BALNEO RESEARCH Balneo and PRM Research Journal
English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

Research article

Mineral Waters with a Potential to Control and Prevent Metabolic Syndrome: A Systematic Review

Todorka Sokrateva [1,*], Bogdan Roussev, [1] Milka Nashar [1] , Ayshe Salim [1] and Diana Ivanova [1]

1 Department of Biochemistry, Molecular Medicine and Nutrigenomics, Faculty of Pharmacy, Medical University of Varna, Bulgaria

* Correspondence: Todorka Sokrateva, sokrateva@mu-varna.bg

Abstract: The morbidity rate of metabolic syndrome (MetS) has increased alarmingly in recent years. The intake of mineral water is among the recommendations for a healthy lifestyle in overweight people. The aim of the study was to investigate the effects of mineral water intake on MetS variables such as lipid status, blood pressure, blood glucose levels, and antioxidant defense. The PRISMA guidelines were followed, focusing on the period from 1990 to 2024. Twenty-four studies met the inclusion criteria. Among these, sixteen were randomized controlled crossover trials, one was crossover, six were interventional, and one was of a cyclic type. The included studies were divided by duration into long-term with mineral water intake for at least one month, postprandial, and treatment including mineral water intake. Mineral waters have been tested according to different protocols regarding water composition, amount consumed, with or without changes in lifestyle and diet in healthy subjects or such with impaired biochemical parameters. Regular mineral water intake may have a positive effects on lipid metabolism, blood pressure, glycemic status, and the antioxidant system. These findings can be used as an additional alternative treatment method in risk groups with MetS, obesity, or hyperglycemia.

Keywords: mineral water; water intake; metabolic syndrome; obesity; prevention

Citation: Sokrateva T., Roussev B., Nashar M., Salim A., Ivanova D. - Mineral Waters with a Potential to Control and Prevent Metabolic Syndrome: A Systematic Review
Balneo and PRM Research Journal
***2025**, 16(1): 773*

Academic Editor(s):
Constantin Munteanu

Reviewer Officer:
Viorela Bembea

Production Officer:
Camil Filimon

Received: 24.01.2025
Published: 31.03.2025

Reviewers:
Mihai Hoteteu
Elena Valentina Ionescu

Publisher's Note: Balneo and PRM Research Journal stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Introduction

Obesity is a global health problem, and the main risk factors for its occurrence are an unhealthy diet and a sedentary lifestyle [1]. In turn, obesity is a major risk factor for the development of health problems, such as excess abdominal adipose tissue and dyslipidemia, increased levels of pro-inflammatory cytokines and reactive oxygen species (ROS) [2, 3]. This depletes the body's defense mechanisms, causing an imbalance in the homeostasis of carbohydrates, fats, and proteins, resulting in the so-called metabolic syndrome (MetS). Some of the MetS characteristics are high blood pressure (BP) nonalcoholic fatty liver, epicardial fat accumulation, endothelial dysfunction, low-grade inflammation, and insulin resistance (IR) [4, 5]. Persistent high levels of cholesterol, especially LDL cholesterol (LDL-C), triglycerides (TG), and low levels of high-density lipoprotein particles (HDL) are a prerequisite for endothelial dysfunction and atherogenesis [6, 7]. On the other hand, a sedentary lifestyle and obesity also contribute to endothelial dysfunction [8]. Increasing the risk of developing cardiovascular events and diabetes, MetS has turned into a major public health concern [4].The prevalence of MetS has increased over time and is reaching epidemic proportions. Approximately one-fifth of the elderly population in Western countries has been affected by MetS. The frequency of this observation is increasing with age [9]. Not all obese people develop MetS. However, obesity could contribute to reference range deviations in MetS diagnostic markers, such as BP, TG, LDL-C, HDL-C, uric acid, glucose, and insulin sensitivity. Impaired health is a result of MetS. However, it has been suggested that changes in lifestyle and diet may contribute to its successful management. New, more

effective, and safer drugs are constantly being developed and natural remedies are being sought [10, 11].

Prevention against MetS includes control over the choice of food and drinks—exclusion of red meat and increased consumption of legumes, whole grains, and fiber, as well as higher intake of greens, fruits, fish, and poultry [12–14]. Recommendations include daily physical activity, moderate quantities of low-alcoholic beverages, preferably red wine, and smoking cessation [14]. Intake of minerals and functional foods affecting one or more MetS parameters is also recommended [15, 16].

Benefits of water intake

1.1. Amount

Despite being an essential ingredient at all levels of organization in the human body, water is often overlooked in dietary recommendations. According to the European Food Safety Agency (EFSA), the daily amount of water intake should be at least 2.5 L for men and 2 L for women [17]. Water amount of less than 0.5 L per day has been determined to carry a significantly higher risk of hyperglycemia, compared to a regular long-term daily water intake above 1 L [18]. A cross-sectional study showed that each glass of water, part of the daily intake, reduces the risk of elevated HbAC1 by 22% in men [19]. Water consumed in sufficient quantity might contribute to weight loss. Regular water consumption suppresses hunger and limits sweetened soft drink intake—a habit known to increase the risk of type 2 diabetes (T2D) [20–24]. Maintaining constant plasma volume (volemia) is crucial for the proper cardiac function. Increased plasma volume can cause hypertension, while decreased volume leads to hypovolemia, which is associated with reduced BP and increased blood viscosity, thus straining the heart. Adequate hydration and balanced water distribution inside and outside the cell are necessary. The major regulator of extracellular fluid volume is aldosterone. Maintaining the reabsorption of sodium and excretion of potassium through the kidney, it controls electrolyte and water balance. High aldosterone is linked to hypertension, endothelial dysfunction, cardiovascular disease (CVD), and others [25, 26]. Being overweight is associated with increasing aldosterone levels, even in non-hypertensive subjects.

1.2. Source of macronutrients and micronutrients

To maintain water balance, both the amount of water consumed daily and its composition, which may confer health benefits, are important (Water & Health. How Water Protects and Improves Health Overall). Mineral waters contain the electrolytes sodium, potassium, and chloride with an important role in the transportation of nutrients within cells, the transmission of nerve impulses, and the formation of hydrochloric acid. In addition, some mineral waters are rich in the macronutrients calcium, magnesium, and phosphate, which are essential in carbohydrate and energy metabolism, bone formation, muscle contraction, heart rate, and BP regulation [27, 28]. For example, intracellular magnesium regulates glucokinase and some calcium channels in pancreatic β-cells preceding insulin secretion. Autophosphorylation of insulin receptors depends on intracellular magnesium concentrations. At the same time, insulin modulates urinary magnesium excretion. Thus, patients with T2D and hypomagnesemia enter a vicious cycle in which hypomagnesemia causes IR, which lowers serum magnesium concentrations. Furthermore, in patients with hypomagnesemia, T2D progresses more quickly and the risk of complications is higher [29]. Other data showed that people living in areas with higher magnesium content in tap water tend to have lower BP [30]. It has been demonstrated that the bioavailability of calcium in mineral waters may be at least comparable to, or possibly above, that present in dairy products and pharmaceutical preparations [31]. In some European countries, the average calcium content in public tap water and bottled mineral waters is in the 50–100 mg/L range and

adequate consumption would provide between 10% and 31% of the recommended daily calcium intake, depending on the individual age [32]. Not by chance, calcium-rich mineral water was recognized as a functional food (EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)) and indicated in cases of increased calcium needs, specifically recommended for postmenopausal women [33]. The long-term consumption of mineral water has been found to lower total cholesterol (TC) and LDL-C in hyperlipidemic patients [34–38]. The blood lipid levels were significantly higher in people living in areas with soft drinking water with total hardness of 40 mg/L, obtained in the summation of magnesium and calcium ions, compared to areas with total drinking water hardness above 80 mg/L [39].

In addition, mineral waters are a source of micronutrients such as silicon, molybdenum, zinc, selenium, cobalt, boron, and others involved in enzymatic reactions in the metabolism of carbohydrates, fats, and lipids, hematopoiesis, immune and antioxidant protection [40]. On the other hand, it is known that people with obesity, CVD, and diabetes often have a diagnosed mineral and vitamin deficiency [41, 42]. The intake of essential minerals by drinking mineral water can be an effective way to replenish deficiencies [43]. Therefore, the sufficient intake of water and its content should no longer be neglected.

1. 3. Mineral composition—the most frequently studied mineral waters

Natural mineral waters (NMWs), unlike public tap water which is chlorinated daily for safety, are of underground origin and are protected against microbial contamination (European Community directives, natural mineral waters). Each kind of NMW has a specific chemical composition, organoleptic characteristics, temperature, and health-promoting properties [40, 44–46]. In addition to natural purity, the minerals contained in them are in ionic form, which makes the essential elements more easily absorbed compared to some foods [47–50].

The effects of carbonate and bicarbonate mineral waters, such containing sodium, magnesium, calcium, potassium, and sulfur on the MetS parameters are frequently the focus of research. Magnesium-, calcium-, and sodium-rich bicarbonate waters with traces of iron, manganese, and selenium have been reported to reduce serum cholesterol levels [51] and alleviate arteriosclerosis [52]. Sodium-bicarbonate-rich mineral waters have a beneficial effect on insulin sensitivity in women [53], postprandial hyperlipidemia [54–56], and cardiovascular health [57]. Water containing magnesium has shown a potential in reducing coronary heart disease mortality in the European population [58]. Sulfurous bicarbonate waters have been indicated to control glycemia, polydipsia, and polyuria, reduce insulin requirements, and neutralize metabolic acidosis in diabetes [46]. Improvement in antioxidant status [59–63], kidney function [64], lipid levels in overweight people [65], and BP [66] after consuming sulfur-containing mineral water has also been reported. Oligomineral waters should not be underestimated as well. In combination with a hypocaloric diet, they can reduce total and extracellular water content and contribute to the maintenance of normal body weight in overweight women [67]. The modulating role of mineral waters on key MetS parameters has already been considered [68]. Some of the potential positive effects of mineral waters have not been described. There are new data on antioxidant effects. Recently, mineral waters have been added to spa therapies to treat MetS [69, 70].

The study aimed to update data about the effects of mineral water consumption associated with MetS parameters.

2. Results

2.1. Literature search

Database search yielded 1551 records of papers. Among them, 1373 were excluded after screening for eligibility according to PICOS criteria, thus leaving 64 studies. After reading the abstracts, or the whole article, another 42 studies were excluded. Two

records identified by the cited literature have been added. Details on the study selection process were reported in a flowchart diagram (Figure 1). The number of included studies is 24.

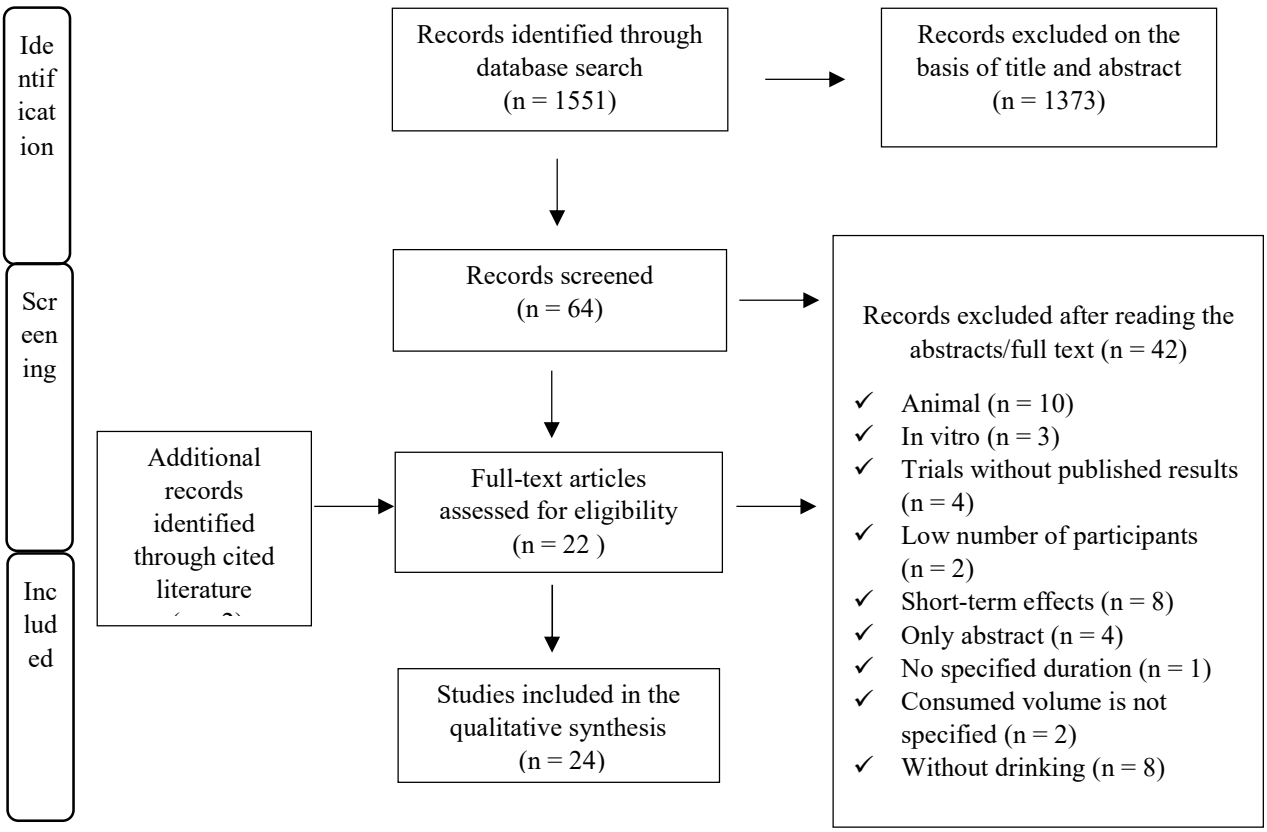

Figure 1. Flow-chart of the literature search.

2.2. Description of included studies

The mineral water content is shown in Table S1, as published in the selected articles.

BALNEO RESEARCH Balneo and PRM Research Journal English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

Table S1. Main composition of the studied mineral waters. The arrangement is by the name of the first author.

Main ions	Aslan abadi et al., 2014 [37]	Balakin et al., 2010 [76]*	Capurso et al., 1999 [34]#	Chala ya et al., 2017 [70]**	Dragom iretska et al, 2023 [77]	Jovicic et al., 2023[79]***	Mansou ri et al., 2024 [71]	Murakami et al., 2015[72]	Perez-Grana dos et al., 2010 [35]; Toxqui et al., 2012 [55]	Roussev et al., 2019 [63], Sokrate va et al., 2019a;b [64-65]	Rylander and Arnaud 2004 [78]	Schoppen et al., 2004 (BSC 1)[73] 2005 (BSC 1,2)[54] 2007 (BSC 1,2 [53] 2008 (BSC 1,2)[75]	Schorr et al., 1996 [74]	Toxqui and Vaquero,2016a, b [36, 56]	Wassefurth et al., 2019 [43]	Zair et al., 2013 [38]
Bicarbonate ion (mg/L)	BCM 1350 LM 29	1300–1600	SM 677	1000–1500	1453	1098	HBS 4368 LBS 228	TW 28 BMW 2485	CSB 2120 LM 104	A 281 DM 268.5	Valvert® LM 204 DWM 12 SCB 403	BSC[1]2094 BSC[2]2013 LM 71.1	LSB < 12 HSB 1983 HSC 879	BSC 2050 LM 74.9	LBHP 403 MBMP1816 HBLP 2451 MBLP 1864	SY 4168 RW 183
Sulphate ion (mg/L)	BCM 165 LM 20	1200–1600	SM 1540	250–500	43		HBS 174 LBS 15	TW 6.9 BMW 355	CSB 45.3 LM 15.6	A 77 DM 50	Valvert® LM 18 DWM 326 SCB 1187	BSC[1] 49.9 BSC[2] 42.9 LM 15.7	LSB < 9.6 HSB 67 HSC 278	BSC 50 LM 10.6	LBHP 1463 MBMP 38.3 HBLP 17 MBLP 39	SY 186 RW 18
Magnesium ion (mg/L)	BCM 250 LM 7	< 100	SM 136	50–120	9	34.9	HBS 11 LBS 6.9	TW 1.9 BMW 291	CSB 9.4 LM 5.0	A 27 DM 24	Valvert® LM 2 DWM 82.3 SCB 84	BSC[1] 5.7 BSC[2] 9.7 LM 2.7	LSB < 2.4 HSB 53 HSC 9.7	BSC 5.8 LM 2.8	LBHP 124 MBMP 108 HBLP 241 MBLP 59.2	SY 11 RW 12
Calcium ion (mg/L)	BCM 149.83 LM 4.99	300–400	SM 670	200–400	10	80.1	HBS 90 LBS 67.5	TW 6.1 BMW 177	CSB 32 LM 33.4	A 43 DM 42	Valvert® LM 4 DWM 67.6 SCB 486	BSC[1] 43.6 BSC[2] 52.1 LM 25.2	LSB < 4 HSB 124 HSC 64	BSC 20.8 LM 22.6	LBHP 528 MBMP 348 HBLP 168 MBLP 98.7	SY 85 RW 48
Potassium ion (mg/L)	BCM 9 LM 2		SM 140			27.3	HBS 110 LBS 2.3	TW < 0.1 BMW 80	CSB 49.5 LM 2.0	A 7 DM 7.8	Valvert® LM 0.2 DWM 0.1 SCB 3,2	BSC[1] 54.7 BSC[2] 47.7 LM 1.4	LSB < 3.9 HSB 27 HSC 70	BSC 47.2 LM 1.7	LBHP 6.9 MBMP 10.5 HBLP 37.4 MBLP 16.1	SY 117 RW 1

Sodium ion (mg/L)	BCM 149.83 LM 4.99	Sodium plus Potassium 800–1100)	SM 5.535	Sodium plus Potassium 50-250	Sodium plus Potassium 617		HBS 1708 LBS 8.4	TW 10 BMW 0.4	CSB 1102 LM 8.7	A 39 DM 69	Valvert® LM 1.9 DWM 2.4 SCB 9.1	BSC[1] 1116 BSC[2] 948 LM 9	LSB < 2 HSB 602 HSC 1295	BSC 1090 LM 7.6	LBHP 28.8 MBMP 118 HBLP 261 MBLP 564	SY 1626 RW 31
Chloride ion (mg/L)		300–500	SM 9.080	50–150	121	22	HBS 322 LBS 11	TW 11 BMW 182	CSB 597 LM 11	A 104 DM 100	Valvert® LM 4 DWM 0.7 SCB 8.6	BSC[1] 583 BSC[2] 592 LM 5.7	LSB < 3.5 HSB 152 HSC 1507	BSC 622 LM 4.8	LBHP 28.9 MBMP 39.7 HBLP 14 MBLP 139	SY 329 RW 48
Silicon (mg/L)		Metasilicic acid H2SiO3 30–70			Metasilicic acid H2SiO3 63.4			Metasilicic acid H2SiO3 TW 10 BMW 207		A 34 DM Metasilicic acid 32.76	Valvert® LM 5.7 DWM 0 SCB 8					
Hydrogen sulfide (mg/L)								TW < 0.1 BMW < 0.1		A 1.7 DM 2.8						
Carbon dioxide (g/L)								TW 0.9 BMW 161	CSB 3.9	DM 11,9		NA				
Fluoride ion (mg/L)								TW < 0.1 BMW 0.3	CSB 0.9 C < 0.2	A 0.71 DM 0.62	Valvert® LM < 0.05 DWM 0 SCB 0.32	BSC[1] 7.9 BSC[2] 1.4 LM 0.2		BSC 0.73 LM 0.2		
Boron (mg/L)					Orthoboric acid 29.13			Metaboric acid TW 0.8 BMW 6.2								
PRAL (mEq/L)															LBHP 10.7 MBMP 10.8 HBLP 19.3 MBLP 22.1	

BCM—bicarbonate-calcium-magnesium-rich mineral water, LM—low mineral content water, SM— Montecatini Regina salt-rich mineral water, HBS—high bicarbonate-sodium mineral water, LBS—low bicarbonate-sodium mineral water, BMW—bicarbonate-rich mineral water, TW—tap water, LSB—low sodium-bicarbonate mineral water, HSB—high sodium-bicarbonate mineral water, HSC—high sodium-chloride mineral water, CSB—carbonated sodium-bicarbonate mineral water, A—Aquarium, DM—Dom Mladost, DWM—distilled water + MgSO4, SCB— Contrex® sulfate-calcium-bicarbonate mineral water, BSC (with or without asterisks)—bicarbonate-sodium-chloride mineral water, LBHP—low bicarbonate, high potential renal acid load (PRAL), MBMP—medium-high bicarbonate, medium PRAL, HBLP—high bicarbonate high PRAL, MBLP—medium-high bicarbonate, low PRAL, SY—Saint-Yorre sparkling high mineral content water, RW—Ogeo referent mineral water, *Novoterskaya (https://novoterskaya.ru), **https://narzanwater.ru/eng/***, Sneznik-1/79 reported in Lalovic et al., 2020; # https://www.termemontecatini.it

BALNEO RESEARCH Balneo and PRM Research Journal English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

According to Directive 2009/54/EC, all used mineral waters have a complex chemical composition, 78% are bicarbonate-rich [34–38, 43, 53–56, 71–77]. The magnesium is above 50 mg/L in seven studies [34, 37, 43, 72, 74, 76, 78], in four studies the calcium is above 150 mg/L [37, 43, 72, 76], in eight studies the potassium is between 50 and 100 mg/L [35, 53–55, 71–74], those containing sodium above 200 mg/L are 12 [34–36, 43, 53, 54, 71, 73–77], chlorine level over 200 mg/L is present in 11 types of mineral waters [35, 36, 38, 53–55, 71, 73–76], the silicon content varies in 6 studies [63, 65, 72, 76–78], carbon dioxide is reported in 5 studies [35, 55, 63, 65, 72], and fluorine level of over 1 mg/L is present in 2 types of mineral waters [53, 54, 73, 75].

The mineral waters of interest were consumed in different amounts, with or without changes in lifestyle and diet, with varying durations of intake. Of the original studies, sixteen were randomized controlled crossover trials (RCTs) [36–38, 43, 53–56, 69–71, 73–75, 77, 78], one crossover study [35–], six—interventional studies [34, 63–65, 76, 79], [43], and one was a cyclic-type study [72].

The included studies were distributed based on the duration of mineral water intake as follows:

Table 1. Studies with mineral water intake lasting at least one month—fifteen studies;
Table 2. Postprandial studies—five studies;
Table 3. Treatments including mineral water intake—five studies.

BALNEO RESEARCH Balneo and PRM Research Journal English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

Table 1. The purpose, design, number of participants, duration, and results of long-term studies, with a duration of more than one month, were sorted by the first author's name.

Reference	Study, Duration	Participants	Aim/Study Design	Comparison	MetS-Related Outcomes
Aslanabadi et al., 2014 [37]	RCT, 4 wks	♂♀ 69; aged 30–60, hyperlipidemia	Hypolipidemic effect of BCM . Case group (♂♀32) 1 L BCSM	Control group (♂♀37) 1 L LM, similar diet	↓TC [mmol/L] Case group: 250.75 ± 6.88 vs. 224.47 ± 5.52, P = 0.0001; Control group: 236.24 ± 6.42 vs. 218.65 ± 7.02 mmol/L, P = 0.0005 ↓LDL-C [mmol/L] Case group: 174.35 ± 6.29 vs. 150.31 ± 5.34, P < 0.05; Control group: 157.40 ± 6.94 vs. 138.48 ± 6.94, P < 0.05 HDL-C and TG-NS;Differences in lipid levels depending on the mineral water content: NS
Capurso et al., 1999 [34]	Interventional, 9 wks	10 (6♂ 4♀), mean age 65 ± 6.7, mild hypercholesterolemia	The influence of SM on lipids status and bile acid excretion. 3 wks of diet stabilization period, 3 wks of SM active treatment period (750 mL Montecatini Regina water in the morning for 30 min, plus standard diet of 2200 kcal/d), 3 wks tap water control period; no antibiotics, lipid-lowering drugs, or milk enzymes	Control period (750 mL tap water)	↓TC [%] 7.5 in the SBM period; ↓LDL-C [%] 12.5 in the SBM period ↓TC/HDL-C [%] 6.3; ↓ApoB [%] 6.3 in the SBM period; HDL-C, TG, Apo-AI, Lp(a) [%]: NS ↑Total fecal bile acid excretion [%] 98.9 in the SBM period; ↓Gallbladder volume [%] 40 in the SBM period; Na^+, K^+, and Mg^{2+} in blood: NS ↑Cl in the SBM period without differences between the diet stabilization and control periods; BP: NS
Jovicic et al., 2023 [79]	Interventional,4 wks	♂♀ 60; aged 30–60, T2DM without diabetic foot, retinopathy, hemodialysis; 62.5% from the patients had constipation	Evaluation of the effects of Snejnik-1/79 low mineral, weakly acidic water on microbiota, metabolic, biochemical, and anthropometric parameters in T2DM patients. The amount of consumed water p/d was dosed individually.	Changes before and after the intervention	Anthropometric and body composition: NS; Glucose: NS; Intestinal peristalsis, daily bowel movements were improved in all patients after the intervention; ↓Dysbiosis [%] in 50; ↓TC, P < 0.05; TG, LDL-C, HDL-C: NS; $\downarrow O_2^-$, P < 0.01;↑NO_2, P < 0.05; ↓H_2O_2: NS; ↑TBARS: NS Antioxidant capacity improved: ↑SOD , P < 0.01; ↑CAT:NS; ↑GSH, P < 0.05
Mansouri et al., 2023 [71]	RCT, 4 wks	85 (25♂ 60♀) healthy volunteers; mean age 53.9 y; BMI 24.2 kg/m^2; omnivorous diet	Evaluation of the effects of HBS on the BP and related factors;HBS group ♂♀43 (15 hypertensive at baseline). The amount of consumed water p/d min 1.5 L, max 2 L. Volunteers kept their usual dietary and lifestyle habits. Dietary assessment.	LBS group ♂♀42 (10 hypertensive at baseline)	Anthropometric parameters at baseline and after intervention: NS; SBP > in the HBS group at baseline. Mineral intake from food and beverages at baseline and after intervention: NS , except ↓K^+ in the LBS group (P < 0.05). ↑Urine volume in all volunteers (P < 0.05). ↓BP in the LBS group (P = 0.002), but not in the HBS group ↓Aldosterone [ng/L] in both groups: HBS group before 103 (61) vs. after 65 (63); LBS group before 104 (94) vs. after 98 (78). ↓Urinary calcium excretion in the HBS group (P < 0.05). ↑Urinary sodium excretion in the HBS group (P < 0.05). No association between urinary sodium excretion and the increase in the SBP in HBS group (B = 0.046, P = 0.170). Changes in urinary sodium excretion did not correlate with changes in

					serum aldosterone in HBS group group (r = -0.146, p = 0.350)
Murakami et al., 2015 [72]	Cyclic type, 4 wks	19 (7♂ 12♀), aged 26-59 y, healthy	Effects of BMW on glycemic control, blood metabolomes, and fecal microbiome. The amount of the consumed water (500 mL) was drunk three times per day (30–60 min before main meals). TW and BMW consumption periods lasted for a week each and this cycle was repeated twice. Volunteers kept their normal dietary habits. Drugs were prohibited.	Commercially available TW	TC, HDL-C, LDL-C, TG, FGL, fasting insulin, HOMA-IR: NS; Blood glucose tended to decrease in the BMW period (P = 0.092) ↓Glycoalbumin [% of total albumin] in BMW period compared with TW period: 14.2 ± 1.7 vs. 14.4 ± 1.7, P < 0.05 Uric acid, Na^+, Mg^{2+}, Cl^-, and cortisol in blood: NS ↑Ca^{2+} [mg/dL], mg/dL—BMW period compared to the TW period 9.4 ± 0.2 vs. 9.3 ± 0.2, P < 0.005; ↑pyruvate, ↑ATP, ↓ADP after the BMW period; ↓tyrosine, ↓methionine and ↓glycine, and ↑UDP-N-AcGlucosamine after the BMW period; ↑Lean-inducible bacteria after the BMW period.
Perez-Granados et al., 2010 [35]	Crossover, 8 wks	18 (8♂ 10♀), mean age 29 ± 8 y, mild cholesterolemia, healthy	Effects of CSB on cardiovascular risk in moderate cholesterolemic young adults. Two consecutive periods lasted 8 wks, each separated by 8 wks washout. In addition to the usual diet, 1 L p/d of CSB. Determination analyses at the end of the control LM period, and on the 4th w and 8th w of the CSB water period (cold season). Dietary intake evaluation.	Commercially available LM	↓SBP [mmHg] at the 4th week in the CSB period vs LM period: 111 ± 14 vs. 120 ± 19, P < 0.05; differences between 4th and 8th weeks: NS; DBP: NS. ↑Urine pH in the CSB period compared with the LM period; 7.01 ± 0.3 vs. 6.43 ± 0.5, P < 0.005; ↑Urine Na^+ and Cl^- in the CSB period, compared with the LM period; ↓TC [mmol/L] in the CSB period compared with the LM period: 5.42 ± 0.67 vs. 5.78 ± 0.73, P < 0.05; ↓LDL-C [mmol/L] after 8 weeks of the CSB period compared with the LM period: 3.40 ± 0.67 vs 3.77 ± 0.69, P < 0.05; HDL-C, TG, Apo A-I - NS The CVD risk indexes (TC/HDL, LDL/HDL, and ApoB) reduced in the CSB period compared with the LM period, P < 0.05; Apo A-1, HDL/Apo -1, LDL/ApoB: NS; Glucose tended to decrease in the CSB period; Insulin: NS; Adiponectin, sICAM-1, sVCAM-1, hs-CRP: NS.
Roussev et al., 2019 [64]	Interventional,8 wks	50 (7♂ 43♀) aged 40–65, mean 50.76 ± 7.38 y, healthy;	The effects of Varna mineral water intake on human metabolism; Two similar publicly available LM hydrogen sulfide waters containing also bicarbonate, calcium, and magnesium, named Dom Mladost and Aquarium. The participants had right to choose one of both. Individual water intake (20 mL/kg bw), but not less than 800 mL p/d; Exclusion criteria: chronic diseases, steroid anti-inflammatory drugs, supplements containing minerals; changes in lifestyle habits during the intervention.	Changes before and after the intervention	↓Creatinine in blood [µmol/L] after the intervention: 77.36 ± 9.99 vs. 72.94 ± 9.38, P = 0.0006; Na+, K+, Cl-, Ca^{2+}, PO^-, aldosterone in blood: NS; ↓hs-CRP [mg/L] after the intervention: 2.76 ± 2.22 vs. 1.88 ± 1.24, P = 0.0003;↑Diuresis [mL] after the intervention: 1849 ± 602.4 vs. 1660 ± 608.9, P = 0.01;↑eGFR [mL/min] after the intervention: 93.22 ± 21.71 vs. 88.19 ± 21.63, P = 0.002; Renal function improved independently of diuresis volume.
Rylander and Arnaud 2004 [78]	RCT, double-blinded, 4 wks	♂♀ 70, aged 45–64 y, borderline hypertension	To evaluate the effects of water with added magnesium (distilled water + MgSO4) and SCB on BP. At least 1 L p/d. Three separate assessments—before, after 2 weeks, and after 4 weeks.	Three types of waters: distilled water + MgSO4 vs. SCB vs. LM	↓SBP in the SCB group among subjects with an initial magnesium level in urine < 0.40 mmol/L: before 156.8 (15.9); after 2 weeks 150.1 (16.1), P < 0.05; after 4 weeks 150.4 (15.5), P < 0.05. ↓DBP in the SCB group among subjects with an initial magnesium level in urine < 0.40 mmol/L: before 148.8 (13.3); after 2 weeks 142.5 (10.1), P < 0.05; after 4 weeks 144.3 (14.4), P < 0.05. ↑Magnesium in 24h urine in all subjects: in distilled water + MgSO4 group (P < 0.01) and the SCB group (P < 0.05) with an initial lower excretion of magnesium or calcium in urine.
Schoppen et al., 2004 [73]	RCT, crossover, 8 wks	18♀ healthy BMI < 30 kg/m^2 amenorrhea (≥ 1 y)	Beneficial effects of consuming Vichy Catalan, BSC mineral water, on lipid metabolism and endothelial dysfunction in postmenopausal women. No smoking, no estrogen replacement therapy, no vitamins and minerals, no diets within 1 y of selection.	LM (Vichy Catalan)	Anthropometric data and BP: NS ↓TC [mmol/L] in the BSC compared with the LM: 5.64 ± 0.67 vs. 6.05 ± 0.84, P < 0.001; ↑HDL-C [mmol/L] in the BSC compared with the LM: 1.63 ± 0.30 vs. 1.50 ± 0.35, P < 0.05; ↓LDL-C [mmol/L] in the BSC compared with the LM: 3.62 ± 0.59 vs. 4.25 ± 0.56, P ≤ 0.00; TG, Apo A, ApoB: NS;

			The amount of the consumed water 1 L p/d. Dietary energy intake did not vary throughout the study.		↓CVD risk indexes (TC/HDL and LDL/HDL) in the BSC, $P < 0.0001$; ↓sICAM-1, sVCAM-1 in the BSC period compared with LM, $P < 0.05$; ↓FGL [mmol/L] in the BSC compared with the LM: 5.1 ± 0.4 vs. 5.54 ± 0.41, $P < 0.001$.
Schorr et al., 1996 [74]	RCT crossover double-blinded, 4 wks	16 (7♂ 9♀) 60–72 y, mean age 64.1 ± 3.6 y, BMI 26.1 ± 3.6 kg/m^2, healthy, low-salt diet (<100 mmol p/d)	Effect of HSB and HSC mineral waters on the BP, glucose, and lipid metabolism in elderly normotensive individuals. Each water in an amount of 1.5 L p/d was drunk for 4 weeks, with a 2-week washout period.	LSB	↓Urine Na^+ during LS water period and ↑ during the HSB and the HSC; ↑Urine Cl^- only during the HSC period;↓BP [mmHb] in LS (-7.0 ± 7.2; $P < 0.001$) and in HSB (-5.7 ± 6.4; $P < 0.05$) periods compared with baseline;During the HSC period, the BP was identical to the baseline and abolished the effect of a low-salt diet. The BP was not affected by the three regimens; ↓Ca^{2+} excretion [mmol/24 urine] in the HSB period: 3.91 ± 1.29 vs. 3.04 ± 1.08, $P < 0.01$, and ↑ in the HSC period: 3.91 ± 1.29 vs. 4.06 ± 1.25, $P < 0.02$) compared to baseline.Glucose, insulin, oral glucose tolerance, and lipids were not affected by the three regimens;↓Renin at the end of the 1st week in the HSC period; ↓Aldosterone at the end of the 1st week in the HSB and the HSC periods.↑Atrial natriuretic factor only at 1st week in the HSB period. These changes were not observed at the end of the interventions and their levels were returned to the baseline. Plasma uric acid, catecholamines, and GGT: NS.
Sokrateva et al., 2019a [63]	Interventional, 8 wks	50 (7♂ 43♀) aged 40–65, mean 50.76 ± 7.38 y, healthy;	To explore the antioxidative and anti-inflammatory effects of Varna mineral water. Two similar publicly available types of LM hydrogen sulfide water containing also bicarbonate, calcium, and magnesium, named Dom Mladost and Aquarium; The study desigh is described in ref.64;	Comparison of the levels of the markers of interest before and after the intervention	↑Total thiols [μmol/L] after the intervention in all participants: 437.5 ± 10.40 vs. 492 ± 10.11, $P < 0.0001$ more clearly expressed in the Dom Mladost subgroup. ↑Total glutathione [μmol/L] after the intervention in all participants: 2.67 ± 0.004 vs. 3.01 ± 0.19, $P < 0.05$, and in the Dom Mladost subgroup; ↑*GCL* expression 1.935 ± 0.34, $P < 0.01$; GSH: nonsignificant increase after intervention by 27.4%; GSSG: NS; GSH/GSSG: tendency of slight elevation by 15.2%; MDA, dROMs: NS; Negative correlation between dROMs and Total glutathione $r = -0.31$, $P < 0.05$. After the intervention the correlation was weaker with borderline significance $r = -0.27$, $P = 0.07$; ↑*ICAM-1* expression 2.63 ± 0.45, $P < 0.01$, but the level of the protein: NS.
Sokrateva et al., 2019b [65]	Interventional,8 wks	50 (7♂43♀) aged 40–65, mean 50.76 ± 7.38 y, healthy;	Investigated whether the mineral water effects varied depending on the lifestyle factors (smoking, alcohol consumption, physical activity, and body mass index) The study desigh is described in ref. 64 All participants were stratified into overweight/normal weight; smokers/non-smokers; alcohol consumption/no alcohol consumption; high physical activity/low physical activity groups.	Comparison of the levels of lipids, thiols, hs-CPR, and MDA before and after the intervention between the groups.	HDL-C, TG [mmoL/L]: NS ↓LDL-C [mmoL/L] in the overweight after intervention: 2.87 ± 0.12 vs 2.70 ± 0.09, $P < 0.05$ TC: nonsignificant decrease in the overweight group after the intervention; ↓hs-CPR in all groups, more pronounced in the overweight, low physical activity, and smokers groups and less pronounced in the alcohol-consumption group; ↑Total thiols in all groups were more pronounced in the normal weight, non-smokers, and no-alcohol-consumption groups. MDA: NS.
Toxqui and Vaquero, 2016a [36]	RCT, crossover, 8 wks	64 (28♂ 36♀), mean age 30.7 ± 7.5 y, moderately hypercholesterolemic, BMI 23.2 ± 2.8 kg/m^2	The effects of BSC mineral water on cardiometabolic risk biomarkers. Amount of BSC 1 L p/d. Two consecutive intervention periods, separated by 8 weeks of washout. Dietary assessment. Determinations at 0, 4th, and 8th w of each water period.	LM	BW, BMI, BP: NS; ↓TC [mmol/L] after both types of water: BSC 5.8 ± 0.77 vs. 5.7 ± 0.73 vs. 5.5 ± 0.73; LM 5.78 ± 0.71 vs. 5.66 ± 0.76 vs. 5.67 ± 0.73, ($P < 0.005$); HDL-C, TG: NS;↓LDL-C [mmol/L] after both waters: BSC 3.79 ± 0.81 vs. 3.7 ± 0.72 vs. 3.57 ± 0.7; LM 3.77 ± 0.71 vs. 3.62 ± 0.70 vs. 3.65 ± 0.74, ($P = 0.001$);Oxi-LDL tended to decrease after both types of water ($P = 0.073$); ↓TC/HDL without water type effect ($P < 0.05$); ↓LDL/HDL without water type effect ($P < 0.05$); HDL/Apo-AI: NS; ↑ApoB [mmol/L] after both typ of water: BSC 114.3 ± 20.7 vs. 119.5 ± 19.1 vs. 119.6 ± 18.9; LM: 114.5 ± 18.8 vs. 119.7 ± 21.1 vs. 122.2 ± 20.3, ($P < 0.001$); ↓LDL/ApoB without water type effect, ($P < 0.001$); Apo-AI: NS, HDL/A AI: NS.↓FGL [mmol/L] without water type effect: BSC 4.95 ± 0.41 vs 4.94 ± 0.46 vs. 4.80 ± 0.4; LM 4.90 ± 0.47 vs. 4.95 ± 0.47 vs. 4.88 ± 0.44, ($P < 0.05$); Insulin: NS; Aldosterone: NS; Ca^{2+}, Na^+, and PO_4^{3-} excretion/24 h urine: NS; ↓K^+/creatinine in both types of water, ($P < 0.05$); ↓Ca^{2+}/creatinine in BSC period ($P < 0.05$); Na+/creatinine and PO_4^3/creatinine: NS;↑Urinary pH in the BSC period befo and after 5.9 ± 0.6 vs. 6.2 ± 0.6, ($P < 0.05$).
Wassefurth et al., 2019 [43]	RCT, 4 wks	108 (83♀ 26♂) aged 18–75 y, healthy BMI ≥ 18 and ≤ 32	Evaluation of the effects of mineral waters with varying bicarbonate content on acid-base status in free-living healthy adults following an omnivorous diet, no intake	LBHP, n = 31 MBMP, n = 37	Anthropometric characteristics and BP—no difference between the groups at t 0. ↓Blood pH in the LBHP and the MBMP groups from 7.37 pH to 7.36, pH, $P < 0.05$; acid-base status (HCO_3^-, pCO_2, pO_2, BE) difference only in the MBLP group at t 4;

		kg/m^2	of magnesium or calcium, no intake of drugs affect mineral absorption and/or acid-base status (laxatives, proton pump inhibitors, diuretics, corticoids, etc.). Amount of water: 1.5–2 L p/d. Intervention: screening phase, 4-week run-in phase, 4-week intervention. Examination: at the beginning (t 0) and at the end (t 4) of the intervention. Dietary records.	HBLP, n = 31 MBLP, n = 30	↓pH of spot urine in the LBHP group, ($P < 0.05$), and ↑ in the MBMP and in the MBLP at t 4 ($P < 0.05$); ↓pH in 24h urine in the LBHP, and ↑ in the HBLP and MBLP at t 4, ($P < 0.05$); ↓TA and NH^{4+} after the MBMP, HBLP, and MBLP waters; ↑HCO^{3-} after the MBMP and HBLP waters; The intergroup comparison in HCO^{3-} excretion at difference at t 4 ($P \leq 0.001$). ↑Net acid excretion (NAE) by 48% within the MBMP group, in the HBLP group—by 68%, and in the MBLP group—by 53% ($P < 0.05$); ↑Serum HCO^{3-} in the HBLP ($P = 0.057$) and MBLP ($P < 0.001$).
Zair et al., 2013 [38]	RCT, double-blind crossover, 8 w	12♂, aged 20–60 years, moderately hypercholesterolemic; BMI 18.5–25 kg/m^2.	To evaluate the effects of the Saint-Yorre (SY) strong bicarbonate mineral water on lipoprotein levels during fasting and in a postprandial state. Two consecutive intervention periods lasting 8 wks each separated by one-week washout. The amount of the consumed water was 1.25 L p/d. Exclusion and inclusion criteria, food intake assessment. Evaluations before water consumption and after water consumption. The effect of 0.5 L from both water types in fasting and a postprandial state was also analyzed.	Ogeo LM sparkling water.	BP: NS; TC TAUC, HDL-C TAUC in the postprandial state after both SY and LMS consumption: NS; ↓TG- after the SY by 23%; VLDL-TG by 31%, and a tendency to a decrease of VLDL-C in fasting; TAUC for both SY and LMS-NS; Postprandial glucose TAUC after SY and LMS consumption: NS; Fasting insulin: NS.

RCT—randomized controlled tral; w—week; ♂—male gender; ♀—female gender; BCM—bicarbonate-calcium-magnesium-rich mineral water; LM—low mineral content water; SM— Montecatini Regina salt-rich mineral water; HBS–high bicarbonate sodium mineral water; CSB—carbonated sodium-bicarbonate mineral water; LBS–low bicarbonate sodium mineral water; BMW—bicarbonate-rich mineral water; SCB—sulfate-calcium-bicarbonate mineral water; TW—tap water; BSC—bicarbonate-sodium-chloride mineral water; LSB—low sodium-bicarbonate mineral water; HSB—high sodium-bicarbonate mineral water; HSC—high sodium-chloride mineral water; LBHP—low bicarbonate, high potential renal acid load (PRAL); MBMP—medium-high bicarbonate, medium PRAL; HBLP—high bicarbonate high PRAL; MBLP—medium-high bicarbonate, low PRAL; TC—total cholesterol; HDL-C—high-density lipoprotein cholesterol; TG—triglycerides; LDL-C—low-density lipoprotein cholesterol; NS—nonsignificant; BP—blood pressure; Apo-AI—apolipoprotein AI; Lp(a)—lipoprotein (a); p/d—per day; TBARS— thiobarbituric acid reactive substances; SBP—systolic blood pressure; DBP—diastolic blood pressure; MAP—mean arterial pressure; FGL—fasting glucose levels; HOMA-IR—homeostatic model assessment for insulin resistance; CVD—cardiovascular diseases; sICAM-1—soluble intercellular adhesion molecule-1; sVCAM-1—vascular cell adhesion molecule-1; hs-CRP—high-sensitivity C-reactive protein; BW—body weight; eGFR—estimated glomerular filtration rate; GGT—gamma-glutamyl transferase; GSH—reduced glutathione; GSSG—oxidized glutathione; MDA—malondialdehyde; dROMs—dissolved reactive oxygen metabolites; PRAL—potential renal acid load; TA—thiobarbituric acid; TAUC—total area under curve

BALNEO RESEARCH Balneo and PRM Research Journal English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

1 **Table 2**. Purpose, design, number of participants, and results of postprandial studies, sorted by first author's name.

First Author, Pub Year	Study, Duration	Participants	Aim/Study Design	Comparison	MetS-Related Outcomes
Schoppen et al., 2005 [54]	RCT triple crossover	18♀, mean age 55.7 y, healthy, BMI 26.89 kg/m^2, amenorrhea (≥ 1 y), non-smokers, no estrogen replacement therapy, standard meal	Whether BSC waters with different mineral content affect postprandial cholesterol and TG metabolism. Two mineral water evaluations with 2-week intervals between each. After specified dinner and 12 hours of overnight fasting, blood samples were obtained in the morning and after a standard meal plus 0.5 L of the studied mineral water BSC. The postprandial effects were investigated at 30, 60, 120, 240, 360, and 420 min. BSC[1](**Table S1**) contained 5.7 times more fluoride. Demineralized water (100 mL) was used for hydration after 240 and 390 min.	LM	Anthropometric data, TC, and TG: baseline. Water consumption effects were observed in TAUC for serum and chylomicron TG (ANOVA, $P < 0.05$). After bicarbonate mineral water TAUC is lower compared to LM water (949.55 ± 249.99 vs. 1123.56 ± 392.34, Bonferroni $P < 0.05$). The peak concentration of TG showed a water-type effect ($P < 0.05$). Changes in chylomicron cholesterol were not significantly affected by the type of water.
Schoppen et al., 2007 [53]	RCT triple crossover	18♀, mean age 55.5 ± 2.28 y, healthy, BMI 26.88 kg/m^2, amenorrhea (≥ 1 y), non-smokers, no estrogen, vitamin, mineral replacement therapy, study meal provided (4,552 kJ)	To study the effects of drinking 0.5 L of two types of BSC water with a standard meal, on postprandial insulin and glucose levels, and whether the effects vary depending on IR. 3 visits of the laboratory with 2-week intervals on each visit. BP, weight, height, and waist-to-hip ratio were measured, and blood samples were obtained after specified dinner and 12 hours of overnight fasting and postprandial period after a standard meal plus 0.5 L of one of the studied mineral water (BSC[1, 2], **TableS1**). Effects were investigated at 30, 60, 120 min. Demineralized water (100 mL) was used for hydration after 240 and 390 min.	LM	Differences in baseline anthropometrics, TC, TG depend on HOMA-IR n-tiles; baseline and postprandial glucose and insulin concentrations were investigated. Baseline weight, BMI, and hip circumference - significant differences depending on the HOMA n-tiles. Glucose: no change; HOMA and QUICKY inversely correlated ($r = -1.000$; $P < 0.0001$). Insulin concentrations showed a significant time effect ($r = -1,000$; and water x time interaction ($P < 0.05$). At 120 min insulin levels with BSC[1] were lower than with LM ($P < 0.05$). The effects were more pronounced in volunteers with higher HOMA values.
Schoppen et al., 2008 [75]	RCT triple crossover	18♀ mean age 55.5 ± 2.28 y, non-obese individuals, non-smokers, no estrogen, vitamin, or mineral replacement	The influence of consuming BSC, (**TableS1)** waters on serum aldosterone and urinary electrolytes. The interventional design was the same as ref. 53	LM	Urinary pH and postprandial excretion of calcium, phosphorus, magnesium, and sodium chlorine for 7 h: no differences observed; ↑Sodium excretion with BSC[1], compared with LM water consumption ($P < 0.05$) ↓Aldosterone in 120 min with BSC[1] and BSC[2] ($P < 0.05$), compared with LM water consumption.

		therapy, study meal provided			
Toxqui et al., 2012 [55]	RCT four-way crossover	21 (10♂ 11♀), moderately hypercholesterolemic, BMI >18 and < 30 kg/m^2, aged 18–40 y, with exclusion criteria	Investigation of the effects of CSB with or without a meal on postprandial TG, CCK, and gallbladder volume. Blood samples were obtained at baseline (after specified dinner and 12 hours of overnight fasting), and in a postprandial state after standard meal. The treatments were as follows: 0.5 L of LM plus standard meal; 0.5 L of CSB plus standard meal; 0.5 L of LM without a meal and 0.5 L of CSB without a meal.	LM	Anthropometrics, BP, lipids, glucose, insulin, and gallbladder volume at the baseline. ↓TG [mmol/L] in CSB with meal compared with control water at 30 min (1.55 ± 0.87 vs. 1.75 ± 0.90, P = 0.01) and 60 min (1.92 ± 0.83 vs. 2.17 ± 0.95, P < 0.05); ↓CCK [pmol/L] in CSB with meal at 30 min compared with control water (2.28 ± 1.95 vs. 3.63 ± 2.25, P < 0.01), CSB water with meal-induced higher gallbladder volume at 30 min (P < 0.05), 60 min (P = 0.01), and 120 min (P < 0.05) and reduced gallbladder emptying. Insulin concentration showed a sign time effect at 30 min, insulin peaked with both waters. When both waters were consumed with meal, the levels of insulin were without significance
Toxqui and Vaquero, 2016b [56]	RCT four-way crossover	21 (10♂ 11♀), moderately hypercholesterolemic, BMI >18 and < 30 kg/m2, Aged 18–40 y	Evaluation of the effects of BSC mineral water, with or without a meal, on aldosterone levels. Blood samples were obtained at baseline (after specified dinner and 12 hours fasting) and in a postprandial state after standard meal consumption. The treatments were: 0.5 L of LM, 0.5 L of BSC, 0.5 L of LM plus standard meal, 0.5 L of BSC plus standard meal; Standard meal similar to the Mediterranean diet. Analysis at 0, 30, 60, and 120 min.	LM	BMI [kg/m^2] is higher in men compared with women at baseline 25.8 ± 2.2 vs. 22.0 ± 2.3, P = 0.001. SBP [mmHg] higher in men compared with women at baseline 122.7 ±11.7 vs. 105.8 ± 11.1, P ≤ 0.01 DSB: NS at baseline HDL-C [mmol/L] is lower in men compared with women at baseline 1.6 ± 0.2 vs. 2.0 ± 0.3, P ≤ 0.01. TC, LDL-C, TG, glucose, insulin, aldosterone, sNa$^+$, and sK$^+$: NS difference at baseline. Serum Na$^+$: NS. ↓Serum K$^+$ without water type effect (P < 0.05). ↓Aldosterone at 30 (P < 0.05), 60 (P = 0.01), and 120 min (P < 0.05) after BSC, and at 120 min (P < 0.05) when consumed with a meal, compared to LM water but the significance was only in women.

2

3 BSC—bicarbonate-sodium-chloride mineral water; CSB—carbonated sodium-bicarbonate mineral water; LM—low mineral content water; TAUC—the total area under the curve; TC—total
4 cholesterol; HDL-C—high-density lipoprotein cholesterol; TG—triglycerides; LDL-C—low-density lipoprotein cholesterol; NS—nonsignificant; HOMA-IR—homeostatic model assessment for
5 insulin resistance; BMI—body massindex; CCK—cholecystokinin; BP – blood pressure; SBP—systolic blood pressure; DBP—diastolic blood pressure

Table 3. Treatment includes mineral water intake.

First Author, Pub Year	Study Type, Duration	Participants	Aim/Study Design	Comparison	MetS-Related Outcomes
Balakin et al., 2010 [76]	Intervention al, two groups, 4 w	105♂♀ obese, BMI > 30 kg/m^2, mean age 41.3 ± 0.48 y, moderate hypertensive	Evaluation of the effect of combined standard therapy for weight loss (diet, exercise, antihypertensive drugs) plus carbonated sulfate calcium magnesium mineral water in amounts 200–250 mL 20 min before main meals (main group, n = 55) The initial patient's condition was evaluated through an additional study with 15 healthy volunteers (aged 40.8 ± 1.22 y, BMI 24–28)	Control group (n = 50), the same combined standard therapy for weight loss (diet, physical exercise, antihypertensive drugs)	↓SBP [mmHg] in both groups: Control 142 ± 1.38 vs. 132 ± 1.20, P < 0.005; Main 144 ± 1.60 vs. 130 ± 1.14, P < 0.005; ↓DBP [mmHg] in both groups: Contol 93 ± 1.02 vs. 86 ± 0.85, P < 0.005; Main 95 ± 1.05 vs. 85 ± 0.77, P < 0.005; ↓TC [mmol/L] in the Main 5.94 ± 0.15 vs. 5.46 ± 0.11 and in the Control: NS; ↑HDL-C: NS in both groups; ↓TG: NS in both groups. ↓The atherogenic coefficient in both groups with significance only in the Main 4.45 ± 0.25 vs. 3.51 ± 0.18, P < 0.05. ↓FPG: NS in both groups; ↓Insulin [µU/ML] in the Main 20.8 ± 0.35 vs. 16.2 ± 0.25, P < 0.01, and in the Control: NS; Cardiovascular activity during exercise was improved in both groups, more clearly in the Main.
Chalaya et al., 2017 [70;	RCT, four groups, resort-based treatment with different duration	100 ♂♀, aged 48–63 y, mean 47 ± 1.3 y, obese, hypertensive	Estimation of the effectiveness of the new therapeutic modalities for the health resort-based treatment of MetS. Three groups, number (n) of patients in each group = 25. In addition to standard treatment 50 ml decoction (motherwort grass, hawthorn and rosehip berries, peppermint); Different duration of treatment. Group 1: 3–4 baths for a 6–7-day stay; Group 2: 8–9 baths for a 13–14-day stay; Group 3: 12–13 baths for a 21-day stay.	Control group (n = 25), standard treatment (hypocaloric diet, exercises, antihypertensive drugs, and 12–13 Narzan baths for 15 min, plus Narzan mineral water (3.5 per kg/bw) 30 min before meals (21 stays)	All patients were hypertensive at baseline (SBP > 140, DBP > 90, Heart rate > 80). ↓BP in all groups after the treatment, (P < 0.05). The period of return to baseline depended on the duration of applied treatment: in Groups 1 and 2—after 3 months, in Group 3—after 6 months, and in the Control group—after 9–12 months.

Dragomiretska et al., 2023 [77]	RCT, two groups, 8 w	71 ♂♀ patients with NAFLD and CVHC who had contracted COVID-19; 36♀, 35♂, mean age 42.13 ± 8.64 y	Assess the effectiveness of including mineral water in the rehabilitation complex in patients with CVHC and NAFLD who had contracted COVID-19. All patients received a complex therapy—Mediterranean diet, atherodinol, and exercise. In addition to complex therapy, the Main group (n = 32) received Shayanskaya silicon-containing bicarbonate mineral water—3 mL per kg/bw, at 30, 40, 60 min, three times per day, before meals, depending on stomach acidity.	Control group (n = 39): Mediterranean diet, atherodinol, exercise therapy	Anthropometrics, liver biochemistry examination, lipid metabolism, peroxidation, cytokine profile, IR, and ultrasonography of the abdominal organs were explored before and after treatment. ↓ALT, mmol/(h·L), before: 58.22 ± 4.08; after: Control group 34.44 ± 2.38, $P < 0.05$; Main 21.28 ± 2.76, $P < 0.05$; DFG, $P < 0.001$; ↓AST, mmol/(h·L), before: 52.71 ± 2.06; after: Control 31.15 ± 2.64, $P < 0.05$; Main 24.74 ± 2.06, $P < 0.05$; DFG, $P < 0.05$; ↓TC [mmol/L], before: 6.04 ± 0.16; after: Control 5.24 ± 0.21, $P < 0.05$; Main 5.11 ± 0.18, $P < 0.05$; DFG: NS; ↓TG [mmol/L] only in the Main, before: 3.15 ± 0.43; after: 2.17 ± 2.12, $P < 0.05$, DFG: NS; ↓LDL-C [mmol/L], before: 4.74 ± 0.18; after: Contol 4.01 ± 0.18, $P < 0.05$; Main 3.61 ± 0.19, $P < 0.05$; DFG, $P < 0.05$; ↑HDL-C [mmol/L] only in tne Main, before: 1.16 ± 0.09 after 1.34 ± 0.08 (after), $P < 0.05$; DFG: NS; ↓coefficient of atherogenicity, only in the Main, before: 4.09 ± 0.46; after: 2.72 ± 0.18, $P < 0.05$, DFG: NS; ↑Adiponectin [ng/mL] only in the Main, before: 12.28 ± 1.14; after: 15.44 ± 1.23, $P < 0.05$, DFG: NS; ↓Leptin [ng/mL] in both groups, before: 23.71 ± 3.36; after: Control 16.02 ± 1.63, $P < 0.05$, Main 15.97 ± 1.55, $P < 0.05$, DFG: NS; ↓MDA [µmol/L] in both groups: before 6.98 ± 0.27; after: Control 5.62 ± 0.26, $P < 0.05$; Main 4.52 ± 0.15, $P < 0.05$; DFG, $P < 0.001$; ↓Diene conjugates, [c.o., IO], before: 1.84 ± 0.19; after: Control 0.96 ± 0.16, $P < 0.05$; Main 0.67 ± 0.13, $P < 0.05$; DFG: NS; ↑Total antioxidant activity [%], only in the Main, before: 35.17 ± 1.89; after 42.12 ± 2.11, $P < 0.05$, DBG: NS; ↓FGL [mmol/L], only in the Main, before: 5.73 ± 0.23; after: 5.19 ± 0.22, $P < 0.05$; DBG: NS; ↓Insulin [µU/ml], only in the Main, before: 19.67 ± 0.84; after: 15.06 ± 1.20, $P < 0.001$, DBG, $P < 0.001$; ↓HOMA-IR, only in the Main, before: 5.10 ± 0.32, after: 3.54 ± 0.39, $P < 0.0001$; DBG, $P < 0.001$.

Zabolotnaya et al., 2016 [69]	RCT, four groups, 21–24 days treatment	120 (♂48, ♀72), 48–64 y, mean 54.53 ± 3.41 y, NAFLD, 81.66% with biliary system disorder	To evaluate the effectiveness of the internal course of mineral waters of different balneological types and a bischofite aqueous solution for the treatment of NAFLD. 4 groups each with 30 patients: Control (C) received standard complex therapy (diet, exercise); Bischofite (B) received in addition bischofite aqueous solution 40 min before main meals; Sulfate (S) received in addition sulfate mineral water; Sodium bicarbonate (SB) received in addition sodium-bicarbonate mineral water. Mineral water (1% of body weight ~150–200 mL), 3 times p/d.	Before and after the treatment	↓TC [mmol/L]: B 6.78 ± 0.18 vs. 5.80 ± 0.3, P < 0.02; S 6.46 ± 0.35 vs. 5.27 ± 0.23, P < 0.02; BS 6.66 ± 0.42 vs. 5.64 ± 0.35, P < 0.05; HDL-C: NS; ↓LDL-C [mmol/L]: SB 4.27 ± 0.24 vs. 3.86 ± 0.19 , P < 0.05; ↓TG [mmol/L]: B 2.10 ± 0.15 vs. 1.68 ± 0.12, P<0,05; S 2.32 ± 0.14 vs. 1.74 ± 0.02, P < 0.02;↓Beta-lipoproteins: B 68.16 ± 2.11 vs. 57.32 ± 2.29, P < 0.001; S 72.22 ± 3.67 vs. 58.32 ± 2.36, P < 0.01; SB 74.25 ± 2.88 vs. 62.62 ± 3.26, P < 0.05; FPG [mmol/L]: S 6.12 ± 0.24 vs. 5.43 ± 0.22, P < 0.05, SB 6.46 ± 0.37 vs. 5.37 ± 0.21, P < 0.01; ↓Insulin [μU/ML]: B 18.73 ± 0.76 vs. 9.21 ± 1.37, P < 0.01, S 19.94 ± 1.67 vs. 14.53 ± 1.42, P<0.05, SB 16.93 ± 0.94 vs. 10.11±1.02, P<0.001; ↓HOMA-IR [μU/ML] B 5.46 ± 0.57 vs. 2.46 ± 0.48, P < 0.01, S 3.78 ± 0.36 vs. 2.69 ± 0.29, P < 0.05, SB 3.98 ± 0.36 vs. 2.26 ± 0.28, P<0.001; ↓Total bilirubin [μmol/L] in the mineral groups, more pronounced in the S 18.15 ± 1.94 vs. 12.17 ± 1.36, P < 0.05; ALT [mmol/h/L]: NS; ↓AST [mmol/h/L]: S 0.56 ± 0.08 vs. 0.33 ± 0.06, P <0.05.

NAFLD—nonalcoholic fatty liver disease; CVHC—chronic viral hepatitis C; ALT—alanine aminotransferase; AST—aspartate aminotransferase; DBG—difference between the groups; TC—total cholesterol; HDL-C—high-density lipoprotein cholesterol; TG—triglycerides; LDL-C—low-density lipoprotein cholesterol; NS—nonsignificant; HOMA-IR—homeostatic model assessment for insulin resistance; BMI—body mass index

The number and age of the populations varied: in four studies the number of volunteers was ≥100 [43, 69–70, 76], in seven—more than 50, and the rest included between 10 and 21 volunteers. Female participants between 50 and 55 years of age predominated. A few studies included young volunteers [35, 36, 55, 56] and three had elderly volunteers ranging from 60 to 75 [34, 43, 74].

Regarding the health status of the participants, seven studies were performed with moderately hyperlipidemic patients [34–38, 55, 56], two—with obese and hypertensive ones [70, 76], two—with nonalcoholic fatty liver disease patients [69, 77], one was with borderline hypertensive ones [78], one had a mixed population of healthy and hypertensive individuals [71], one included T2D patients [79], and ten focused on healthy volunteers [43, 53–54, 63–65, 72–75].

Assessment of fasting lipid status was reported by several studies [34–38, 65, 72, 74, 76, 77, 79] and postprandial status was part of two studies [38, 54]. Postprandial cholecystokinin and gallbladder volume were also studied [55]. Apoproteins A and B have been analyzed [34–36, 73] as well as the cardiovascular risk [35, 73] and the coefficient of atherogenicity [36, 76, 77]. Bile acid excretion was reported in one study [34] and peristalsis, daily bowel movements, microbiome, and metabolome analysis were included in two [72, 79].

The effects on blood pressure and related parameters were studied [34–36, 38, 43, 64, 70–76, 78]. Of these, the aldosterone levels [36, 64, 71, 74–75] and the renin and atrial natriuretic factor were reported [74]. One study examined the effect of bicarbonate-rich water intake on the acid-base status [43].

Glycemic control was the subject of the following studies: 35–36, 38, 72–74, 76–77, 79, which examined fasting blood glucose and insulin levels, while Zair et al., 2013 [38], Toxqui et al., 2012 [55], and Schoppen et al., 2007 [53] additionally examined postprandial glucose and insulin levels. In three studies [69, 72, 73] IR (HOMA-IR) was calculated, and glycoalbumin was analyzed by Murakami et al., 2015 [72].

Oxidative and antioxidant status after mineral water intake was investigated in five studies [36, 63, 65, 77, 79] and some authors have also investigated changes in pro-inflammatory and anti-inflammatory parameters [35, 63–65, 73]. The levels of the cytokines adiponectin and leptin were also studied [35, 77].

3. Discussion

3.1. Effects of mineral water on lipid status

The imbalance of lipids such as TC, LDL-C, TG, and HDL-C is a condition known as dyslipidemia [80]. Dyslipidemia is one of the abnormalities in the etiology of MetS [81]. The development of MetS has been studied in various animal models [82, 83]. After the diagnosis of MetS, a therapy combining a calorie-restricted diet and the intake of different types of mineral waters is used. Sulfate, magnesium, bicarbonate, and low mineral waters are more effective in improving lipid and glucose status [84]. The specific effect of these waters is characterized by the combination of the effects of naturally carbonated and pure hydrogen carbonate waters, partly from the sulfates, calcium, etc. contained in them. These effects are not always synergistic, but antagonistic. It is known that carbonic acid ions increase the acidity of gastric secretion, and alkaline hydrogen carbonate ions decrease it [85].

Of the selected studies, of great interest are Vaquero's RCTs [35, 36, 73]. In the beginning, the team tested the effects of carbonated sodium-bicarbonate mineral water (Vichy Catalan) and low mineral water in 18 postmenopausal healthy women in an 8-week trial [73]. The long-term consumption of 1 liter/day of Vichy Catalan significantly lowered TC, LDL-C and adhesion molecules, and increased HDL-C, compared with low

mineral water. The protective postprandial effects of Vichy Catalan compared to other mineral waters with similar composition or low mineral water were also explored [54]. The results showed a significantly reduced postprandial serum and chylomicron TG in 18 postmenopausal healthy women after carbonated sodium-bicarbonate mineral water drinking, compared to low mineral water [54]. Curiously, in an earlier study with salty mineral water, similar results were observed in 10 moderately cholesterolemic adults [35]. In addition to the improved lipid profile during fasting, an increase in the excretion of bile acids and a decrease in gall bladder volume were also found [34].

Vaquero`s team also observed the effects of mineral-rich Vichy Catalan in relatively young volunteers with moderate cholesterolemia [35]. After long-term consumption, significant reductions in TC and LDL-C, TC/HDL-C, LDL/HDL, and ApoB were observed. However, serum TG, Apo A-I, and adhesion molecule levels did not change in this study. Despite similar results, the effect of water appeared to be stronger in healthy postmenopausal women than in younger individuals with moderate hypercholesterolemia (72% vs. 66%, respectively). A reduction in the levels of postprandial TG was found [54]. The researchers assumed that the observed increase in urine pH after mineral water intake may also be relevant to the intestinal lumen, suggesting a possible decreased absorption of dietary lipids.

Unexpectedly, in a recent study with a cohort of 64 volunteers (mean age 30.7 ± 7.5 years), the effects of similar mineral water, compared to low mineral water [36], showed reduced cardiovascular risk regardless of the mineral composition. The TC and LDL-C levels, and the ApoB levels ($P < 0.001$) were significantly reduced independently of the mineral water type ($P < 0.005$), and a tendency to decrease oxidized LDL-C was observed as well ($p = 0.073$). Triglycerides, HDL-C, and Apo-AI were unchanged (Table 1). The authors reported that examination of the participants' food and beverage consumption diary revealed a decreased intake of sweetened soft drinks, suggesting that the decrease in the TC level was probably due to the replacement of caloric soft drinks with pure mineral water. When consumed with meals, the carbonated sodium-bicarbonate mineral water lowered postprandial TG levels at 30 min ($p = 0.01$) and at 60 min ($p = 0.03$), compared to low mineral water [34, 35]. Carbonated sodium-bicarbonate mineral water was shown to interfere with lipid absorption in the first two hours of digestion by inhibiting cholecystokinin and gallbladder emptying [55]. In contrast, in long-term studies, alternating an 8-week period of low mineral water with 8 weeks of carbonated sodium-bicarbonate mineral water, found a reduced cardiovascular risk only after the mineral-rich water period [35, 73]. Toxqui and Vaquero suggest that the free choice of foods and the observed consumption of more saturated fat during the intake of carbonated sodium-bicarbonate mineral water period, but not during the low mineral water period, probably neutralized the previously found positive effect of carbonated sodium-bicarbonate mineral water. The observed increased levels of ApoB and decreased LDL-C/ApoB in both periods are explained by the possible appearance of smaller, denser, and TG-poor LDL in the blood [36].

The independent effects due to the type of mineral water consumed were also established in other RCTs with an intake of 1 L/d for one month [37]. The TC and LDL-C levels significantly decreased, but the TG and the HDL-C levels did not change in adult volunteers (30–60 y) with dyslipidemia with a similar diet in the morning and at lunchtime according to Aslanabadi et al., 2014. The studied mineral water was rich in calcium, magnesium, and bicarbonate. Interestingly, the same effects were observed in the control group after intervention with commercially available low mineral water.

In T2D patients, only the TC levels were significantly reduced, while the reduction of TG, HDL-C, and LDL-C was insignificant. In this study with low-mineral bicarbonate water intake (bicarbonate ions 1098.0 mg/L) and similar duration, the daily water amount was individually calculated and varied from 1.5 to 3 L per person [79]. According to the authors, the duration of mineral water intake was perhaps insufficient to induce metabolic changes—the anthropometric parameters and the adipose tissue activity remained unchanged. When two types of water were alternated every other

week, as in the intervention of Murakami et al., 2015 [72], no significant changes were found in the lipid profile of healthy volunteers who kept their normal dietary habits. Such intervention design resulted in significantly positively changed blood metabolites and microbiome after mineral-rich water consumption.

Zair et al., 2013 [38], also examined the effects of the Saint-Yorry carbonated mineral-rich water (bicarbonates 4168 mg/L, sodium 1626 mg/L, chlorides 329 mg/L, and potassium 117 mg/L), comparing them to the Ogeo lightly carbonated mineral water (control water), on the lipid profile of 12 men aged 20–60 years with normal body weight and moderate cholesterolemia. Long-term daily intake of Saint-Yorry, compared to Ogeo, significantly reduced the TG and very-low-density-lipoprotein cholesterol (VLDL-C) levels of in 12 moderate cholesterolemic men [38]. Very-low-density-lipoprotein cholesterol was non-significantly decreased in the fasting state. The lipid status remained unchanged in the postprandial state. In contrast to other studies, which reported decreased LDL-C levels alone [34, 35] or together with increased HDL-C levels [73], in the study by Zair et al., 2013, these markers did not change [38]. Triglycerides decreased postprandially but not during fasting [34, 35, 74) as in the study by Zair et al. [38]. The difference in postprandial results is probably due to the standard diet—higher calorie intake in the studies of Schoppen and Toxqui [55, 74] compared to that of Zair [38] (1089 kcal vs. 798 kcal). The different mineral composition of the waters might also contribute to the different results. For example: the Montecatini Regina mineral water has the lowest HCO_3^-/Cl molar ratio 0/43 [34], Vichy Catalan has an intermediate HCO_3^-/Cl molar ratio 2/1 [35, 55], and Saint-Yorry is the richest in bicarbonates, intermediate in chlorine, and has the highest HCO_3^-/Cl molar ratio 7/3 [38] (Table S1). It is likely that intermediate-bicarbonate, high-chloride mineral waters have a fiber-like effect and may decrease the TC and LDL-C, whereas high-bicarbonate, intermediate-chloride waters have a potential to decrese the TG and VLDL-C levels by inhibiting fat absorption [38].

Recently, sulfur-containing mineral water has also been studied. A significant reduction in LDL-C levels was observed in overweight but not in normal-weight volunteers after two months of mineral water consumption [65]. Non-significant reduction in TC levels was observed only in the overweight volunteers. The HDL-C and TG levels in the blood were unchanged.

One-month standard spa therapy resulted in a significant decrease in the TC levels in obese patients with moderately high BP who drank Novoterskaya medicinal water (n = 55), compared to a control group (n = 50) without mineral water intake. Only in the mineral water group, the coefficient of atherogenicity was decreased, and the TG and HDL levels remained unchanged [76]. This type of mineral water is commercially available. It contains bicarbonate (1300–1600 mg/L), sodium (800–1100 mg/L), sulfate (1200–1600 mg/L), calcium (300–400 mg/L), and chlorine (300–500 mg/L).

In patients with fatty liver disease (n = 120, 48 males/72 females, average age about 55 years), the effects of different mineral waters and bischofite solution were studied [69]. After a three-week therapy, a significant decrease in the TC levels in all groups was observed (Table 3). This study did not confirm the hypothesis of Zair et al., 2013 [38], that bicarbonate waters with intermediate chloride content lower the TG levels. The TG levels decreased in the patients in the bischofite and sulfate groups, who received more chloride and no bicarbonate, compared to the patients in the sodium-bicarbonate group, who consumed less chloride via water. The TG levels in the sodium-bicarbonate group remained unchanged, but a significant decrease in the LDL-C levels was found. Another effect of the therapy was a decrease in the ApoB levels observed only in the mineral water groups. There was no change in HDL-C after therapy in all studied groups (Table 3).

In chronic fatty liver disease patients after COVID-19 infection, silicon-containing mineral water with a complex composition (Shayanskaya) was added to their rehabilitation course, Tables 1, 3 [77]. The two-month rehabilitation course reduced the TC and LDL-C levels in all patients, with no differences in the TC levels between the groups. Significant decrease in the LDL-C and TG levels was found only in the mineral

water group (Table 3). After the rehabilitation, the HDL-C levels increased and the atherogenic ratio decreased, again only in the mineral water group.

In conclusion, the TC and LDL-C levels were lowered regardless of the type of water consumed—after bicarbonate-calcium-magnesium or table water in dyslipidemic participants [37]; after carbonated sodium-bicarbonate or low mineral water in moderately cholesterolemic subjects [36]; only after the carbonated sodium-bicarbonate mineral water period in young volunteers with moderate cholesterolemia [35] and in menopausal women [73]. After the salty magnesium-calcium mineral water intake, the TC and LDL-C, as well as the TC/LDL ratio, were reduced in elderly healthy volunteers [34]. After consumption of sulfur-containing mineral water with complex composition, the LDL-C decreased only in overweight healthy volunteers [65]. Following the consumption of low-mineral bicarbonate water, only the TC was lowered in people with T2D [79]. The fasting TG levels were significantly decreased in moderately cholesterolemic men in a study with bicarbonate-rich mineral water [38]. The levels of HDL-C were increased in two studies: in patients with chronic hepatitis C after silicon-containing mineral water consumption [77], and in healthy postmenopausal women after carbonated sodium-bicarbonate mineral water consumption [73]. In some studies with bicarbonate-rich water containing essential macro- and microelements, no changes in plasma lipids were reported [72, 74]. When added to standard spa therapy, not excluding medication or BP supplements, mineral waters of different compositions contribute to improving the lipid profile of overweight patients by lowering the TC after carbonated sulfate-calcium-magnesium water consumption [76] and after a bischofite aqueous solution consumption [69] in all patients regardless of the water intake [77]. A decrease was registered in the LDL-C levels in the sodium-bicarbonate water group [69] in all patients regardless of the water intake [77]. The TG levels were decreased in the bischofite and sulfate drinking groups [69].

It is likely that the sodium-bicarbonate waters taken during meals have a slight alkalizing effect [35, 54] and neutralize the stomach's acidic environment, necessary for activating gastric lipase [86]. Decreased functionality of gastric lipase decreases the hydrolysis of the TG to MG, DG, and fatty acids, on which cholecystokinin secretion and the activation of pancreatic lipase and colipase depend [87]. Undigested TG in the intestinal lumen are probably the cause of the inhibition of cholecystokinin secretion and gallbladder emptying [55], leading to a reduction in the amount of secreted bile acids in the intestinal lumen. Through a combination of actions at a digestive level, the bicarbonate mineral water might decrease the absorption of both TC and TG. Salty mineral waters also lower TC and LDL-C, TC/HDL-C, and ApoB but the mechanism of action is associated with accelerated emptying of the gallbladder and increased excretion of bile acids with feces. Interrupting the enterohepatic circulation of bile acids, salty mineral waters can exhibit a hypolipidemic effect. Further controlled studies, confirming the reported positive effects on lipid status after the intake of silicon- and sulfur-containing mineral waters, are needed.

3.2. Effects of mineral water on blood pressure and related parameters

It is known that high dietary sodium chloride intake is a risk factor for developing hypertension [88–91]. It would be interesting to know what the effect of mineral-rich water would be on BP. It has already been shown that magnesium- and calcium-rich waters improve osmolarity and reduce the risk of CVD [92], while low mineral water improves diuresis, supporting the excretion of sodium, uric acid, and urea, and may have beneficial effects in urinary infections, urolithiasis, gout, and high BP [93].

More than half of the selected studies examine the influence of mineral waters on BP and related parameters, some postprandially [56, 75] and others in the long-term [35–36, 38, 64, 70–74, 76, 78]. Many of the studied waters have a wide variety of minerals present in them, with bicarbonate, sodium, sulfate, and chlorine ions being the most common. Some of these waters are gaseous, containing both carbon dioxide and

hydrogen sulfide. Another common feature is the presence of calcium, magnesium, and potassium (Table S1).

Sodium-bicarbonate waters and sodium-chloride waters have different effects on BP. Consumption of low sodium-bicarbonate (LSB) or high sodium-bicarbonate mineral water (HSB) in an amount of 1.5 L/d had a positive effect on 21 healthy elderly volunteers with limited salt intake. High sodium-bicarbonate mineral water had neither a positive nor a negative effect but the positive effect of a low-salt diet on the BP was lost after HSC water intake. There was no change in the BP of the volunteers after HSC water intake. It is likely that the potassium (70 mg/L) in the HSC water, together with the salt-limited diet, regulates the electrolyte balance. As expected, the excretion of sodium decreased during the intake of LSB mineral water, increased during the intake of both HSB and HSC water, and the chloride excretion increased during HSC water intake [74]. No adverse effects on the BP after consumption of bicarbonate-sodium-chloride mineral water (BSC) were also reported [36, 38, 56 71, 73]. Long-term intake of carbonated mineral water rich in bicarbonate, sodium and chloride (2094 mg/L, 1116 mg/L, 600 mg/L, respectively) by healthy menopausal women had no negative effect on the BP after 2 months [73]. Despite the addition of about 1 g of salt per day when consuming 1 L/d of mineral water, the BP did not increase. This could be due either to the greater tolerance of the female gender to salt or to potassium intake (54.7 mg/L). Studies have reported that potassium removes the negative effects of sodium chloride intake [94]. Toxqui and Varuero [36] also did not observe changes in the systolic blood pressure (SBP) and in the diastolic blood pressure (DBP) in 64 volunteers with moderate cholesterolemia who took an extra intake of 1 g of sodium per day through consumption of 1 L per day of the almost the same BSC with 4.5 g/L carbon dioxide, compared to low mineral water (Table S1). According to the authors, the lack of a negative effect on the BP might be due to aldosterone, which tended to decrease after 8 weeks compared with its pre-intervention levels. It is shown that increased consumption of BSC, with or without food, affects the renin-angiotensin-aldosterone system (RAAS) with a subsequent aldosterone-lowering and sodium-excretion-increasing effect [53, 56, 75]. Mansouri et al., 2023 [71] also investigated the influence of the consumption of HSB mineral water (HSB group, $n = 43$), comparing it with low in bicarbonate and sodium (LBS) control water (LBS group, $n = 42$), on BP in different baseline BP subjects (Table 1). In response to different mineral water intake in normotensive and hypertensive subjects, the BP changes were similar, without significance between the groups. In all hypertensive subjects, a decrease in the SBP was established. The significance was only in the LBS group ($p = 0.002$), revealing a beneficial effect of regular consumption of low mineral water in people with high BP. Urinary calcium and sodium excretion increased in the HBS group, thus the additional sodium intake was effectively excreted. Serum aldosterone decreased significantly without water type effect, more pronounced in the HBS group [71]. A similar decrease in serum aldosterone levels, regardless of the type of mineral water, was observed by Schorr et al., 1996 [74]. At the end of the first week of a 4-week intervention, the levels of aldosterone and renin decreased. The atrial natriuretic factor increased after the HSB water intervention. These changes were not observed at the end of interventions and their levels returned to the baseline.

Drinking one liter of BSC mineral water with about 50 mg/L potassium content had a small contribution to exerting a hypotensive effect [36]. After the intervention, an increase in urinary pH was observed, accompanied by a decrease in calcium excretion. Similar results were observed in an 8-week study with carbonated sodium-bicarbonate mineral water (CSB) intake (bicarbonate 2120 mg/L, sodium 1102 mg/L, and chlorine 597 mg/L), suggesting systemic alkalinization [35]. High-protein diets can cause mineral deficiency by a mechanism related to impaired reabsorption through the kidneys due to an acid load in the blood and urine. In this sense, bicarbonate mineral water can improve mineral reabsorption through the kidneys [95]. Consumption of bicarbonate-rich mineral water can significantly decrease net acid excretion (NAE) by reducing the amount of dietary acid supplied to the body and, at the same time, it can replenish the

mineral deficiency [43]. In 19 healthy volunteers who drank bicarbonate-rich mineral water, no BP and electrolyte changes were observed, except for calcium whose level in the blood increased after mineral water intake ($p < 0.05$). The calcium content in the bicarbonate mineral water was 177 mg/kg [72].

In 18 young normotensive dyslipidemic volunteers (TC > 5.17 mmol/L, LDL-C > 2.58 mmol/L), in the fourth week after the start of a CSB intervention, the SBP decreased significantly compared to the low mineral water period [35]. Another observed effect was an increase in sodium and chloride ion elimination only after the CSB water consumption. It is likely that in young people the kidneys are capable of excreting an additional dietary salt [35]. The reason may also be the lack of equimolar concentrations of sodium and chloride in the mineral water. It was discovered that an increase in sodium intake without equimolar intake of chloride did not increase extracellular fluid volume and BP [96]. Similar results were obtained by Zair Y et al. [38] who explored the influence of mineral water reach in sodium, potassium, and relatively little chloride in 12 young moderate cholesterolemic men. After 8-week consumption, this type of water did not change the BP. The intake of mineral water rich in sodium does not appear to pose a risk of BP elevation [38].

The participants' kidney function was likely improved after mineral water consumption, as observed by Roussev et al., 2019 [64] in a study with sulfur-containing low-mineral waters with a variety of ions and metasilicic acid (Table S1). In 50 healthy middle-aged volunteers, an 8-week water intake reduced the level of creatinine in the blood and increased the glomerular filtration rate of the kidneys, regardless of the increased diuresis. After the intervention, the electrolytes and aldosterone levels in the blood remained unchanged. A decrease was observed in the DBP, but not in the SBP [66].

A change in lifestyle, including the intake of mineral water (Novoterskaya) before meals, can improve the health status of patients with obesity and moderately high BP. A one-month complex therapy affected carbohydrate and lipid metabolism and significantly reduced the BP parameters [76]. In T2D patients, the Narzan mineral water (hydrocarbon, magnesium, calcium, and potassium-rich water, Table S1), in addition to the standard balneotherapy for weight loss, also contributed to lowering BP [70]. The achieved effects were maintained for more than 9 months only in patients with the longest therapy duration of three weeks (Table 3).

In conclusion, the data in the selected articles regarding the effect of mineral waters on BP and related parameters are contradictory and difficult to compare. In some studies, after taking BSC water with traces of magnesium and calcium, the BP did not change [73, 56]. The same effect was observed when bicarbonate waters were more saturated with magnesium and calcium [72]. Waters with medium and low levels of mineralization are more likely to have a positive effect, as shown by a decrease in systolic and diastolic BP in borderline high BP participants after consumption of low mineral water compared to distilled water with added magnesium sulfate [78]. It is likely that intake of sodium-bicarbonate or BSC waters has no negative effect in healthy elderly people with borderline high BP without kidney disease but abolishes the positive effect of a limited salt diet [74, 78]. Similar mineral water in middle-aged volunteers did not affect normotensive subjects [71]. Blood pressure significantly decreased in hypertensive subjects only after LSB water consumption [71]. Diastolic BP was reduced in healthy volunteers following ingestion of low-mineral hydrocarbonated water with dissolved sulfides [66]. Acute consumption of BSC water taken on an empty stomach or with meals led to a significant decrease in aldosterone [56, 73]. The same effect was observed with long-term intake regardless of the type of water [71], but not in Schorr's, Toxqui and Vaquero's, and Roussev's studies [36, 64, 74]. The kidneys of healthy subjects likely adapt to the challenge of mineral-rich water by increasing the excretion of excess ions without negative consequences on the BP. Conversely, regular intake of low mineral water leads to reduced excretion of ions. The intake of waters with medium and

high content of bicarbonate and low potential renal acid load containing magnesium and calcium can contribute to maintaining the acid-base status [43].

3. 3. Effects of mineral water on blood glucose levels

From selected human studies, fasting glucose levels (FGL) are significantly reduced by 6.7% ($P < 0.001$) in 18 healthy, nonobese women with amenorrhea (> 1 y) after a two-month intervention with BSC compared with low mineral water [73]. Bicarbonate-sodium chloride-rich mineral water, under controlled conditions (no smoking, no estrogen, vitamin, mineral replacement therapy, diet providing 4,552 kJ), can increase insulin sensitivity in healthy postmenopausal women with higher HOMA-IR [53]. In another RCT with CSB or low mineral water (both Vichy Catalan), a significant decrease in glucose levels ($P < 0.05$) was found in 64 volunteers with moderate cholesterolemia, with no significant differences between the two periods of mineral water drinking. Plasma insulin levels were not affected in either the carbonated bicarbonate water period or the low mineral water period [36]. In young volunteers (mean age 29 years) with moderate hypercholesterolemia, the two-month intake of CSB, compared with low mineral water, showed a tendency to lower serum glucose levels ($P = 0.056$). Insulin levels remained unchanged, as did the insulin sensitivity-related hormone adiponectin [35].

Sulfate or sodium-bicarbonate mineral waters, in addition to standard therapy (diet and physical exercise), improved carbohydrate metabolism in patients with non-alcoholic fatty liver disease and biliary system disorder. Only in the subgroups that received sulfate or sodium-bicarbonate mineral water as a supplement, FGL significantly decreased, more distinctly in the sodium-bicarbonate group ($P < 0.05$ vs. $P < 0.01$, respectively), compared to the control and bischofite groups. The average values of fasting insulin decreased significantly in the three mineral water groups, more clearly in the sodium-bicarbonate group ($P < 0.001$). After treatment, IR was positively affected in all patients, with the HOMA index decreasing below 2.5 μU/mL in the bischofite and sodium-bicarbonate groups, Table 3 [69]. Similar results were observed by Balikin et al., 2010 [76]. Only in the mineral water group, after a four-week weight loss therapy including Novoterskaya mineral water, a significant decrease in fasting insulin levels (FIL) was achieved in patients with moderate hypertension. The FGL was not significantly changed after the therapy. An improvement in carbohydrate metabolism through significant FGL and FIL decrease in patients with chronic liver disease and after COVID-19 was observed [77]. A two-month recovery period including Shayanskaya mineral water, containing orthoboric and metasilicic acids, decreased IR only in patients from the mineral water group, compared to the control group—patients on standard healing therapy (Table 3). Glycoalbumin was significantly reduced in 19 healthy volunteers after the consumption of bicarbonate-rich water (bicarbonate content 2485 mg/L), compared with tap water consumption [72]. The performed metabolomic analysis revealed significant differences in metabolites from carbohydrate and amino acid metabolism. The microbiome was also changed as *Christensenellaceae* typical of non-obese people increased after the mineral water intake [72].

No changes in glycemic control were observed in the study by Shorr et al., 1996 [74]. Three types of mineral water, HSB, HSC, and low sodium-bicarbonate mineral water (LSB) taken for four weeks, each with a two-week washout period, by healthy elderly people ($n = 16$) without changes in plasma glucose and insulin levels. No variation in glucose levels was observed in a study with a similar design and with moderate cholesterolemia patients ($n = 12$) who consumed two kinds of carbonated waters (Saint-Yorre or Ogeo) or low-mineral water used as a reference [38]. A lack of correlation between Snejnik-1/79 low-mineral water, consumed for 4 weeks, and glucose levels in T2D patients was also observed [79]. The authors did not report the composition of the water but said that the content of calcium ions (80.1 mg/L) and magnesium ions (34.9 mg/L) in Snejnic-1/79, supporting the absorption of glucose by the

cell, might be insufficient for the manifestation of a hypoglycemic effect, or the intake of water should be longer. The same water showed a hypoglycemic and antioxidant effect in TD2 rats after one month [97]. The effects appear less pronounced in young adults whose BMI, insulin, and glucose concentrations were within normal baseline ranges compared to elderly subjects [55]. The intake of CSB water did not show a significant effect on insulin levels. The glucose concentration did not change in fasting and postprandial states. The mineral water used was not rich in calcium (32 mg/L) and magnesium (9.4 mg/L). Curiously, other studies reported positive effects on glycemic control for similar mineral water [35, 54, 73].

The mechanisms of impaired glucose tolerance due to insufficient water intake in T2D are still being elucidated. Arginine vasopressin (AVP) probably plays a key role. In addition to maintaining the water balance in the body, it exhibits a hyperglycemic effect in humans [98]. Elevated levels of AVP or its precursor copeptin are positively and independently associated with new-onset T2D [99, 100], and also with insufficient water intake people [98]. Increased water consumption was found to significantly reduce mean circulating copeptin levels in healthy volunteers with habitually low to moderate daily water intake [101]. Better hydration likely affects the secretion of AVP involved in BP regulation, glucose homeostasis, and IR [100]. Insufficient hydration and increased osmolality can activate the RAAS [102]. Some data has shown that elevated aldosterone levels interrupt normal insulin signaling and slow down the removal of glucose from the bloodstream [103]. Furthermore, the increased renin activity is associated with increased ROS production of and impaired insulin signaling [104].

The influence of mineral waters on the signaling pathways of hormones regulating blood sugar has been studied in fructose-induced MetS in experimental animal models [82, 105, 106, 109]. The Pedras Salgadas hypersaline carbonated mineral water has been shown to improve glucocorticoid signaling and increased sirtuin 1 in the liver, subcutaneous (SCAT) and visceral adipose tissues [107]. Sirtuin 1 is thought to exert its beneficial effect by inhibiting the glucocorticoid receptor (GR) [108], whose increased activity is associated with IR and obesity [106, 108, 109]. The effects of mineral water on insulin signaling, lipid deposition, and endoplasmic reticulum stress have also been studied [110]. Fructose-induced IR is associated with overactivation of hepatic protein-tyrosine phosphatase 1B (PTP1B), a key regulator of insulin signaling, dephosphorylating the tyrosine residues of the insulin receptor and insulin receptor substrate (IRS) (active, phosphorylated), thereby promoting their dissociation, which interrupts insulin signaling way [110]. Mineral-rich water intake can fully or partially modulate fructose-induced effects by increasing phosphorylated extracellular-signal related kinase (p-ERK/ERK), activating inositol requiring enzyme-1 alpha (IRE1α) increasing undisplaced X-box binding protein 1 (XBP1), and partially preventing a fructose-induced increase in total ERK in visceral adipose tissue. According to the authors, mineral-rich water can protect the body from oxidative stress and IR [110].

In conclusion, studies evaluating the mineral water effects on glycemia have been performed with a relatively low number of volunteers and with different types of mineral water. Some of the studies were focused on mineral waters with high availability of magnesium and calcium [72, 76]. Murakami's study observed a decrease in glycoalbumin and a positive change in metabolites and microbiome in 19 healthy volunteers consuming 500 mL of mineral-rich water daily. In Balikin's study of 55 obese and moderately hypertensive volunteers undergoing weight loss therapy, FILs were lowered without a change in FGLs. The remaining studies with positive effects were performed with CSB mineral waters, with a trace of calcium and magnesium ions. Water consumption lowered the FGL in 18 postmenopausal women [73] and in 64 volunteers with moderate cholesterolemia [36]. Both studies tested BSC mineral water. Zabolotnaya et al., 2016 [69] compared the effects of sulfate, bicarbonate, or sodium-bicarbonate mineral water in a total of 120 volunteers, divided into 30 subjects in a group. In this study, the levels of glucose and insulin were reduced in all three groups. The IR was improved in patients after low mineral water consumption [77]. In healthy elderly,

moderately cholesterolemic, with TD2, or young healthy subjects [38, 55, 74, 79] no changes in the glucose and insulin levels were observed. Probably the low number of participants or the amount of macro- and microelements received with these mineral waters were insufficient to exert a hypoglycemic effect.

3.4. Effects of mineral water on antioxidant defense

Hyperglycemia, hyperlipidemia, chronic inflammation and endothelial dysfunction, and the characteristic vitamin and mineral deficiency of obesity generate oxidative stress [111]. In recent years, there has been a growing interest in sulfur mineral waters due to their antioxidant and anti-inflammatory properties [62, 112, 113].

Of the selected articles, 8 tracked the antioxidant and anti-inflammatory effects of mineral waters. All studies had the same duration of two months. Five of them were carried out with low mineral waters [63–65, 77, 79], with four of them containing sulfur and metasilicic acid [63–65, 77]. The other three articles were carried out with BSC mineral waters [35, 36, 74].

Antioxidant capacity was improved by increasing the activity of the antioxidant enzyme superoxide dismutase and reducing the level of the intracellular antioxidant glutathione [79]. Superoxide dismutase is responsible for neutralizing the superoxide anion radical to hydrogen peroxide. This explains the significant decrease in superoxide anion radicals in T2D patients after bicarbonate-calcium-magnesium mineral water drinking (Tables S1 and Table 1). A significant increase in nitric oxide was also reported after the intervention [79].

Increased levels of glutathione and total thiols, as well as increased expression of a regulatory enzyme of glutathione synthesis, gamma-glutamyl-cysteinyl ligase (GCL), in peripheral blood mononuclear cells (PBMCs) of healthy volunteers after 8-week sulfur-containing mineral water intake with similar low magnesium and calcium content, was also reported [63]. Concomitantly, an increase in mRNA for the intracellular adhesion molecule (ICAM-1) was also observed but the levels of the protein in the blood remained unchanged after the intervention. An anti-inflammatory effect of sulfur mineral water has been observed in healthy volunteers, due to a decrease in the levels of highly sensitive C-reactive protein (hs-CRP) after the intervention [64], more pronounced in overweight people, individuals with low physical activity, and smokers. For those consuming high-alcohol beverages the effect was less pronounced. Total thiols were significantly increased in normal-weight volunteers without harmful habits [65]. A similar lack of differences in the levels of adhesion molecules (sICAM-1, sVCAM-1) and adiponectin due to the consumption of CSB water was reported [35]. In contrast to studies with low mineral water containing sulfur and metasilicic acid [63–65, 77], this involved only 18 volunteers, and no positive change was reported in the analyzed hs-CRP protein. In Schoppen's study almost the same bicarbonate water significantly lowered sICAM-1 and sVCAM-1 in menopausal women [73]. An effective complex therapy was reported with silicon-containing low mineral water, which was added in the long-term rehabilitation of patients with chronic hepatitis C after COVID-19 infection. The treatment resulted in a significant restoration of the balance in the LPO/AOS system in all patients (n = 71). Only in the mineral water group, there was a significant increase in the total antioxidant activity compared with the control group. In the mineral water group, the reduction in malondialdehyde (MDA) levels was more pronounced [77]. The tendency to lower oxidized LDL regardless of the type of mineral water (BSC or low mineral water) was observed in the study by Toxqui and Vaquero, 2016a [36]. Antioxidant defense increased in studies with clinically healthy or osteoarthritic subjects. This beneficial effect was accompanied by reduced levels of lipid and protein oxidation products, reduced inflammation, and reduced cartilage degradation after twelve days of balneological spa treatments with sulfur mineral water [59–61]. There is data that sulfide mineral water can protect against DNA damage and has a therapeutic effect in upper and lower respiratory tract inflammatory diseases. Furthermore, a possible influence on the metabolism of xenobiotics through the

activation of the conjugating enzymes from phase II 3-phosphoadenosine-5-phosphosulfate synthase was reported in human intestinal cells [114]. A significant decrease in ROS and FGL was found after 12-day sulfurous hydropinotherapy in patients suffering from several chronic disorders [115, 116]. Mineral waters containing sulfur in the form of sulfate (SO_4^{2-} > 200 mg/L) or hydrogen sulfide (H_2S > 1 mg/L) have a variety of applications in the prevention of various clinical skin relief conditions, such as atopic dermatitis and psoriasis [62, 117–119], degenerative osteoarthritis [59, 120–122], gastrointestinal, urological and cardiovascular diseases [85]. Antioxidant, membrane stabilizing, detoxifying, and immunomodulating effects were found in rats after experimental MetS development and subsequent therapy combining intake of sulfate mineral water and low-intensity electromagnetic radiation [123]. Similar results were reported in other animal models [113, 124].

The healing properties of this type of mineral water are probably due to the sulfur. Sulfur is involved in the synthesis, native conformation, and post-translational modification of proteins. It is a component of amino acids, methionine—a precursor of the universal donor of methyl groups S-adenosyl-L-methionine (S-AM); cysteine—a part of glutathione, a cofactor of antioxidant enzymes (cysteine is also a precursor of 3'-phosphoadenosine-5'-phosphosulfate (PAPS) donor of sulfate groups, necessary for the synthesis of glycosaminoglycans, complex glycoproteins, and receptors); of taurine—involved in the synthesis of bile salts. The ROS-neutralizing abilities of these waters are probably due to dissolved sulfides, including hydrogen sulfide. Effects on signaling pathways activating the expression of antioxidant enzymes have been reported [125]. The trace elements in mineral water, such as molybdenum, zinc, selenium, cobalt, etc., may also contribute to the reported antioxidant and anti-inflammatory action.

4. Materials and Methods

The PRISMA guidelines were followed for this review. The Medline database was searched through PubMed and the Cochrane Library for comparative studies evaluating the biological effects of NMW consumption in healthy volunteers or with deviations in some parameters related to MetS until February 2024. Titles, abstracts, and full-text articles were examined by the primary reviewer (TS) to assess eligibility for review by using PICOS criteria (Participants, Intervention, Comparison, Outcomes, Study type) for inclusion and exclusion of studies.

PICOS were set as follows:

Participants: individuals without age, sex, or race restrictions, healthy or at risk of CVDs and TD2, normal weight or overweight/obese, with hyperlipemia or not, with hypertension or not;

Intervention: the durations were set as follows: at least four weeks for mineral water consumption and three weeks for balneotherapy; the postprandial examinations did not have a set time period. No restrictions on type, degree of mineralization, serving temperature, or drinking quantity;

Comparisons: interventions examining changes before and after consumption of mineral water, or comparing changes with control groups drinking tap water, low mineral water, or another type of mineral-rich water—alone or in addition to complex therapy;

Outcomes: biochemical or physiological effects relevant to MetS parameters;

Study type: randomized and non-randomized trials, blinded and non-blinded interventions, crossover, sequential, and parallel studies.

In the first stage, the titles of all searches found were read. The searches whose titles fell within the scope were selected. In the second stage, the abstracts of the selected searches were read, and in the third stage, searches involving mineral water consumption in humans were read in full. The reference lists were also reviewed to include all the related articles. To track the effects of mineral waters on MetS parameters, the following keywords alone or in combination were used: mineral water, metabolic

syndrome, obesity, hyperglycemia, hypertension, type 2 diabetes, dyslipidemia, and blood pressure. Search strategies are shown below:

PubMed: mineral water AND (metabolic syndrome OR obesity); mineral water AND (glucose OR glycemic OR hyperglycemia); mineral water AND (cholesterol OR dyslipidemia OR lipid metabolism)—All fields.

Filters activated: publication period 1990–2024.

Cochrane: mineral water* and hyperglycemia or metabolic syndrome or hypertension or type 2 diabetes, obesity, or lipid metabolism—All fields.

Data extraction

The primary author extracted relevant study information such as the physicochemical characteristics of drinking mineral waters, population, type, design, and primary and secondary results. In cases of uncertainty, items were discussed by the authors (T.S., B.R., and D.I.) until agreement was achieved.

5. Conclusions

The results from this systematic review revealed that NMWs, depending on the mineral composition and mineral levels, could positively affect the main risk factors defining MetS, such as lipid status, blood pressure, blood glucose levels, and redox status. Bicarbonate mineral waters may inhibit the emulsification of lipids and the activation of pancreatic lipase, preventing its absorption and deposition in adipose tissue. By accelerating the excretion of bile acids, saline mineral waters could decrease cholesterol levels. Positive health effects have also been found after consumption of moderate mineral water, such as hydrocarbonate and sulfurous waters which lowered the blood pressure in hypertensive people compared to mineral-rich waters. At the same time, the consumption of mineral waters with medium and low potential renal acid load (PRAL), containing relatively fewer calcium and magnesium ions, such as hydrocarbon waters, might help to restore the body's acid-base balance. On the other hand, moderate to high calcium and magnesium mineral hydrocarbonate waters may reduce some markers related to glycemic status (glycoalbumin and FIL) in healthy and hypertensive volunteers undergoing weight loss therapy. Therefore, different carbonated (sparkling), sulfate, sodium-bicarbonate, and low mineral waters, could improve glycemic control. Whether the observed effects are due to the mineral content or to increased regular water intake remains unclear. Moreover, similar antioxidant properties and anti-inflammatory effects have been established after interventions with mineral waters of completely different compositions among which sulfurous water stands out. In order to use mineral water consumption as an additional alternative therapy in patients with MetS, obesity or hyperglycemia, new carefully controlled studies confirming the reported effects are needed.

Supplementary Materials: Table S1: Main composition of the studied mineral waters. The arrangement is by the name of the first author.

Author Contributions: Conceptualization, T.S. and M.N.; methodology, T.S; software, T.S. and B.R.; investigation, T.S.; resources, T.S. and B.R; data curation, T.S., B.R., and D.I.; writing—original draft preparation, T.S..; writing—review and editing, M.N., A.S., B.H., and D.I.; visualization, T.S.; supervision, D.I.; project administration, D.I.; funding acquisition, D.I. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the European Union-NextGenerationEU through the National Recovery and Resilience Plan of the Republic of Bulgaria, project no. BGRRP-2.004-0009-C02, Research group 3.1.1., Natura4Health.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Mozaffarian D.; Hao T.; Rimm E.B.; Willett W.; Hu F.B. Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med*, **2011**, 364 (25): 2392–404.
2. Santillán E.; Bautista M.; Esquivel-Soto J.; Morales-González A.; Esquivel-Chirino C.; Durante-Montiel I.; Sánchez-Rivera G.; Valadez-Vega C.; Morales-González J.A. Inflammation, oxidative stress, and obesity. *Int J Mol Sci* **2011**, *12*, 3117–32.
3. Marseglia L.; Manti S.; D'Angelo G.; Nicotera A.; Parisi E.; Di Rosa G.; Gitto E.; Arrigo T. Oxidative stress in obesity: a critical component in human diseases. *Int J Mol Sci* **2014**, *16*, 378-400.
4. O'Neill S.; O'Driscoll L. Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obes Rev* **2015,** *16*, 1-12.
5. Bjornstad P.; Eckel R.H. Pathogenesis of lipid disorders in insulin resistance: a brief review. *Curr Diab Rep* **2018**, *18* (12):127. doi: 10.1007/s11892-018-1101-6.
6. Bae J.H.; Schwemmer M.; Lee I.K.; Lee H.J.; Park K.R.; Kim K.Y.; Bassenge E. Postprandial hypertriglyceridemia-induced endothelial dysfunction in healthy subjects is independent of lipid oxidation. *Int J Cardiol* **2003**, *87*, 259-67.
7. Gotto A.M. Jr.; Brinton E.A. Assessing low levels of high-density lipoprotein cholesterol as a risk factor in coronary heart disease: a working group report and update. *J Am Coll Cardiol* **2004**, *43*, 717–24.
8. Badimon L.; Vilahur G. Thrombosis formation on atherosclerotic lesions and plaque rupture. *J Intern Med*, **2014**, *276*, 618-32.
9. Beltran-Sanchez H.; Harhay M.O.; Harhay M.M.; McElligott S. Prevalence and trends of metabolic syndrome in the adult U.S. population, 1999–2010. *J Am Coll Cardiol* **2013**, *62*, 697–703.
10. Feingold K.R. Cholesterol Lowering Drugs. [Updated 2024 Feb 12]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK395573/.
11. Rauf A.; Akram M.; Anwar H.; Daniyal M.; Munir N.; Bawazeer S.; Bawazeer S.; Rebezov M.; Bouyahya A.; Shariati M.A.; Thiruvengadam M.; Sarsembenova O.; Mabkhot Y.N.; Islam M.N.; Emran T.B.; Hodak S.; Zengin G.; Khan H. Therapeutic potential of herbal medicine for the management of hyperlipidemia: latest updates. *Environ Sci Pollut Res Int* **2022**, *29*, 40281-301.
12. Walker K.Z.; O'Dea K.; Gomez, M.; Girgis, S.; Colagiuri R. Diet and exercise in the prevention of diabetes. *J Hum Nutr Diet* **2010,** *23*, 344–52.
13. Salas-Salvadó J.; Martinez-González M.Á.; Bulló M.; Ros E. The role of diet in the prevention of type 2 diabetes. *Nutr Metab Cardiovasc Dis* **2011**, *21*, 32–48.
14. Pérez-Martínez P.; Mikhailidis D.P.; Athyros V.G.; Bullo M.; Couture P.; Covas M.I.; de Koning L.; et al. Lifestyle recommendations for the prevention and management of metabolic syndrome: an international panel recommendation. *Nutr Rev* **2017**, *75*, 307-26.
15. Cicero, A.F.; Colletti, A. Role of phytochemicals in the management of metabolic syndrome. *Phytomedicine* **2016**, *23*, 1134-44.
16. Rochlani, Y.; Pothineni, N.V.; Kovelamudi, S.; Mehta, J.L. Metabolic syndrome:pathophysiology, management, and modulation by natural compounds. *Ther Adv Cardiovasc Dis* **2017**, *11*, 215–25.
17. Agostoni C.V.; Bresson J.L.; Fairweather-Tait S. Scientific opinion on dietary reference values for water. *EFSA J*, **2010**, 8 (3): 1459.
18. Roussel R.; Fezeu L.; Bouby N.; Balkau B.; Lantieri O.; Alhenc-Gelas F.; Marre M.; Bankir L; D.E.S.I.R. Low water intake and risk for new-onset hyperglycemia. *Diabetes Care* **2011**, *34*, 2551–4.
19. Carroll, H.A.; Betts, J.A.; Johnson, L. An investigation into the relationship between plain water intake and glycated Hb (HbA1c): A sex-stratified, cross-sectional analysis of the UK National Diet and Nutrition Survey(2008–2012). *Br J Nutr* **2016**, *116*, 1770–80.
20. Hu F.B. Resolved: there is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. *Obes Rev* **2013**, *14*, 606-19.
21. Dennis E.A.; Dengo A.L.; Comber D.L.; Flack K.D.; Savla J.; Davy K.P.; Davy B.M. Water consumption increases weight loss during a hypocaloric diet intervention in middle-aged and older adults. *Obesity* **2010**, *18*, 300-7.
22. Malik V.S.; Schulze M.B.; Hu F.B. Intake of sugar-sweetened beverages and weight gain: a systematic review. *Am J Clin Nutr*, **2006**, *84*, 274-88.
23. Tate D.F.; Turner-McGrievy G.; Lyons E.; Stevens J.; Erickson K.; Polzien K.; Diamond M.; Wang X.; Popkin B. Replacing caloric beverages with water or diet beverages for weight loss in adults: main results of the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. *Am J Clin Nutr* **2012**, *95*, 555-63.
24. Stookey J.D.; Constant F.; Gardner C.D.; Popkin B.M. Replacing sweetened caloric beverages with drinking water is associated with lower energy intake. *Obesity* **2007**, *15*, 3013–22.
25. Atlas S.A. The renin-angiotensin aldosterone system: pathophysiological role and pharmacologic inhibition. *J Manag Care Pharm* **2007**, *13*, 9-20.
26. Wagner C.A. Effect of mineralocorticoids on acid-base balance. *Nephron Physiol* **2014**, *128*, 26-34.
27. Baker S.B.; Worthley L.I. The essentials of calcium, magnesium and phosphate metabolism: part I. Physiology. *Crit Care Resusc* **2002**, *4*, 301-6.
28. Volpe S.L. Magnesium in disease prevention and overall health. *Adv Nutr* **2013**, *4*, 378–83.
29. Gommers L.M.; Hoenderop J.G.; Bindels R.J.; de Baaij J.H. Hypomagnesemia in Type 2 Diabetes: A Vicious Circle? *Diabetes* **2016**, *65*, 3-13.

30. Rasic-Milutinovic Z.; Perunicic-Pekovic G.; Jovanovic D.; Gluvic Z.; Cankovic-Kadijevic M. Association of blood pressure and metabolic syndrome components with magnesium levels in drinking water in some Serbian municipalities. *J Water Health* **2012**, *10*, 161-9.
31. Bohmer H.; Müller H.; Resch K.L. Calcium supplementation with calcium-rich mineral waters: a systematic review and meta-analysis of its bioavailability. *Osteoporos Int* **2000**, *11*, 938-43.
32. Vitoria I.; Maraver F.; Ferreira-Pêgo C.; Armijo F.; Moreno Aznar L.; Salas-Salvadó J. The calcium concentration of public drinking waters and bottled mineral waters in Spain and its contribution to satisfying nutritional needs. *Nutr Hosp* **2014**, *30*, 188-99.
33. Burckhardt P. Calcium revisited, part III: effect of dietary calcium on BMD and fracture risk. *Bonekey Rep* **2015** *4*:708. doi: 10.1038/bonekey.2015.77.
34. Capurso A.; Solfrizzi V.; Panza F.; Mastroianni F.; Torres F.; Del Parigi A.; et al. Increased bile acid excretion and reduction of serum cholesterol after crenotherapy with salt-rich mineral water. *Aging* **1999**, *11*, 273-6.
35. Pérez-Granados A.M.; Navas-Carretero S.; Schoppen S.; Vaquero M.P. Reduction in cardiovascular risk by sodium-bicarbonated mineral water in moderately hypercholesterolemic young adults. *J Nutr Biochem* **2010**, *21*, 948-53.
36. Toxqui L.; Vaquero M.P. An intervention with mineral water decreases cardiometabolic risk biomarkers. a crossover, randomised, controlled trial with two mineral waters in moderately hypercholesterolaemic adults. *Nutrients* **2016a**, *8*, 400. doi: 10.3390/nu8070400.
37. Aslanabadi N.; Habibi Asl. B.; Bakhshalizadeh B.; Ghaderi F.; Nemati M. Hypolipidemic activity of a natural mineral water rich in calcium, magnesium, and bicarbonate in hyperlipidemic adults. *Adv Pharm Bull* **2014,** *4*, 303-7.
38. Zair Y.; Kasbi-Chadli F.; Housez B.; Pichelin M.; Cazaubiel M.; Raoux F.; Ouguerram K. Effect of a high bicarbonate mineral water on fasting and postprandial lipemia in moderately hypercholesterolemic subjects: a pilot study. *Lipids Health Dis* **2013**, *12*, 105. doi: 10.1186/1476-511X-12-105.
39. Nerbrand C.; Agréus L.; Lenner R.A.; Nyberg P.; Svärdsudd K. The influence of calcium and magnesium in drinking water and diet on cardiovascular risk factors in individuals living in hard and soft water areas with differences in cardiovascular mortality. *BMC Public Health* **2003**, *3*, 21. doi: 10.1186/1471-2458-3-21.
40. Quattrini S.; Pampaloni B.; Brandi M.L. Natural mineral waters: chemical characteristics and health effects. *Clin Cases Miner Bone Metab* **2016**, *13*, 173–80.
41. Teegarden D.; White K.M.; Lyle R.M.; Zemel M.B.; Van Loan M.D.; Matkovic V.; Craig B.A.; Schoeller D.A. Calcium and dairy product modulation of lipid utilization and energy expenditure. *Obesity* **2008**, *16*, 1566–72.
42. Major G.C.; Alarie F.P.; Doré J.; Tremblay A. Calcium plus vitamin D supplementation and fat mass loss in female very low-calcium consumers: Potential link with calcium-specific appetite control. *Br J Nutr* **2009**, *101*, 659–63.
43. Wasserfurth P.; Schneider I.; Ströhle A.; Nebl J.; Bitterlich N.; Hahn A. Effects of mineral waters on acid-base status in healthy adults: results of a randomized trial. *Food Nutr Res* **2019**, *63*. doi: 10.29219/fnr.v63.3515.
44. Casado Á.; Ramos P.; Rodríguez J.; Moreno N.; Gil P. Types and characteristics of drinking water for hydration in the elderly. *Crit Rev Food Sci Nutr*, **2015**, *55*, 1633–41.
45. De Giglio O.; Quaranta A.; Lovero G.; Caggiano G.; Montagna M.T. Mineral water or tap water? An endless debate. *Ann Ig* **2015** *27*, 58-65.
46. Petraccia L.; Liberati G.; Masciullo S.G.; Grassi M.; Fraioli A. Water, mineral waters and health. *Clin Nutr* **2006,** *25*, 377–85.
47. Bacciottini L.; Tanini A.; Falchetti A.; Masi L.; Franceschelli F.; Pampaloni B.; Giorgi G.; Brandi M.L. Calcium bioavailability from a calcium-rich mineral water, with someobservations on method. *J Clin Gastroenterol* **2004**, *38*, 761–6.
48. Greupner T.; Schneider I.; Hahn A. Calcium bioavailability from mineral waters with different mineralization in comparison to milk and a supplement. *J Am Coll Nutr* **2017**, *36*, 386–90.
49. Sabatier M.; Grandvuillemin A.; Kastenmayer P.; Aeschliman J.M.; Bouisset F.; Arnaud M.J.; et al. Influence of the consumption pattern of magnesium from magnesium-rich mineral water on magnesium bioavailability. *Br J Nutr*, **2011**, *106*, 331–4.
50. Galan P.; Arnaud M.J.; Czernichow S.; Delabroise A.M.; Preziosi P.; Bertrais S.; et al. Contribution of mineral waters to dietary calcium and magnesium intake in a French adult population. *J Am Diet Assoc* **2002**, 102, 1658-62.
51. Sheu M.J.; Chou P.Y.; Lin W.H.; Pan C.H.; Chien Y.C.; Chung Y.L.; Liu F.C.; Wu C.H. Deep sea water modulates blood pressure and exhibits hypolipidemic effects via the AMPK-ACC pathway: an in vivo study. *Mar Drugs* **2013** *11*, 2183-202.
52. Katsuda S.; Yasukawa T.; Nakagawa K.; Miyake M.; Yamasaki M.; Katahira K.; et al. Deep-sea water improves cardiovascular hemodynamics in Kurosawa and Kusanagi-Hypercholesterolemic (KHC) rabbits. *Biol Pharm Bull*, **2008**, *31*, 38-44.
53. Schoppen S.; Sánchez-Muniz F.J.; Pérez-Granados M.; Gómez-Gerique J.A.; Sarriá B.; Navas-Carretero S.; Pilar Vaquero M. Does bicarbonated mineral water rich in sodium change insulin sensitivity of postmenopausal women? *Nutr Hosp* **2007**, *22*, 538-44.
54. Schoppen S.; Pérez-Granados A.M.; Carbajal A.; Sarriá B.; Sánchez-Muniz F.J.; Gómez-Gerique J.A.; Pilar Vaquero M. Sodium bicarbonated mineral water decreases postprandial lipaemia in postmenopausal women compared to a low mineral water. *Br J Nutr* **2005**, *94*, 582-7.
55. Toxqui L, Pérez-Granados AM, Blanco-Rojo R, Vaquero MP. A sodium-bicarbonated mineral water reduces gallbladder emptying and postprandial lipaemia: a randomised four-way crossover study. Eur J Nutr. 2012 Aug;*51*:607-14.
56. Toxqui, L., Vaquero, M.P. Aldosterone changes after consumption of a sodium-bicarbonated mineral water in humans. A four-way randomized controlled trial. *J Physiol Biochem* **2016b**. 72, 635–41.

57. Bastos P.; Araújo J.R.; Azevedo I.; Martins M.J.; Ribeiro L. Effect of a natural mineral-rich water on catechol-O-methyltransferase function. *Magnes Res* **2014**, *27*, 131-41.
58. Jiang L.; He P.; Chen J.; Liu Y.; Liu D.; Qin G.; Tan N. Magnesium levels in drinking water and coronary heart disease mortality risk: A Meta-Analysis. *Nutrients* **2016**, 8, 5. doi: 10.3390/nu8010005.
59. Benedetti S.; Pagliari S.; Benvenuti F.; Marini D.; Galli T.; F. Oliva et al. Antioxidative effects of sulphurous water from Macerata Feltria Thermal resort in patients with osteoarthritis. *Progress in Nutrition* **2007**, *9*, 46-52.
60. Benedetti S.; Benvenuti F.; Nappi G.; Fortunati N.A.; Marino L.; Aureli T.; et al. Antioxidative effects of sulfurous mineral water: protection against lipid and protein oxidation. *Eur J Clin Nutr* **2009**, *63*, 106-12.
61. Benedetti, S.; Canino C.; Tonti G.; Medda V.; Calcaterra P.; Nappi G.; Salaffi F.; Canestrari F. Biomarkers of oxidation, inflammation and cartilage degradation in osteoarthritis patients undergoing sulfur-based spa therapies. *Clin Biochem* **2010**, *43*, 973-8.
62. Carbajo J.M.; Maraver F. Sulphurous mineral waters: new applications for health. *Evid Based Complement Alternat Med* **2017**;2017:8034084. doi: 10.1155/2017/8034084.
63. Sokrateva T.D.; Roussev B.H.; Nashar M.A.; Kiselova-Kaneva Y.D.; Mihaylova G.M.; Todorova M.N.; et al. Effects of sulphur-containing mineral water intake on oxidative status and markers for inflammation in healthy subjects. *Arch Physiol Biochem* **2021,** *127*, 327-36.
64. Roussev B.H.; Sokrateva T.D.; Nashar M.A.; Radanova M.; Komosinska-Vassev K.; Olczyk P. Effect of sulfur-containing mineral water on renal function. *C R Acad Bulg Sci* **2019**, 72, 1577-84.
65. Sokrateva T.D.; Nashar M.A.; Salim A.S.; Tatyana V.; Ivanova D.I. Health effects of sulfurous mineral water may vary depending on lifestyle. *J of IMAB* **2019b,** *25*, 2828-37.
66. Sokrateva T.D. Research on the molecular mechanisms of sulfur-containing mineral waters from the Varna Basin on human metabolism in regards to their usage as a drinking remedy. PhD Thesis, Medical University – Varna, Varna, Date of defense 17.02.2020. Bulgarian, Pages 174.
67. Farnetti S.; Capristo E.; Gasbarrini G. Decrease in extra-cellular water compartment in overweight women after administration of oligomineral water associated to a hypocaloric diet regimen. *Minerva Gastroenterol Dietol* **2004**, *50*, 277-82.
68. Costa-Vieira D.; Monteiro R.; Martins M.J. Metabolic syndrome features: is there a modulation role by mineral water consumption? A Review. *Nutrients* **2019,** *11*:1141. doi: 10.3390/nu11051141.
69. Заболотная И.Б. Перспективы применения природных и преформированных лечебных факторов в терапии больных неалкогольной жировой болезнью печени. *Вопросы курортологии, физиотерапии и лечебной физической культуры* **2016**, 4, doi: 10.17116/kurort2016442-48.
70. Чалая Е.Н.; Ботвинева Л.А.; Цаллагова Л.В.; Ахкубекова Н.К.; Ефименко Н.В.; Кайсинова А.С.; Амиянц, В.Ю.; Васин В.А. Санаторно-курортное лечение метаболического синдрома при различной продолжительности лечебного цикла по результатам отдаленных наблюдений. *Вопросы курортологии, физиотерапии и лечебной физической культуры* **2017**, *3*, doi.org/10.17116/kurort201794327-31.
71. Mansouri K.; Greupner T.; Hahn A. Blood pressure stability and plasma aldosterone reduction: the effects of a sodium and bicarbonate-rich water - a randomized controlled intervention study. *Blood Press* **2024,** *33*: 2291411. doi: 10.1080/08037051.2023.2291411.
72. Murakami S.; Goto Y.; Ito K.; Hayasaka S.; Kurihara S.; Soga T.; Tomita M.; Fukuda S. The consumption of bicarbonate-rich mineral water improves glycemic control. *Evid Based Complement Alternat Med*, **2015**:824395. doi: 10.1155/2015/824395.
73. Schoppen S.; Pérez-Granados A.M.; Carbajal A.; Oubiña P.; Sánchez-Muniz F.J.; Gómez-Gerique J.A.; Vaquero M.P. A sodium-rich carbonated mineral water reduces cardiovascular risk in postmenopausal women. *J Nutr* **2004** *134*:1058-63. doi: 10.1093/jn/134.5.1058.
74. Schorr U.; Distler A.; Sharma A.M. Effect of sodium chloride- and sodium bicarbonate-rich mineral water on blood pressure and metabolic parameters in elderly normotensive individuals: a randomized double-blind crossover trial. *J Hypertens* **1996**, 14, 131-5.
75. Schoppen S.; Pérez-Granados A.M.; Carbajal A.; Sarriá B.; Navas-Carretero S.; Pilar Vaquero M. Sodium-bicarbonated mineral water decreases aldosterone levels without affecting urinary excretion of bone minerals. *Int J Food Sci Nutr* **2008**, *59*, 347-55. doi: 10.1080/09637480701560308.
76. Балакин С. А.; Разумов А. Н.; Михайленко Л. В.; Юсупова Р. М.; Гильмутдинова Л. Т.; Кудаярова Р. Р.; Янтурина Н. Х. Питьевые минеральные воды в комплексной терапии метаболических нарушений при мягкой артериальной гипертонии. *Медицинский вестник Башкортостана* **2010**, *3*. URL: https://cyberleninka.ru/article/n/pitievye-mineralnye-vody-v-kompleksnoy-terapii-metabolicheskih-narusheniy-pri-myagkoy-arterialnoy-gipertonii (дата обращения: 19.04.2024).
77. Dragomiretska N.; Zabolotna I.; Gushcha S.; Sierpińska L.; Izha G.; Plakida A.; Bezverhnyuk T. The advantages of drinking mineral water in the rehabilitation of patients with viral hepatitis C with accompanying non-alcoholic fatty liver disease after suffering from COVID-19. *Ann Agric Environ Med* **2023**, *30*, 266-72.
78. Rylander R.; Arnaud M.J. Mineral water intake reduces blood pressure among subjects with low urinary magnesium and calcium levels. *BMC Public Health* **2004**, *30*, *4*:56. doi: 10.1186/1471-2458-4-56.
79. Jovicic N.; Andjic M.; Novakovic J.; Jeremic N.; Zivkovic V.; Srejovic I.; et al. The effects of low mineral content water on microbiota, metabolic, and oxidative stress parameters in patients with type 2 diabetes mellitus. *Heliyon* **2023,** *26*, 9:e18725. doi: 10.1016/j.heliyon.2023.e18725.
80. Pappan N.; Rehman A. Dyslipidemia. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560891/.

81. Rochlani Y.; Pothineni N.V.; Kovelamudi S.; Mehta J.L. Metabolic syndrome: pathophysiology, management, and modulation by natural compounds. *Ther Adv Cardiovasc Dis* **2017**, *11*, 215-25.
82. Pereira C.D.; Severo M.; Araújo J.R.; Guimarães J.T.; Pestana D.; Santos A.; et al. Relevance of a hypersaline sodium-rich naturally sparkling mineral water to the protection against Metabolic Syndrome induction in fructose-fed Sprague-Dawley rats: a biochemical, metabolic and redox approach. *Int J Endocrinol* **2014**;2014:384583.
83. Gushcha S.; Nasibullin B.; Plakida A.; Volyanska V.; Balashova I.; Mohylevska T. Metabolic syndrome: the corrective effect of mineral water with an increased content of organic substances. *American Journal of Chemistry and Materials Science*, **2018** 5, 85-90.
84. arciso L.; Martinelli A.; Torriani F.; Frassanito P.; Bernardini R.; Chiarotti F.; Marianelli C. Natural mineral waters, and metabolic syndrome: insights from obese male and female C57BL/6 mice on caloric restriction. *Front Nutr* **2022**, 24;9:886078. doi: 10.3389/fnut.2022.886078.
85. Albertini M.; Dachà M.; Teodori L.; Conti M. Drinking mineral waters:biochemical effects and health implications – the state-of-the-art. *IJEHR*, **2007**, *1*, 153-69.
86. Aloulou A.; Carriere F. Gastric lipase: an extremophilic interfacial enzyme with medical applications. *Cell Mol Life Sci* **2008**, *65*, 851–54.
87. Embleton J.K.; Pouton C.W. Structure and function of gastro-intestinal lipases. *Adv Drug Deliv Rev* **1997**, *25*, 15–32.
88. Bentley-Lewis R.; Adler G.K.; Perlstein T.; Seely E.W.; Hopkins P.N.; Williams G.H.; Garg R. Body mass index predicts aldosterone production in normotensive adults on a high-salt diet. *J Clin Endocrinol Metab* **2007,** *92*, 4472-5. doi: 10.1210/jc.2007-1088.
89. Talukder M.R.; Rutherford S.; Huang C.; Phung D.;.Islam M.Z.; Chu C. Drinking water salinity and risk of hypertension: A systematic review and meta-analysis. *Arch Environ Occup Health* **2017** *4*, 72, 126-38.
90. Mutchler S.M.; Kirabo A.; Kleyman T.R. Epithelial sodium channel and salt-sensitive hypertension. *Hypertension*. **2021**, *77*, 759–67.
91. Adrogué H.J.; Madias N.E. The impact of sodium and potassium on hypertension risk. *Semin Nephrol* **2014**, *34*, 257–72.
92. Nerbrand C.; Agreus L.; Lenner R.A.; Nyberg P.; Svardsudd K. The influence of calcium and magnesium in drinking water and diet on cardiovascular risk factors in individuals living in hard and soft water areas with differences in cardiovascular mortality. *BMC Public Health* **2003**, *3*:21. doi: 10.1186/1471-2458-3-21.
93. Petraccia L.; Liberati G.; Masciullo S.G.; Grassi M.; Fraioli A. Water, mineral waters and health. *Clin Nutr* **2006**, *25*, 377-85.
94. Liu F.; Zhang R.; Zhang W.; Zhu L.; Yu Q.; Liu Z.; Zhang Y.; et al. Potassium supplementation blunts the effects of high salt intake on serum retinol-binding protein 4 levels in healthy individuals. *J Diabetes Investig* **2021,** *12*, 658-63.
95. Rylander R. Drinking water constituents and disease. *J Nutr* **2008** *138*, 423-25.
96. Ziomber A.; Machnik A.; Dahlmann A.; Dietsch P.; Beck F.X.; Wagner H.; et al. Sodium-, potassium-, chloride-, and bicarbonate-related effects on blood pressure and electrolyte homeostasis in deoxycorticosterone acetate-treated rats. *Am J Physiol Renal Physiol* **2008**, *295*, 1752–63.
97. Lalovic D.; Jakovljevic V.; Radoman K.; Bradic J.; Jeremic N.; Vranic A.; et al. The impact of low mineral content water on cardiac function in diabetic rats: focus on oxidative stress. *Mol Cell Biochem* **2020**, *472*, 135-144.
98. Johnson E.C.; Bardis C.N.; Jansen L.T.; Adams J.D.; Kirkland T.W.; Kavouras S.A. Reduced water intake deteriorates glucose regulation in patients with type 2 diabetes. *Nutr Res* **2017**, *43*, 25-32.
99. Bankir L.; Bardoux P.; Ahloulay M. Vasopressin and diabetes mellitus. *Nephron* **2001**, *87*, 8-18.
100. Enhorning S.; Wang T.J.; Nilsson P.M.; Almgren P.; Hedblad B.; Berglund G.; et al. Plasma copeptin and the risk of diabetes mellitus. *Circulation* **2010** *121*, 2102–08.
101. Lemetais, G.; Melander, O.; Vecchio, M.; Bottin J.H.; Enhörning S.; Perrier E.T. Effect of increased water intake on plasma copeptin in healthy adults. *Eur J Nutr* **2018**, *57*, 1883–90.
102. Underwood P.C.; Adler G.K. The renin angiotensin aldosterone system and insulin resistance in humans. *Curr Hypertens Rep* **2013,** *15*, 59-70.
103. Wada T.; Ohshima S.; Fujisawa E.; Koya D.; Tsuneki H.] Sasaoka T. Aldosterone inhibits insulin-induced glucose uptake by degradation of insulin receptor substrate (IRS) 1 and IRS2 via a reactive oxygen species–mediated pathway in 3T3-L1 adipocytes. *Endocrinology* **2009**, *150*, 1662–9.
104. Lastra G.; Habibi J.; Whaley-Connell A.T.; Manrique C.; Hayden M.R.; Rehmer J, et al. Direct renin inhibition improves systemic insulin resistance and skeletal muscle glucose transport in a transgenic rodent model of tissue renin overexpression. *Endocrinology* **2009**, *150*, 2561–8.
105. Almeida C.; Araújo J.R.; Monteiro R.; Severo M.; Guimarães J.T.; Azevedo I.; Martins M.J. Chronic ingestion of a hypersaline sodium-rich carbonated natural mineral water on an animal model of the metabolic syndrome – effects on blood pressure and plasma metabolic profile. *Press Therm Climat* **2010**, *147*, 110–11.
106. Pereira C.D.; Monteiro R.; Constancia M.; Martins M.J. 11b-hydroxysteroid dehydrogenases in the regulation of tissue glucocorticoid availability. In: Steroids—From Physiology to Clinical Medicine. Rijeka, Croatia: InTech **2012**a, 83-106.
107. Pereira C.D.; Severo M.; Neves D.; Ascensão A.; Magalhães J.; Guimarães J.T.; et al. Natural mineral-rich water ingestion improves hepatic and fat glucocorticoid signaling and increases sirtuin 1 in an animal model of metabolic syndrome. *Horm Mol Biol Clin Investig* **2015**, *21*, 149-57.
108. Rose A.J.; Herzig S. Metabolic control through glucocorticoid hormones: an update. *Mol Cell Endocrinol* **2013**, *380*, 65-78.

109. Pereira C.D.; Araújo J.; Pestana D.; Rosário M.; Severo M.; Martins M.J. Protection of the hepatic redox status by chronic ingestion of a hypersaline sodium-rich carbonated Portuguese natural mineral water in an animal model of the metabolic syndrome. *Rev Port Cirur* **2012**b, 56.
110. Pereira C.D.; Passos E.; Severo M.; Vitó I.; Wen X.; Carneiro F.; et al. Ingestion of natural mineral-rich water in an animal model of metabolic syndrome: effects in insulin signaling and endoplasmic reticulum stress. *Horm Mol Biol Clin Investig* **2016,** *26*, 135-50.
111. Manna P.; Jain S.K. Obesity, oxidative stress, adipose tissue dysfunction, and the associated health risks: causes and therapeutic strategies. *Metab Syndr Relat Disord*, **2015**, *13*, 423-44.
112. Costantino M.; Izzo V.; Conti V.; Manzo V.; Guida A.; Filippelli A. Sulphate mineral waters: A medical resource in several disorders. *J Tradit Complement Med*, **2019**, 22, 320-26.
113. Karagülle M.Z.; Karagülle M. Effects of drinking natural hydrogen sulfide (H2S) waters: a systematic review of in vivo animal studies. *Int J Biometeorol*, **2020**, 64, 1011-22.
114. Sokrateva T.; Tasinov O.; Stoeva S.; Ivanova D.; Nazifova-Tasinova N.; Nashar M. Sulfur containing mineral water as a dietary factor challenging the phase II detoxification enzymes in human intestinal cells. *J of IMAB*, **2022**, *28*, 4541-47.
115. Costantino M.; Conti V.; Corbi G.; Filippelli A. Hydropinotherapy with sulphurous mineral water as complementary treatment to improve glucose metabolism, oxidative status, and quality of life. *Antioxidants* **2021**, 10 (11):1773. doi: 10.3390/antiox10111773.
116. Costantino M.; Giampaolo C.; Filippelli A. Effetti della creno-terapia idropinica sullo stress ossidativo [Effects of drinking spa therapy on oxidative stress]. *Clin Ter* **2012**;163(1):e13-7. Italian.
117. Huang A.; Seité S.; Adar T. The use of balneotherapy in dermatology. *Clin Dermatol* **2018**, 36, 363-68.
118. Matz H.; Orion E.; Wolf R. Balneotherapy in dermatology. *Dermatol Ther* **2003**, *16*, 132-40.
119. Costantino M.; Marongiu M.G.; Iannotti S.; Filippelli A. Sulphurous mud-balneotherapy: an possible strategy for the plaque psoriasis. *PARIPEX – Indian J Res* **2015**, 4, 69-74.
120. Ekmekcioglu C.; Strauss-Blasche G.; Holzer F.; Marktl W. Effect of sulfur baths on antioxidative defense systems, peroxide concentrations and lipid levels in patients with degenerative osteoarthritis. *Forsch Komplementarmed Klass Naturheilkd* **2002**, *9*, 216-20.
121. Karagülle M.Z.; Tütüncü Z.N.; Aslan O.; Basak E.; Mutlu A. Effects of thermal sulphur bath cure on adjuvant arthritic rats. *Phys Rehab Kur Med* **1996**, *6*, 53-7.
122. Kovács C.; Pecze M.; Tihanyi Á.; Kovács L.; Balogh S.; Bender T. The effect of sulphurous water in patients with osteoarthritis of hand. Double-blind, randomized, controlled follow-up study. *Clin Rheumatol* **2012**, *31*, 1437-42.
123. Korolev Y.N.; Nikulina L.A.; Mikhailik L.V. The use of drinking mineral water and low-intensity electromagnetic radiation at an early stage of metabolic syndrome development (experimental study)]. *Vopr Kurortol Fizioter Lech Fiz Kult* **2022**, *99*, 54-9. Russian.
124. Costantino M.; Giuberti G.; Caraglia M.; Lombardi A.; Misso G.; Abbruzzese A.; Ciani F.; Lampa E. Possible antioxidant role of SPA therapy with chlorine-sulphur-bicarbonate mineral water. *Amino Acids* **2009**, *36*, 161-5.
125. Costa-Vieira D.; Monteiro R.; Martins M.J. Metabolic syndrome features: is there a modulation role by mineral water consumption? A Review. *Nutrients* **2019**, *11*, 1141. doi: 10.3390/nu11051141.