects in larger and more diverse populations.

A limited number of small-scale studies have investigated the potential effects of dihydrogen on appetite and related mediators within experimental and clinical nutrition contexts. A Japanese study was among the first to show that a 4-day supplementation with hydrogen water can influence mRNA expression for ghrelin in mice (Matsumoto et al., 2013), an appetite-stimulating and glucose-regulating hormone that plays a key role in increasing caloric intake and fat deposition. Similarly, another animal study indicated that hydrogen-rich water, consumed over 25 days, could influence daily weight gain, feed intake, and upregulate serum levels of appetite-regulating hormones such as peptide YY and cholecystokinin in female-only piglets fed a mycotoxin-contaminated diet, compared to a control group (Zheng et al., 2018). Furthermore, a 12-week hydrogen-rich water intervention in five overweight women demonstrated effects on the brain's glutamate-glutamine-GABA cycle, which involves critical amino acid neurotransmitters in neural activation related to appetite regulation (Korovljev et al., 2023a). A recent human study explored hydrogen-related appetite control pathways

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in eight patients (1 male, 7 female) with obesity who had undergone Roux-en-Y gastric bypass (RYGB) surgery (Steinert et al., 2024). The authors found that a single dose of a hydrogen-producing compound (inulin) acutely enhanced the glucose-lowering and appetite-suppressive effects of surgery, correlating with breath hydrogen concentrations, though with no measurable effects on plasma GLP-1 and peptide YY. Our study corroborates some findings from these prior investigations, demonstrating positive effects of hydrogen-rich water on appetite markers and lipid profiles. It also expands on these findings by utilizing a longer supplementation period, a larger and gender-diverse sample, and a more comprehensive evaluation of appetite and body composition, focusing specifically on obese individuals.

Our primary finding indicates that hydrogen-rich water was significantly more effective than placebo in suppressing appetite, evidenced by a reduction of 7.4 points in total cravings score in the experimental group compared to 1.3 points in the control group. This suggests that dihydrogen may act as an appetite suppressant, particularly in individuals with obesity. The effect was more pronounced in the female subsample, likely targeting physiological mechanisms underlying cravings, as reflected by a significant intervention-specific difference in this appetite subdomain. Dihydrogen may suppress appetite in individuals with obesity through several interconnected physiological and biochemical pathways. It has been proposed to modulate gut hormones, such as ghrelin, and gut-derived metabolites like SCFAs, which are involved in appetite regulation (McCarty, 2015; Korovljev et al., 2023a). Additionally, dihydrogen may influence appetite-related brain regions and neurotransmitter systems, contributing to its effects on central appetite control (Ostojic, 2021; Korovljev et al., 2023a). By mitigating oxidative stress and inflammation—key factors in dysregulated appetite observed in obesity—dihydrogen could normalize hunger and satiety signals (Kamimura et al., 2011). Furthermore, it may address insulin resistance, which is known to impair the regulation of hunger and fullness (Xie et al., 2023), and alter fatty acid availability, which is closely linked to appetite control (Iio et al., 2013). H_2 may also enhance hydration levels, independently promoting a sense of fullness and thereby reducing caloric intake (Xiao et al., 2022). Lastly, dihydrogen may influence brain estrogen levels, which are implicated in appetite regulation, as demonstrated in an animal study (Houe et al., 2018). The findings indicate that these effects are more pronounced in females, suggesting a potential gender-specific mechanism of action. Our previous study highlights the potential involvement of gut-derived SCFAs in appetite regulation, with hydrogen-rich water significantly elevating fecal propionic levels in individuals with obesity (Korovljev et al., 2023a). SCFAs, produced through colonic fermentation, are known to activate hormonal and neural pathways that suppress appetite and reduce energy intake (Chambers et al., 2015). However, the mechanisms by which hydrogen-induced SCFA production in the gut translates into systemic circulation and influences the brain to regulate appetite remain poorly understood. The present study revealed a reduction in circulating levels of propionic and butyric acid following hydrogen-rich water consumption, with the effects similar to placebo. This decrease in gut-derived propionic acid may result from its utilization by the liver through first-pass metabolism (Tian et al., 2020) or potentially increased uptake by other tissues, including the brain (Ostojic, 2021a; Ostojic, 2021b). Recent studies have highlighted the intricate interplay between the fecal microbiota and plasma metabolites following hydrogen intervention (Xie et al., 2022; Liang et al., 2023), underscoring the need for further research to elucidate the liberation, absorption, distribution, metabolism, and clearance of endogenous SCFAs after hydrogen intake. However, hydrogen-rich water appears to influence GLP-1, a key hormone in appetite regulation. Our trial observed mild-to-moderate increases in serum GLP-1 levels following hydrogen-rich water consumption. GLP-1 plays a critical role in managing appetite by acting on gastrointestinal and brain satiety pathways (Shah and Vella, 2014). These findings suggest that hydrogen-rich water may serve as a novel dietary intervention, potentially modulating GLP-1 metabolism through mechanisms affecting its secretion, cellular uptake, or elimination. Further clinical research is essential to elucidate these pathways and confirm the effectiveness of hydrogen-rich water in appetite suppression among individuals with obesity.

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No significant differences in body size or composition between interventions were observed in the present study, likely attributable to the relatively short duration of the intervention. Previous research has indicated a trend toward weight reduction in individuals with non-alcoholic fatty liver disease following 8 weeks of hydrogen-rich water supplementation (Kura et al., 2022). However, extended supplementation with hydrogen-rich water, ranging from 12 to 24 weeks, has been demonstrated to reduce body weight in overweight individuals (Korovljev et al., 2023b) and patients with metabolic syndrome (LeBaron et al., 2020). This suggests that achieving significant weight-related changes with hydrogen-based interventions may require a longer treatment period. However, our findings revealed a notable reduction in body weight (2.0 kg on average) in obese men who consumed hydrogen-rich water, indicating a potential weight-reducing effect specific to this subgroup. Prior studies have shown that men tend to lose weight more rapidly than women after dietary interventions, primarily due to differences in body composition, energy expenditure, and hormonal factors influencing metabolism (Christensen et al., 2018; Susanto et al., 2022). These physiological and metabolic differences may explain the observed male-specific response to hydrogen-rich water. Although the magnitude of this effect appears modest, the possibility of a gender-specific response to hydrogen highlights the importance of incorporating sex as a biological variable in future research. Further investigation is warranted to explore the mechanisms underlying these effects and to optimize intervention strategies for different populations.

We observed significant lipid-lowering effects of hydrogen-rich water, evidenced by reductions in total cholesterol and LDL cholesterol levels in individuals with obesity. Specifically, total cholesterol decreased by an average of 0.32 mmol/L (95% CI, from 0.10 to 0.54), while LDL cholesterol declined by 0.21 mmol/L (95% CI, from 0.02 to 0.54) following eight weeks of hydrogen-rich water consumption, outperforming placebo in modulating these metabolic biomarkers. These findings align with prior studies demonstrating the cholesterol-reducing potential of dihydrogen across diverse clinical populations (for a comprehensive review, see Todorovic et al., 2023). Although the underlying mechanisms remain to be fully elucidated, it is hypothesized that hydrogen-rich water may exert lipid-lowering effects through antioxidative and anti-inflammatory pathways, modulation of lipid metabolism, or improved insulin sensitivity. These promising results suggest that hydrogen-rich water could serve as a safe and effective dietary supplement for managing dyslipidemia in obesity, warranting further investigation in larger, long-term studies.

Our findings also reveal that hydrogen-rich water significantly improved sleep quality compared to placebo, with a large interaction effect observed in our cohort of individuals with obesity ($\eta_p^2 = 0.21$). Given that sleep quality is frequently compromised in individuals with obesity—due to interrelated physiological, metabolic, and psychological factors (Beccuti and Pannain, 2011)—our data suggest that hydrogen-rich water may represent a novel therapeutic option for addressing sleep disturbances in this population. Emerging evidence aligns with our results, supporting the potential role of dihydrogen in modulating sleep-related outcomes. Preclinical research indicates that dihydrogen can enhance sleep architecture and consolidation through the activation of neuronal pathways in brain regions involved in sleep promotion (Vincent et al., 2023). Furthermore, a recent clinical study demonstrated that hydrogen gas inhalation improved total sleep duration, sleep efficiency, and reduced sleep latency in patients with glioma, positioning hydrogen as a potential therapeutic agent in sleep medicine (Wu et al., 2024). Hydrogen's potent antioxidant and anti-inflammatory properties may underlie these effects by alleviating oxidative and inflammatory stress, which are known disruptors of circadian rhythms and the sleep-wake cycle, particularly under conditions of physiological or psychological stress (Zanini et al., 2020; Todorovic et al., 2021). These properties may be particularly beneficial in the context of obesity, where chronic inflammation and oxidative stress are prevalent. While these findings underscore the promising utility of dihydrogen in improving sleep quality, additional research is necessary to clarify the mechanisms involved and to validate its clinical efficacy, particularly in populations with conditions that compromise sleep health.

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While the study design demonstrates methodological rigor, several limitations should be acknowledged. The relatively small sample size restricts statistical power and limits the generalizability of the findings, underscoring the need for larger, more diverse cohorts to validate these results across broader populations. Self-reported questionnaires for assessing appetite, sleep, and quality of life introduce potential biases, including social desirability and recall inaccuracies, which may affect the reliability of subjective outcomes. Despite instructions to avoid additional dietary supplements and weight management interventions, the absence of formal dietary intake and physical activity monitoring presents a risk of confounding variables influencing the results. The 8-week intervention period, while sufficient for initial assessments, is inadequate for evaluating the long-term effects of hydrogen-rich water on body composition, appetite regulation, or metabolic biomarkers, thereby limiting insights into sustained outcomes. Although biochemical markers such as GLP-1 and SCFA levels were measured, the study lacks detailed mechanistic exploration to elucidate direct pathways linking these markers to observed physiological changes. Furthermore, the exclusion of participants with chronic diseases, recent use of obesity-related pharmaceuticals, or dietary supplements narrows the study population, reducing its relevance to real-world scenarios where such conditions are prevalent among individuals with obesity. Future research addressing these limitations could significantly strengthen the robustness and external validity of findings related to hydrogen-rich water and its potential therapeutic benefits for obesity.

Conclusion

In conclusion, this study provides promising evidence that hydrogen-rich water may offer a safe and effective intervention for managing appetite, improving lipid profiles, and enhancing sleep quality in individuals with obesity. Over the eight-week intervention, participants consuming hydrogen-rich water showed significant reductions in food cravings, total and LDL cholesterol levels, and improvements in sleep quality compared to the placebo group. These effects were particularly pronounced in women, suggesting potential gender-specific responses. Although no major differences were observed in body composition or obesity-related quality of life, the findings support the need for further investigation into the long-term benefits and mechanistic pathways of hydrogen-rich water in obesity management.

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Conflict of Interest Statement: NT, SB, DN, JK, DK, DJ, KB, NK and SMO declare there are no competing interests. AT is employed by Natural Wellness Now Health Products Inc., the company that supplied the supplements examined in this study.

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