Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 2026

Effects of an 8-Week Aquatic Training Program and Red Grape Juice Supplementation on Gut Permeability, Inflammatory Markers, and Neuromuscular Performance in Female Patients with Multiple Sclerosis

Protocol summary

Study aim

To investigate the effect of 8 weeks of aquatic exercise and red grape juice supplementation on intestinal permeability, inflammation, and neuromuscular function in women with Multiple Sclerosis.

Design

Randomized, controlled, parallel-group, double-blind clinical trial (blinding of participants to the beverage, and blinding of assessors and analysts), Sample size: 70 (5 groups of 14). Simple randomization using a random number generator software, with allocation concealment via coded bottles.

Settings and conduct

Exercise in an indoor pool (26-28°C). Blood sampling 48h before/after intervention, after 12h fasting. Measurements: inflammation (IL-2, IL-10, TNF-alpha) and cortisol by ELISA; intestinal permeability (LPS, zonulin) and stool SCFAs by GC; neuromuscular function by EMG-NCV, dynamometer, and balance platform. All measurements by blinded assessors.

Participants/Inclusion and exclusion criteria

Inclusion: Women with RRMS; confirmed 2017 McDonald criteria; EDSS 1-4.5; aquatic exercise capability; no recent relapse; no severe cardiac, metabolic, or GI disease; no antioxidants/regular exercise in 3 months; no grape allergy; signed consent. Exclusion: Relapse during study; medication change; non-cooperation; severe systemic disease; new antioxidant use; exercise outside protocol; smoking.

Intervention groups

Five parallel groups (n=14): 1) Aquatic exercise + grape juice, 2) Aquatic exercise + placebo, 3) Supplement only, 4) Placebo only, 5) Control. Exercise: 8 weeks, 3 sessions/week, 60 min at 50-70% HRmax. Supplement: 250 ml grape juice or placebo, 3 times/week.

Main outcome variables

Intestinal permeability: LPS, zonulin. Systemic inflammation: IL-2, IL-10, TNF-alpha, cortisol. Stool short-chain fatty acids: acetate, propionate, butyrate. Neuromuscular function: nerve conduction velocity (EMG-NCV), muscle strength (dynamometer), balance (Stability Platform).

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20211020052826N2**
Registration date: **2026-10-07, 1405/07/15**
Registration timing: **prospective**

Last update: **2026-10-07, 1405/07/15**
Update count: **0**

Registration date

2026-10-07, 1405/07/15

Registrant information

Name
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Name of organization / entity
Razi University of Kermanshah
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Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-11-05, 1405/08/14

Expected recruitment end date

2026-12-05, 1405/09/14

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Effects of an 8-Week Aquatic Training Program and Red Grape Juice Supplementation on Gut Permeability, Inflammatory Markers, and Neuromuscular Performance in Female Patients with Multiple Sclerosis

Public title

Effect of Aquatic Exercise and Red Grape Juice Supplementation on Intestinal Permeability, Inflammation, and Neuromuscular Function in Women with Multiple Sclerosis

Purpose

Supportive

Inclusion/Exclusion criteria

Inclusion criteria:

Women with Relapsing-Remitting Multiple Sclerosis (RRMS). Definitive diagnosis based on the 2017 revised McDonald criteria confirmed by a neurologist. Expanded Disability Status Scale (EDSS) score between 1 and 4.5. Ability to perform physical activity in water. No relapse in recent months. No severe cardiovascular, metabolic, or gastrointestinal diseases. No use of antioxidant supplements or regular exercise programs in the past three months. No known allergy to grape products. Willingness to participate and sign the written informed consent form.

Exclusion criteria:

Relapse of the disease during the study. Any medication change during the study. Unwillingness to continue cooperation at any stage of the research. Having severe metabolic, cardiovascular, or gastrointestinal diseases. Consumption of new antioxidant supplements during the study. Performing exercise outside the study protocol. Smoking.

Age

From **20 years** old to **40 years** old

Gender

Female

Phase

N/A

Groups that have been masked

- Participant
- Investigator
- Outcome assessor
- Data analyser

Sample size

Target sample size: **70**

Randomization (investigator's opinion)

Randomized

Randomization description

Simple randomization was performed using a computer-generated random number sequence. Participants were allocated into five groups of 14. For allocation concealment, coded bottles were used, and only one person outside the data collection and analysis process had access to the allocation codes.

Blinding (investigator's opinion)

Double blinded

Blinding description

In this study, blinding for the nutritional intervention (red grape juice supplement vs. placebo) has been fully implemented. Since there is no 'exercise-alone' group among the exercise groups, and both exercise groups receive a beverage (one supplement and one placebo), participants cannot distinguish whether their beverage is active or not. The supplement and placebo are completely identical in color, taste, volume, and packaging. Furthermore, outcome assessors and data analysts are blinded to the group allocation of the participants. Given the nature of the exercise intervention, blinding to 'performing exercise' is not feasible; however, this limitation has been compensated for by the precise blinding of assessors and analysts.

Placebo

Used

Assignment

Parallel

Other design features

Randomized parallel-group double-blind clinical trial (blinding of participants to the type of beverage, and blinding of outcome assessors and data analysts), with five intervention and control groups.

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research Ethics Committee (Sport Sciences Research Institute)

Street address

No. 3, 5th Alley, Mir Emad St., Ostad Motahari St., Tehran, Iran

City

Tehran

Province

Tehran

Postal code

1587653111

Approval date

2026-09-01, 1405/06/10

Ethics committee reference number

IR.SSRC.REC.1405.096

Health conditions studied

1

Description of health condition studied

Relapsing-Remitting Multiple Sclerosis (RRMS)

ICD-10 code
G35
ICD-10 code description
Multiple sclerosis

Primary outcomes

1

Description
Lipopolysaccharide (LPS) level
Timepoint
All outcome variables are measured at two time points:Pre-test: 48 hours before the first intervention session Post-test: 48 hours after the last intervention session Blood sampling is performed after a 12-hour fast, between 8:00 and 9:00 AM.
Method of measurement
Measurement by ELISA method

2

Description
Zonulin level
Timepoint
All outcome variables are measured at two time points:Pre-test: 48 hours before the first intervention session Post-test: 48 hours after the last intervention session Blood sampling is performed after a 12-hour fast, between 8:00 and 9:00 AM.
Method of measurement
Measurement by ELISA method

3

Description
Interleukin-2 (IL-2) level
Timepoint
All outcome variables are measured at two time points:Pre-test: 48 hours before the first intervention session Post-test: 48 hours after the last intervention session Blood sampling is performed after a 12-hour fast, between 8:00 and 9:00 AM.
Method of measurement
Measurement by ELISA method

4

Description
Interleukin-10 (IL-10) level
Timepoint
All outcome variables are measured at two time points:Pre-test: 48 hours before the first intervention session Post-test: 48 hours after the last intervention session Blood sampling is performed after a 12-hour fast, between 8:00 and 9:00 AM.
Method of measurement
Measurement by ELISA method

5

Description
Tumor Necrosis Factor-alpha (TNF-α) level
Timepoint
All outcome variables are measured at two time points:Pre-test: 48 hours before the first intervention session Post-test: 48 hours after the last intervention session Blood sampling is performed after a 12-hour fast, between 8:00 and 9:00 AM.
Method of measurement
Measurement by ELISA method

6

Description
Cortisol level
Timepoint
All outcome variables are measured at two time points:Pre-test: 48 hours before the first intervention session Post-test: 48 hours after the last intervention session Blood sampling is performed after a 12-hour fast, between 8:00 and 9:00 AM.
Method of measurement
Measurement by ELISA method

7

Description
Stool acetate level
Timepoint
All outcome variables are measured at two time points:Pre-test: 48 hours before the first intervention session Post-test: 48 hours after the last intervention session Blood sampling is performed after a 12-hour fast, between 8:00 and 9:00 AM.
Method of measurement
Measurement by Gas Chromatography (GC) method

8

Description
Stool propionate level
Timepoint
All outcome variables are measured at two time points:Pre-test: 48 hours before the first intervention session Post-test: 48 hours after the last intervention session Blood sampling is performed after a 12-hour fast, between 8:00 and 9:00 AM.
Method of measurement
Measurement by Gas Chromatography (GC) method

9

Description
Stool butyrate level
Timepoint
All outcome variables are measured at two time points:Pre-test: 48 hours before the first intervention session Post-test: 48 hours after the last intervention session Blood sampling is performed after a 12-hour fast, between 8:00 and 9:00 AM.
Method of measurement
Measurement by Gas Chromatography (GC) method

10

Description
Nerve Conduction Velocity (EMG-NCV)
Timepoint
Neuromuscular assessments including nerve conduction velocity (EMG-NCV), are performed at two time points: pre-test (48 hours before the first intervention session) and post-test (48 hours after the last intervention session). These assessments do not require fasting and are performed during standard daytime hours.
Method of measurement
Electromyography and Nerve Conduction Velocity (EMG-NCV)

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Description
Muscle strength
Timepoint
Neuromuscular assessments including muscle strength (dynamometer), are performed at two time points: pre-test (48 hours before the first intervention session) and post-test (48 hours after the last intervention session). These assessments do not require fasting and are performed during standard daytime hours.
Method of measurement
Dynamometer

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Description
Balance
Timepoint
Neuromuscular assessments including balance (Stability Platform) are performed at two time points: pre-test (48 hours before the first intervention session) and post-test (48 hours after the last intervention session). These assessments do not require fasting and are performed during standard daytime hours.
Method of measurement
Stability Platform

Secondary outcomes

empty

Intervention groups

1

Description
Intervention group: Aquatic Exercise + Red Grape Juice Supplement
Category
Rehabilitation

2

Description
Intervention group: Aquatic Exercise + Placebo
Category
Rehabilitation

3

Description
Intervention group: Red Grape Juice Supplement without Exercise
Category
Treatment - Other

4

Description
Intervention group: Placebo without Exercise
Category
Placebo

5

Description
Control group: Control Group (No Intervention)
Category
N/A

Recruitment centers

1

Recruitment center
Name of recruitment center
Shohada Ashayer Hospital, Khorramabad (Neurology Department)
Full name of responsible person
Nahid Hosseini Nezhad
Street address
Shohada Ashayer Teaching Hospital, Shahid Shiroudi St., Khorramabad, Lorestan, Iran
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Lorestan University
Full name of responsible person
Vahid Valipour Dehno
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Lorestan University, Kamalvand, 5th Km of Tehran-Khorramabad Road, Khorramabad, Lorestan, Iran
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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
No

Title of funding source
Personal Funds (PhD Thesis)

Proportion provided by this source
100

Public or private sector
Private

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Persons

Person responsible for general inquiries

Contact

Name of organization / entity
Lorestan University

Full name of responsible person
Amin Jalili Sarqaleh

Position
PhD Student

Latest degree
Ph.D.

Other areas of specialty/work
Physiology

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Latest degree
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
No - There is not a plan to make this available

Justification/reason for indecision/not sharing IPD
Public sharing of Individual Participant Data (IPD) is not planned for this study. This decision is made to ensure the confidentiality of participants' personal information and to fully comply with the ethical principles outlined in the informed consent forms. The raw data will be used solely for the statistical analyses of this research and will remain accessible only to the research team.

Study Protocol
No - There is not a plan to make this available

Statistical Analysis Plan
No - There is not a plan to make this available

Informed Consent Form
No - There is not a plan to make this available

Clinical Study Report

No - There is not a plan to make this available

Analytic Code

No - There is not a plan to make this available

Data Dictionary

No - There is not a plan to make this available