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Acute Effects of *Sideritis scardica* (SidTea+) Supplementation on Time to Exhaustion During High-Intensity Running in Active Adults: An Exploratory Randomized, Double-Blind, Placebo-Controlled Crossover Trial

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Abstract

Background: *Sideritis scardica* is a medicinal plant rich in flavonoids and phenylethanoid glycosides with reported antioxidant, anti-inflammatory, and vasodilatory properties. Although chronic supplementation has been associated with improvements in cardiovascular and redox-related outcomes, its acute effects on exercise performance remain largely unexplored. Therefore, the aim of the present study was to investigate the effects of an acute 950 mg dose of *Sideritis scardica* extract (SidTea+) on time to exhaustion during high-intensity running performance in healthy, physically active individuals. **Methods**: Ten physically active adults (2 men, 8 women; age 21.4 ± 2.2 years; $\dot{V}O_2$max 44.2 ± 5.1 mL·kg^{-1}·min^{-1}) completed two experimental trials, with a randomized, double-blind, placebo-controlled, crossover design, separated by ≥1 week. One hour before exercise they ingested 950 mg of SidTea+ (SID) or placebo (PLA). Participants subsequently completed 60 min of running at 70–75% $\dot{V}O_2$max followed by running to exhaustion at 90–95% $\dot{V}O_2$max. Heart rate (HR), oxygen uptake ($\dot{V}O_2$), respiratory exchange ratio (RER), blood lactate (BL), glucose (GLU) and time to exhaustion (TEX) were assessed. **Results**: TEX was longer with SID than PLA (327 ± 141 vs. 229 ± 120 s; absolute paired difference 98 s, 95% CI 20–176 s; relative difference 42.8% based on condition means; $p = 0.019$, $d^z = 0.90$). No statistically significant differences between conditions were observed for HR, $\dot{V}O_2$, RER, blood lactate, or blood glucose (all $p > 0.05$). **Conclusions**: Acute ingestion of 950 mg of SidTea+ was associated with a longer TEX during high-intensity running in this specific protocol, with no statistically significant differences in the cardiorespiratory or metabolic variables (HR, $\dot{V}O_2$, RER, blood lactate, or blood glucose). This preliminary finding from a small exploratory trial does not establish efficacy; confirmation in larger independent samples, replication using alternative exercise protocols and investigation of the underlying mechanisms are required.

Keywords: Greek mountain tea; ergogenic aid; endurance exercise; time to exhaustion; blood lactate; phytochemicals

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1. Introduction

Nutritional supplements are widely used to support exercise performance and recovery, although their efficacy depends on the bioactive compound, dose, supplementation regimen, exercise modality, and training status of the individual [1,2]. In recent years, increasing attention has focused on plant-derived bioactive compounds because of their potential antioxidant, anti-inflammatory, metabolic, and vasoactive properties [3,4]. Several polyphenol-rich botanical supplements have been investigated in the context of exercise, with proposed mechanisms including modulation of vascular function, oxidative stress, inflammatory signalling, mitochondrial function, and post-exercise recovery [3,5–7]. However, their physiological and ergogenic effects vary considerably according to phytochemical composition, dose, timing and duration of supplementation, bioavailability, and exercise conditions [3,7].

Among plant-derived nutritional interventions, beetroot juice has received considerable attention for its potential ergogenic effects, which are primarily attributed to dietary nitrate and its subsequent conversion to nitric oxide. Nitrate supplementation has been associated with reduced oxygen cost during exercise and improved tolerance to high-intensity exercise [8–10]. Other botanical interventions, including tart cherry and blackcurrant extracts, have been investigated for their potential effects on exercise recovery, vascular function, and performance [5,11]. Collectively, these findings provide a rationale for investigating other phytochemical-rich medicinal plants with biological properties that may influence exercise tolerance.

Sideritis scardica, commonly known as Greek mountain tea, is a Balkan endemic medicinal herb traditionally consumed as an infusion and used for its anti-inflammatory, digestive properties and to promote vitality and reduce fatigue [12,13]. It contains a diverse range of bioactive constituents, including flavonoids, phenylethanoid glycosides, phenolic acids, and terpenoids, whose abundance varies according to geographical origin, cultivation conditions, and extraction procedures [13–17]. These compounds have been associated with several biological activities of *Sideritis scardica*, particularly its antioxidant, anti-inflammatory, and neuroprotective properties.

Laboratory studies indicate that *Sideritis* extracts and isolated constituents exert antioxidant and anti-inflammatory effects, including scavenging of reactive oxygen species, attenuation of lipid peroxidation, and modulation of redox-sensitive signaling pathways [18–21]. These properties are of interest in exercise physiology because prolonged or strenuous exercise increases reactive oxygen species production, which has been linked to fatigue and muscle damage, although reactive oxygen species also contribute to adaptive redox signaling [22]. However, such findings come from cellular and animal models and do not establish effects on human exercise tolerance. In humans, evidence is limited and derives from studies that did not examine exercise performance. Four weeks of supplementation with the standardized extract SidTea+ (1500 mg·day^{-1} in three divided doses) was associated with favorable changes in physiological, metabolic, and redox-related outcomes in healthy adults [23], while a single dose of a different *Sideritis scardica* extract (475 and 950 mg) improved aspects of cognitive performance and modulated cerebral blood-flow responses in adults aged 50–70 years [24]. To our knowledge, no study has examined whether acute ingestion of *Sideritis scardica* influences exercise performance.

Therefore, the aim of this exploratory study was to examine the effects of a single 950-mg dose of SidTea+ ingested 60 min before exercise on high-intensity running performance following 60 min of submaximal exercise, assessed through time to exhaustion, and on the associated cardiorespiratory (HR, $\dot{V}O_2$, and RER) and metabolic (blood lactate and glucose) responses. We hypothesized that SidTea+ ingestion would improve exercise performance compared with placebo. The 950-mg dose corresponds to the higher of the

two doses tested acutely in [24], whereas the product used here is the extract characterized and tested in our previous 4-week study [23]. The high-intensity test began approximately 2 h after ingestion, within the post-ingestion window assessed in [24]. Nevertheless, the extract in [24] differs from SidTea+ and was studied in an older population, while [23] used a divided daily dose; neither study provides direct evidence of ergogenic effects. Nominally equal doses of different extracts do not guarantee comparable phytochemical exposure, and systemic exposure was not measured here. The dose and timing should therefore be regarded as an informed but untested choice for this protocol, and a possible role of the previously reported antioxidant activity [25] was examined only indirectly.

2. Materials and Methods

2.1. Participants

Given the lack of previous studies investigating the acute effects of *Sideritis scardica* on exercise performance, the present study was designed as an exploratory randomized, double-blind, placebo-controlled, crossover design trial. The crossover design was selected to reduce inter-individual variability by allowing each participant to serve as his or her own control. Twelve participants completed the first experimental period. Two adverse events were reported among the 12 randomized participants. Following the first experimental period, one participant (P03, SID-first sequence) experienced an ankle sprain, while another participant (P11, PLA-first sequence) experienced a hamstring strain. Both injuries occurred outside the laboratory and were reported to the research team by telephone. As a result, both participants withdrew before completing the second experimental period. The remaining 10 participants completed both experimental trials. Participant characteristics are presented in Table 1. Eligible participants were physically active adults aged ≥18 years who were free from injury and had no history of cardiovascular, respiratory, or metabolic disease. Participants were students enrolled in a Physical Education and Sport Science program or current and former track-and-field athletes who continued to engage in regular exercise training. Their classification as physically active was based on their known exercise and training backgrounds. No standardized physical activity questionnaire or predefined quantitative exercise criteria were used. Participants were also required to refrain from consuming any dietary supplements throughout the study period. None of the female participants were using hormonal contraceptives. Information regarding menstrual-cycle phase was not collected, and menstrual-cycle phase was not standardized between experimental trials. To minimize dietary variation between experimental trials, participants recorded all food and beverages consumed for two days preceding the first experimental trial (visit 3) and were instructed to replicate the same intake before the second experimental trial (visit 4) and to record their intake again. Intake was recorded using estimated household-measure food records and analyzed with Science Fit Diet 200A software (Sciencefit, Athens, Greece); the records of the two days preceding each experimental trial were used for Table 2. Compliance was based on self-report only. Participants were asked to avoid mountain tea and other polyphenol-rich foods and beverages during the study period.

Table 1. Physical and physiological characteristics of the participants.

Characteristic	Mean ± SD	Range (Min–Max)	Median	Q1–Q3	IQR
Age (years)	21.4 ± 2.2	18.5–24.7	20.6	20.2–23.5	3.3
Height (m)	1.73 ± 0.12	1.57–1.89	1.73	1.61–1.81	0.19

Table 1. *Cont.*

Characteristic	Mean ± SD	Range (Min–Max)	Median	Q1–Q3	IQR
Body mass (kg)	62.4 ± 13.0	47.9–90.3	60.0	52.4–68.5	16.2
Body mass index ($kg \cdot m^{-2}$)	20.8 ± 2.1	18.5–25.3	20.2	19.3–21.4	2.1
Body fat (%)	17.7 ± 2.6	14.5–22.5	17.0	16.0–19.1	3.1
Systolic blood pressure (mmHg)	110 ± 11	90–120	117	100–120	20
Diastolic blood pressure (mmHg)	64 ± 6	52–70	66	62–68	6
Resting heart rate (bpm)	67 ± 7	59–80	64	64–71	7
Maximal heart rate (bpm)	195 ± 11	181–209	196	185–204	18
$\dot{V}O_2$max ($mL \cdot kg^{-1} \cdot min^{-1}$)	44.2 ± 5.1	34.9–52.0	44.8	41.6–48.0	6.4
Maximal treadmill speed ($km \cdot h^{-1}$)	14.7 ± 1.8	11.0–17.0	15.0	14.2–15.0	0.8
Submaximal running speed (70–75% $\dot{V}O_2$max; $km \cdot h^{-1}$)	10.4 ± 1.2	8.0–12.0	10.7	9.5–11.4	1.9
High-intensity running speed (90–95% $\dot{V}O_2$max; $km \cdot h^{-1}$)	13.7 ± 1.6	10.4–16.0	14.1	12.9–14.4	1.5

$\dot{V}O_2$max, maximal oxygen uptake. Values are rounded for display; IQR, interquartile range.

Table 2. Dietary intake in the *Sideritis* (SID) and placebo (PLA) conditions (n = 10; mean ± SD).

Variable	SID	PLA	t(9)	p	d^z
Energy ($kcal \cdot day^{-1}$)	2125.8 ± 540.8	1965.2 ± 547.5	1.53	0.161	0.48
Carbohydrate ($g \cdot day^{-1}$)	239.1 ± 49.9	221.2 ± 56.5	1.18	0.268	0.37
Carbohydrate (% energy)	45.5 ± 4.4	46.3 ± 5.4	−0.38	0.714	−0.12
Protein ($g \cdot day^{-1}$)	87.1 ± 25.5	89.4 ± 28.8	−0.39	0.705	−0.12
Protein (% energy)	16.5 ± 2.2	18.2 ± 2.7	−1.69	0.125	−0.54
Fat ($g \cdot day^{-1}$)	84.0 ± 34.4	77.3 ± 26.3	— †	0.625 †	r = 0.18
Fat (% energy)	35.4 ± 6.1	34.1 ± 5.3	0.49	0.634	0.16
Vitamin C ($mg \cdot day^{-1}$)	87.9 ± 46.9	86.7 ± 40.8	0.09	0.928	0.03
Vitamin E ($mg \cdot day^{-1}$)	8.43 ± 2.99	8.01 ± 2.64	0.94	0.371	0.30
Selenium ($\mu g \cdot day^{-1}$)	124.5 ± 61.7	123.4 ± 60.6	0.15	0.888	0.05

SID, *Sideritis*; PLA, placebo; d^z, Cohen's effect size for paired data. † Fat intake ($g \cdot day^{-1}$) was analyzed using the Wilcoxon signed-rank test because the paired differences were not normally distributed; therefore, a t statistic is not reported, and the rank-based effect size (r) is presented instead of d^z. Valid observations: n = 10 per condition for every variable.

2.2. Ethics Approval

All procedures were conducted in accordance with the Declaration of Helsinki (2013 revision) and were approved by the Internal Research Ethics Committee of the Department of Physical Education and Sport Science, University of Thessaly (protocol no. 2604; 8 October 2025). The approval covered both the preliminary tolerability assessment and the main exercise performance study. After being fully informed of the study aims, proce-

dures, benefits, and potential risks, all participants, including the five volunteers involved in the preliminary tolerability assessment, completed a medical-history questionnaire and provided written informed consent before participation. Separate informed consent forms were used for the two phases. The trial was registered at ClinicalTrials.gov (NCT07555288). Participant recruitment began on 10 December 2025, before trial registration. The trial record was initially submitted on 21 April 2026 and first publicly posted on 29 April 2026. The first participant was enrolled in the main experimental study on 2 May 2026, and the final experimental assessment was completed on 15 June 2026.

2.3. Experimental Design

The study employed a randomized, double-blind, placebo-controlled, crossover design. Participants completed two experimental conditions—*Sideritis scardica* (SID) and placebo (PLA)—in a counterbalanced order, separated by a washout period of at least one week. The actual washout interval between the two experimental trials was a median of 10.5 days (range: 7–17 days) among the 10 participants who completed both conditions. The one-week washout was selected because it was the minimum interval considered sufficient to minimize carryover effects between the two experimental conditions while maintaining participant adherence, consistent with the exploratory crossover design. Participants were randomly assigned in a 1:1 ratio to one of two treatment sequences (SID–PLA or PLA–SID) using a computer-generated randomization list created with Research Randomizer (web-based randomization software; www.randomizer.org), with six participants allocated to each sequence. Of the 12 randomized participants, 10 completed both experimental conditions, with five participants completing each treatment sequence. The randomization procedure was performed by an independent researcher who was not involved in participant assessment or data analysis. Participants visited the Laboratory of Exercise Biochemistry, Physiology and Nutrition (SmArT Lab) on four separate occasions. During the first visit, participants were informed about the study objectives and experimental procedures, provided written informed consent, the dietary recording and replication requirements were also explained verbally and underwent baseline assessments, including body mass, height, body composition, blood pressure, resting heart rate, and resting blood lactate and glucose concentrations. During the first visit, participants were also familiarized with treadmill running, including the high running speeds subsequently used during the time-to-exhaustion assessment. During the second visit, participants completed an incremental treadmill test to determine maximal oxygen uptake (VO_2max). The third and fourth visits involved the two experimental supplementation trials, performed in a randomized, double-blind, placebo-controlled crossover design, with a washout period of at least one week between trials. The supplements were pre-packaged in identical capsules and coded to ensure allocation concealment. Participants, investigators administering the supplements, and investigators conducting the exercise tests and collecting outcome measurements remained unaware of treatment allocation throughout the experimental procedures. The allocation code was revealed only after completion of data analysis. The registered primary outcomes were selected to address two related scientific objectives: to evaluate the effect of acute *Sideritis scardica* supplementation on exercise performance, assessed by time to exhaustion (TEX), and to investigate whether potential performance differences were accompanied by changes in cardiorespiratory and metabolic responses. Accordingly, HR, VO_2, RER, blood lactate, and blood glucose were assessed as potential explanatory physiological variables. Although these measurements were classified as primary outcomes in the ClinicalTrials registration, TEX represented the principal performance outcome of interest. No formal statistical testing hierarchy or multiplicity-adjustment strategy was prospectively specified.

The flow of participants through the study, including enrollment, randomization, allocation, follow-up, and analysis, is presented in Figure 1.

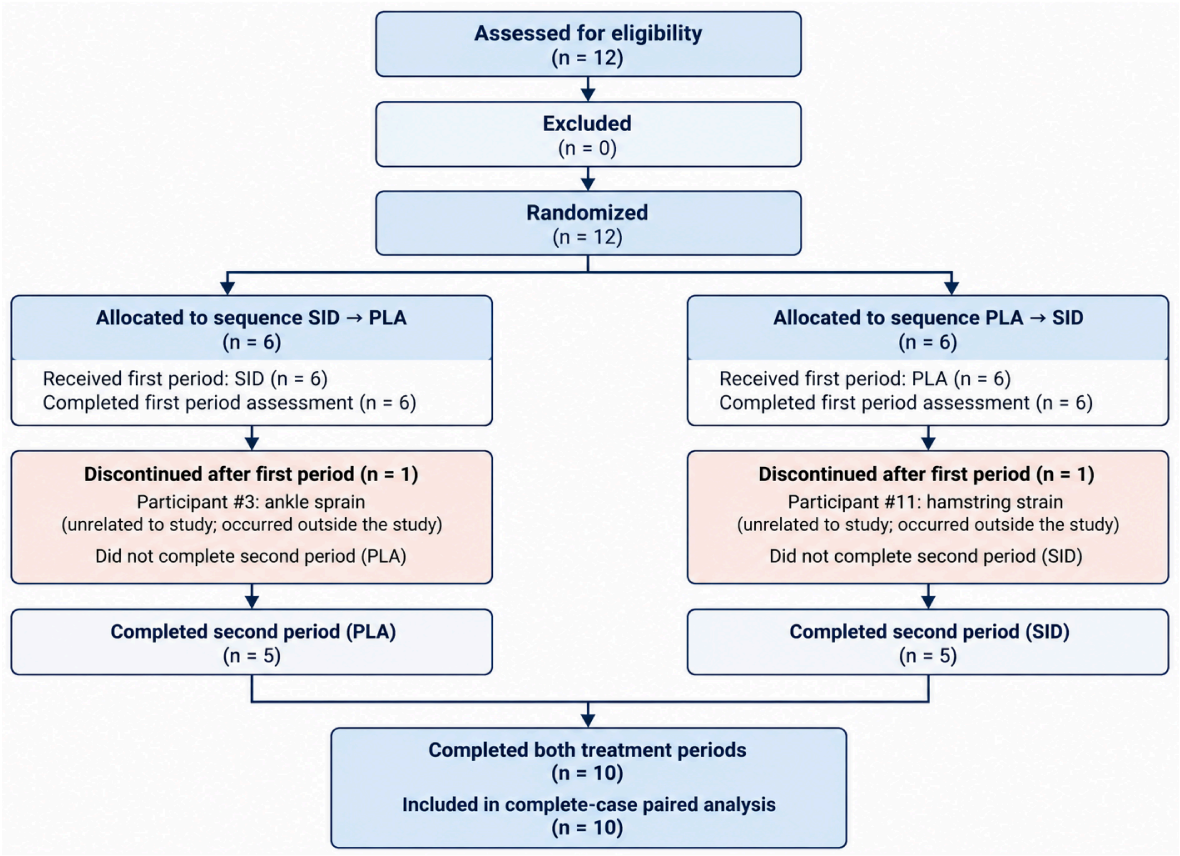


Figure 1. CONSORT flow diagram illustrating recruitment, randomization, treatment sequence, crossover, follow-up, and analysis.

2.4. Supplementation Protocol

Approximately 60 min before the initiation of each experimental trial, participants ingested a single capsule containing 950 mg of SidTea+ *Sideritis scardica* extract or a visually identical placebo, corresponding to approximately 120 min before the TEX assessment. This timing was selected to allow for potential absorption and acute biological activity of the extract's constituents, although the optimal supplementation interval has not been established through pharmacokinetic studies. The SidTea+ extract and placebo were identical to those described previously by Papanikolaou et al. [23]. The *Sideritis scardica* extract was developed and manufactured by the Department of Pharmacy, National and Kapodistrian University of Athens, Greece, and subsequently provided to Pharmainnovations (Trikala, Greece), the holder of the SidTea+™ name. Pharmainnovations supplied the extract to our research team, and the active capsules were prepared in-house at our laboratory. The placebo capsules contained maltodextrin (Merck, Athens, Greece) and were prepared to be visually indistinguishable from the active capsules, as in the previous study [23]. The extract was from production batch PGMTD_3/20, also used in the earlier study [23]. The product was initially tested in January 2024, with a retest date set at 24 months. It was subsequently retested in January 2026, and a new expiry date of January 2027 was assigned. According to the batch certificate of analysis, the dry preparation comprised 80% native extract and 20% maltodextrin and had a total phenolic content of 112 mg GA/g and a DPPH IC_{50} of 157.82 µg/mL. The certificate reported conformity with its specifications for heavy metals, microbiological quality, pesticide residues, and HPLC/HPTLC profiling. The

previously published UPLC-HRMS analysis identified more than 35 metabolites, principally phenolic acids, phenylethanoid glycosides, and flavonoid glucosides [23].

Prior to commencement of the experimental trials, the acute tolerability of the selected 950-mg dose of SidTea+ was assessed in five individuals who were not included in the main study. Each individual ingested a single 950-mg dose of SidTea+ orally in the morning, consistent with the administration procedure used in the experimental trials. Adverse symptoms were monitored for 48 h following ingestion using a standardized adverse-symptom questionnaire. The questionnaire assessed the occurrence and type of adverse symptoms, their time of onset and severity, and whether medical attention was required.

2.5. Measurements

Height was measured using a wall-mounted stadiometer (SECA, Hamburg, Germany), and body mass was determined with a calibrated beam balance (SECA, Hamburg, Germany). Body fat percentage was assessed using a Tanita BC-418 MA Segmental Body Composition Analyzer (Tanita Corporation, Tokyo, Japan). Maximal oxygen uptake ($\dot{V}O_2max$) was determined during an incremental treadmill test on a motorised treadmill (h/p/cosmos, Nußdorf-Traunstein, Germany), in which running speed increased by 1 km·h^{-1} every 2 min at a 0% incline until volitional exhaustion. Respiratory gases were measured continuously using a breath-by-breath metabolic cart (COSMED, Quark CPET, Rome, Italy). The gas analyzers were calibrated using reference gas mixtures with known O_2 and CO_2 concentrations before testing. Heart rate was monitored throughout the test using a Polar FT1 heart-rate monitor (Polar Electro Oy, Kempele, Finland). Criteria for attainment of $\dot{V}O_2max$ included a plateau in $\dot{V}O_2$, defined as an increase of less than 2 mL·kg^{-1}·min^{-1} despite a further increase in treadmill running speed during the final stages of the incremental test, attainment of a heart rate within 10 beats·min^{-1} of age-predicted maximal heart rate (220 − age), a respiratory exchange ratio (RER) ≥ 1.10, and volitional exhaustion. All 10 participants fulfilled the $\dot{V}O_2$ plateau criterion (less than 2 mL·kg^{-1}·min^{-1} increase despite increasing exercise intensity), achieved an RER > 1.10, and reached volitional exhaustion. Eight participants also fulfilled the age-predicted maximal heart rate criterion (within ±10 beats·min^{-1} of 220 − age), whereas two did not. Given that all participants demonstrated a VO_2 plateau supported by the other indicators of maximal effort, VO_2max was considered to have been attained in all participants. The individual relationship between treadmill running speed and oxygen uptake obtained during the incremental test was used to determine the running speeds corresponding to 70–75% and 90–95% of each participant's measured VO_2max. These individualized running speeds were subsequently used to prescribe the submaximal and high-intensity exercise workloads, respectively, during both experimental trials. Blood pressure was measured after an overnight fast following at least 10 min of seated rest using a calibrated sphygmomanometer (Precisa N R-1362, Rudolf Riester GmbH, Jungingen, Germany). Capillary blood glucose (Accu-Chek Instant; Roche Diabetes Care, Mannheim, Germany) and blood lactate (Lactate Plus; Nova Biomedical, Waltham, MA, USA) concentrations were determined from fingertip capillary blood samples collected under aseptic conditions pre-exercise, every 15 min during the submaximal exercise bout, and immediately following exhaustion.

2.6. Exercise Protocol

All experimental trials were performed in the morning under controlled laboratory conditions. Environmental conditions were comparable between the SID and PLA trials, with a mean temperature of 22.2 ± 0.4 °C and relative humidity of 45.4 ± 4.6%. Participants completed both trials following an overnight fast of at least 8–10 h and were instructed to abstain from caffeine and alcohol for 48 h and from strenuous exercise for 72 h before each trial.

They were also instructed to maintain their usual hydration status and replicate their dietary intake during the two days preceding each experimental session, as described in Section 2.1. Sleep duration was recorded before each trial and did not differ between conditions.

Thirty minutes after capsule ingestion, resting blood lactate and glucose concentrations were measured, while pre-exercise blood pressure and heart rate were also assessed during the pre-exercise period. It should be noted that the pre-exercise heart-rate measurements obtained during the experimental trials were distinct from the resting heart-rate measurements obtained during the initial visit for baseline participant characterization. Consequently, these measurements represent different assessment occasions and should not be considered directly equivalent. Participants were then fitted with a heart-rate monitor and the facemask of the metabolic cart before completing a 3-min jogging warm-up followed by 2 min of passive recovery. All pre-exercise assessments and warm-up procedures were completed within the 60-min post-ingestion period, allowing the experimental exercise protocol to commence 60 min after capsule ingestion.

The exercise protocol was performed on a motorized treadmill (h/p/cosmos, Nußdorf-Traunstein, Germany) and consisted of 60 min of running at an individualized treadmill speed corresponding to 70–75% of each participant's measured VO_2max, as determined directly from the speed–VO_2 relationship obtained during the incremental VO_2max test. Participants stepped off the treadmill for approximately 20 s for each blood sample. Following completion of the 60-min exercise phase, treadmill speed was increased to the individualized workload corresponding to 90–95% of VO_2max, and participants continued running until exhaustion. For each participant, identical absolute treadmill speeds were maintained during the corresponding exercise phases in both supplementation conditions (SID and PLA), with treadmill incline set at 0% throughout the protocol. Treadmill speed was increased to elicit the prescribed high-intensity workload without stopping the treadmill (the increase took approximately 1–4 s), and participants continued running until volitional exhaustion. Timing of TEX started when the target speed was reached. Participants were familiarized with treadmill running, including the high running speeds used during the TEX assessment, before completing the experimental trials.

Water consumption was permitted during exercise, with the volume consumed during the first trial recorded and the same volume permitted during the second trial. During the submaximal phase, fingertip blood samples were collected every 15 min to determine blood lactate and glucose concentrations, while $\dot{V}O_2$, respiratory exchange ratio (RER), and heart rate were recorded at the same time points. Immediately after the submaximal phase, treadmill speed was increased to elicit the prescribed high-intensity workload, and participants continued running until volitional exhaustion. The same investigator supervised both experimental trials and provided verbal encouragement using a consistent approach to minimize potential motivational differences between conditions. Volitional exhaustion was defined as the point at which participants were unable or unwilling to maintain the prescribed running speed despite standardized verbal encouragement. Participants indicated exhaustion using a pre-agreed thumbs-down gesture, upon which the treadmill was immediately stopped. TEX was defined as the elapsed time from the beginning of the high-intensity phase until exercise termination. Capillary blood samples were collected immediately after exhaustion for the determination of blood lactate and glucose concentrations. Following each experimental trial, participants were informally asked about their general condition and recovery. No standardized adverse-event questionnaire or systematic symptom checklist was administered. Adverse events were identified through informal communication with participants and spontaneous reports, including telephone notifications of events occurring outside the laboratory.

2.7. Statistical Analysis

Normality of the paired differences was assessed using the Shapiro–Wilk test, and no significant deviations from normality were detected for any variable except fat intake, which was analyzed using the Wilcoxon signed-rank test.

To assess the robustness of the TEX findings, two complementary sensitivity approaches were employed. First, a leave-one-participant-out analysis was performed by sequentially excluding each participant and repeating the paired-samples *t*-test to evaluate the influence of individual observations. Second, an exact Wilcoxon signed-rank test and a sign-flip permutation test were performed to examine the consistency of the findings across alternative statistical approaches, given the small sample size and the limited power of normality tests. The Wilcoxon signed-rank test assessed a rank-based location shift in the paired differences, whereas the sign-flip permutation test evaluated the mean paired difference under the assumption of sign-exchangeability. The Hodges–Lehmann estimator and its 95% confidence interval were used to characterize the paired location shift. For the Wilcoxon signed-rank test of TEX, the exact *p*-value, smaller rank sum (W), and matched-pairs rank-biserial correlation $[r = (T^+ - T^-)/(T^+ + T^-)]$ were reported, with positive values indicating longer TEX following SID supplementation. Zero differences were excluded from the rank calculation. All sensitivity analyses were considered exploratory.

Submaximal physiological and metabolic responses were analyzed using two-way repeated-measures ANOVA, with supplementation condition (SID and PLA) and time (15, 30, 45, and 60 min) as within-subject factors. Separate analyses were performed for blood lactate, blood glucose, heart rate, oxygen uptake (VO_2), and respiratory exchange ratio (RER). Main effects of condition and time, as well as condition × time interactions, were examined. Sphericity was assessed using Mauchly's test, and Greenhouse–Geisser corrections were applied, where appropriate, to the main effect of time and the condition × time interaction. Effect sizes were expressed as partial eta squared (ηp^2).

Mean submaximal HR, $\dot{V}O_2$, RER, blood lactate, and blood glucose were calculated for each participant by averaging measurements obtained at 15, 30, 45, and 60 min of the submaximal exercise phase. Differences between SID and PLA in time to exhaustion, mean submaximal HR, $\dot{V}O_2$, RER, blood lactate and glucose, and blood lactate and glucose concentrations at exhaustion were assessed using paired-samples *t*-tests. Results were expressed as t statistics, two-sided *p* values, and Cohen's d^z as the standardized effect size for paired data. Where reported, 95% confidence intervals (CIs) were calculated for mean paired differences. The rank-based effect size r was calculated for the Wilcoxon signed-rank test.

To assess the potential influence of experimental period on TEX, an additional period-adjusted linear model was fitted, with supplementation condition (SID vs. PLA) and experimental period (first vs. second trial) as fixed effects, accounting for repeated observations within participants. The treatment effect was estimated after adjustment for period, and the corresponding 95% confidence interval was calculated. Treatment sequence-specific descriptive statistics were also calculated. Given the small sample size ($n = 10$), these additional analyses were considered exploratory, and nonsignificant period effects were not interpreted as evidence that period-related influences or carryover effects were absent. First-period data were successfully collected for the two withdrawn participants; however, these available observations were excluded from the complete-case analysis. Consequently, the primary paired analyses included only the 10 participants who completed both experimental periods. No adjustment for multiple comparisons was applied; therefore, statistical findings should be interpreted cautiously.

The trial registration prospectively specified the use of a two-way repeated-measures ANOVA. Although the initial analyses were performed using paired-samples *t*-tests, the registered two-way repeated-measures ANOVA was subsequently implemented during

manuscript revision to examine the main effects of supplementation condition (SID vs. PLA), time (15, 30, 45, and 60 min), and their interaction on time-dependent physiological variables. Additional sensitivity analyses, including a period-adjusted model, leave-one-participant-out analysis, Wilcoxon signed-rank test, and sign-flip permutation test, were conducted post hoc to assess the robustness of the findings.

Statistical analyses were performed using IBM SPSS Statistics, version 29.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $p < 0.05$. Data are presented as mean ± SD.

3. Results

No adverse symptoms were reported by any of the five individuals included in the preliminary tolerability assessment during the 48-h period following oral ingestion of a single 950-mg dose of SidTea+. Dietary intake data are presented in Table 2. No statistically significant differences between SID and PLA were detected for total energy intake, carbohydrate, protein, or fat intake, whether expressed as absolute intake or percentage of total energy (all $p > 0.05$). However, mean energy and carbohydrate intake were higher before the SID trial (by about 161 kcal·day^{-1} and 18 g·day^{-1}, corresponding to approximately 3.8 vs. 3.5 g·kg^{-1}·day^{-1} of carbohydrate, calculated from mean body mass), and with ten participants meaningful differences cannot be excluded. Vitamin C, vitamin E, and selenium intake also showed no statistically significant differences (all $p > 0.05$).

Individual and mean TEX responses following placebo (PLA) and *Sideritis scardica* (SID) supplementation are presented in Figure 2, while the corresponding paired differences and leave-one-participant-out sensitivity analyses are presented in Table 3. TEX was significantly greater following SID than PLA (327 ± 141 vs. 229 ± 120 s), corresponding to a mean paired difference of 98.0 s (95% CI 20–176 s; $t(9) = 2.85$, $p = 0.019$, $d^z = 0.90$; Figure 2). This corresponds to a 42.8% difference between condition means relative to placebo mean, rather than the mean individual responses. Seven of the ten participants demonstrated longer TEX following SID supplementation.

Table 3. Individual time to exhaustion differences between *Sideritis* (SID) and placebo (PLA) supplementation and leave-one-participant-out sensitivity analysis.

Participant	Treatment Sequence	Individual TEX Diff (s)	Mean Diff After Exclusion (s)	*p*-Value After Exclusion
P01	SID–PLA	+112	+96.4	0.0364
P02	PLA–SID	+177	+89.2	0.0433
P04	PLA–SID	+247	+81.4	0.0422
P05	SID–PLA	−14	+110.4	0.0151
P06	PLA–SID	−26	+111.8	0.0132
P07	SID–PLA	+94	+98.4	0.0337
P08	PLA–SID	+19	+106.8	0.0208
P09	SID–PLA	+109	+96.8	0.0360
P10	SID–PLA	+275	+78.3	0.0381
P12	PLA–SID	−13	+110.3	0.0153
All participants	$n = 10$	+98.0 (mean)	—	0.0192

SID, *Sideritis*; PLA, placebo; Individual TEX difference = TEX under SID − TEX under PLA. Positive values indicate longer TEX following SID supplementation. Each leave-one-participant-out analysis excludes the participant identified in the corresponding row and repeats the paired-samples *t*-test using the remaining nine participants. All *p*-values are two-sided and unadjusted for multiple comparisons.

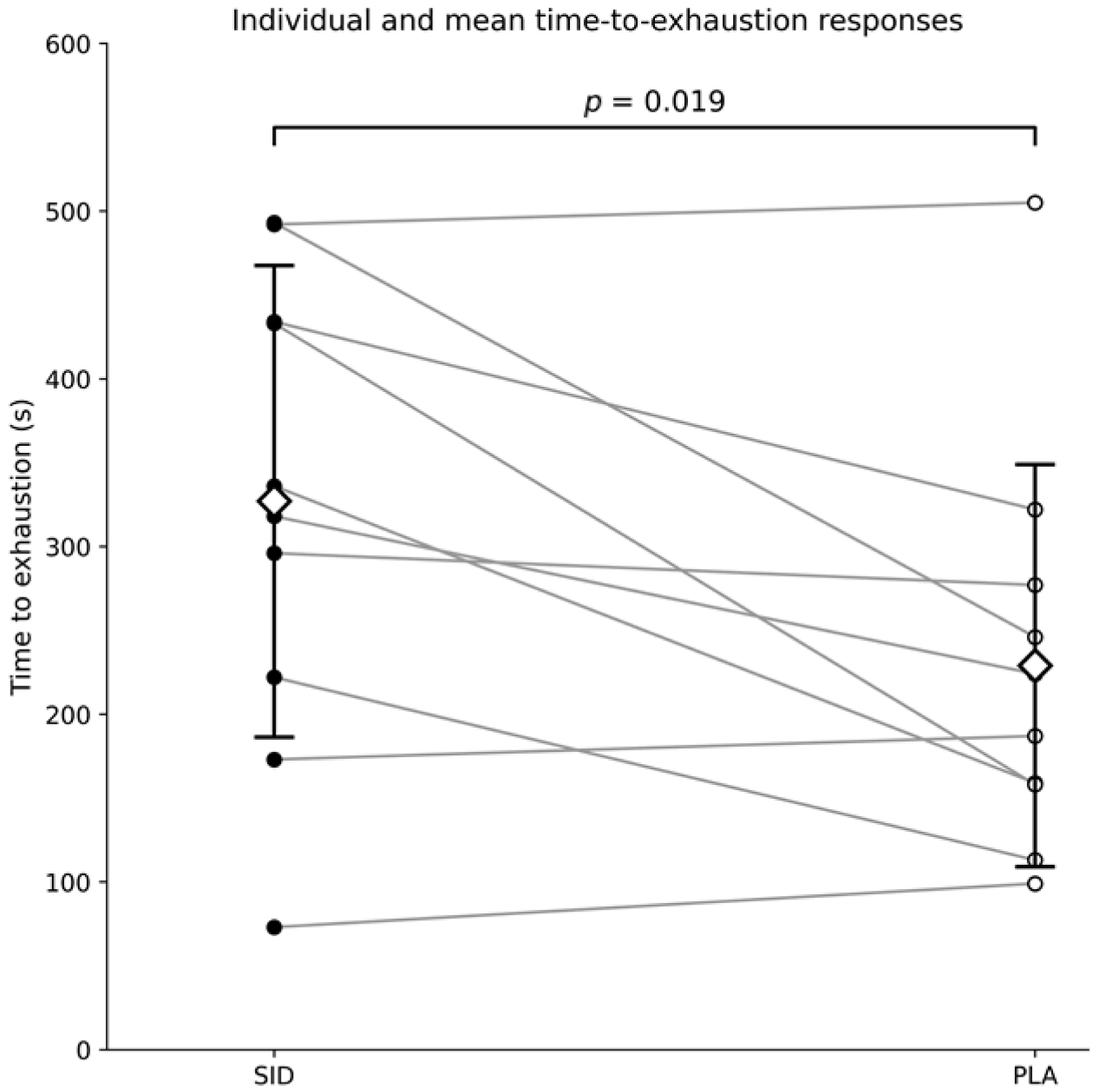


Figure 2. Individual and mean time to exhaustion responses in the *Sideritis* (SID) and placebo (PLA) conditions. Individual responses are represented by circles connected by lines. Open diamonds represent mean values, with error bars indicating SD. $p = 0.019$ for the paired comparison between conditions.

The treatment effect remained positive after adjustment for experimental period (estimated difference: 98.0 s; 95% CI: 15.0–181.0 s; $p = 0.026$), whereas the period effect was not statistically significant (−17.2 s; $p = 0.646$). In the SID–PLA sequence ($n = 5$), mean TEX was 316.0 ± 119.3 s during Period 1 (SID) and 200.8 ± 79.0 s during Period 2 (PLA), corresponding to a mean within-participant difference of +115.2 s. In the PLA–SID sequence ($n = 5$), mean TEX was 257.2 ± 155.4 s during Period 1 (PLA) and 338.0 ± 173.0 s during Period 2 (SID), corresponding to a mean within-participant difference of +80.8 s. Leave-one-participant-out sensitivity analyses yielded positive mean paired differences ranging from 78.3 to 111.8 s, with unadjusted *p*-values between 0.013 and 0.043 (Table 3). Exclusion of the participant with the largest improvement (+275 s) yielded a mean paired difference of 78.3 s ($p = 0.0381$), whereas exclusion of the participant with the second-largest improvement (+247 s) yielded a mean difference of 81.4 s ($p = 0.0422$). Thus, the observed treatment difference was not attributable

exclusively to any single participant. Although this pattern suggests some consistency in the direction of the performance response, individual changes should be interpreted cautiously given the small sample size.

As complementary sensitivity analyses, the exact Wilcoxon signed-rank test (W = 7, Z = −2.09, exact two-sided $p = 0.037$, matched-pairs rank-biserial correlation r = 0.745) and the exact sign-flip permutation test (two-sided $p = 0.025$; 26 of 1024 possible sign combinations) yielded results consistent with the primary paired-samples *t*-test (t(9) = 2.85, $p = 0.019$). The Hodges–Lehmann estimate of the paired location shift was 101.5 s (95% CI: 3–180 s). These analyses provided additional evidence of a positive treatment-associated difference in TEX, although they rely on different statistical assumptions and do not necessarily estimate the same quantity.

Mean performance, cardiorespiratory, and metabolic outcomes are presented in Table 4. Mean HR during submaximal exercise did not differ between SID and PLA (175.0 ± 7.2 vs. 169.2 ± 15.7 bpm; t(9) = 1.20, $p = 0.260$, $d^z = 0.38$). Similarly, no differences were observed for mean $\dot{V}O_2$ (33.5 ± 5.2 vs. 33.6 ± 3.2 mL·kg^{-1}·min^{-1}; t(9) = −0.06, $p = 0.953$, $d^z = -0.02$) or RER (0.92 ± 0.04 vs. 0.92 ± 0.06; t(9) = −0.24, $p = 0.817$, $d^z = -0.08$). Mean submaximal blood lactate was lower on average following SID than PLA (2.77 ± 1.00 vs. 3.30 ± 1.23 mmol·L^{-1}), but the difference was not statistically significant (t(9) = −2.01, $p = 0.076$, $d^z = -0.63$). Blood lactate at exhaustion also did not differ between conditions (6.96 ± 1.09 vs. 6.24 ± 2.34 mmol·L^{-1}; t(9) = 1.19, $p = 0.263$, $d^z = 0.38$). No statistically significant difference in mean glucose was detected between SID and PLA (5.0 ± 0.6 vs. 5.0 ± 0.6 mmol·L^{-1}; t(9) = 0.03, $p = 0.977$, $d^z = 0.01$). Likewise, blood glucose at exhaustion did not differ between conditions (6.0 ± 1.6 vs. 6.2 ± 1.4 mmol·L^{-1}; t(9) = −0.91, $p = 0.388$, $d^z = -0.29$).

Table 4. Mean performance, cardiorespiratory and metabolic responses in the *Sideritis* (SID) and placebo (PLA) conditions ($n = 10$; mean ± SD).

Variable	SID	PLA	Difference [95% CI]	t(9)	*p*	d^z	95% CI for d^z
TEX (s)	327 ± 141	229 ± 120	98 [20.1, 175.8]	2.85	0.019 *	0.90	0.14 to 1.63
Mean heart rate (bpm)	175.0 ± 7.2	169.2 ± 15.7	5.84 [−5.2, 16.8]	1.20	0.260	0.38	−0.27 to 1.01
Mean $\dot{V}O_2$ (mL·kg^{-1}·min^{-1})	33.5 ± 5.2	33.6 ± 3.2	−0.05 [−1.84, 1.76]	−0.06	0.953	−0.02	−0.64 to 0.60
Mean RER	0.92 ± 0.04	0.92 ± 0.06	−0.004 [−0.041, 0.031]	−0.24	0.817	−0.08	−0.69 to 0.55
Mean submaximal lactate (mmol·L^{-1})	2.77 ± 1.00	3.30 ± 1.23	−0.53 [−1.12, 0.07]	−2.01	0.076	−0.63	−1.31 to 0.06
Lactate at exhaustion (mmol·L^{-1})	6.96 ± 1.09	6.24 ± 2.34	0.72 [−0.65, 2.09]	1.19	0.263	0.38	−0.28 to 1.01
Mean submaximal glucose (mmol·L^{-1})	5.0 ± 0.6	5.0 ± 0.6	0.01 [−0.62, 0.63]	0.03	0.977	0.01	−0.61 to 0.63
Glucose at exhaustion (mmol·L^{-1})	6.0 ± 1.6	6.2 ± 1.4	−0.18 [−0.62, 0.27]	−0.91	0.388	−0.29	−0.91 to 0.35

TEX, Time to exhaustion; CI, confidence interval; RER, respiratory exchange ratio; $\dot{V}O_2$, oxygen uptake; d^z, Cohen's effect size for paired observations. Differences are SID − PLA, in the units shown for each variable, and 95% CIs were calculated from unrounded participant-level data (paired t distribution, df = 9). The 95% CIs for d^z were calculated from the unrounded t statistics using the noncentral t distribution. Valid observations: $n = 10$ per condition for every variable; Positive d^z values indicate higher values in SID than PLA. * $p < 0.05$.

The temporal patterns of physiological and metabolic responses during the 60-min submaximal exercise period are presented in Table 5. Two-way repeated-measures ANOVA revealed no significant main effects of supplementation condition for blood lactate ($F(1, 9) = 4.03$, $p = 0.076$, $\eta p^2 = 0.309$), blood glucose ($F(1, 9) = 0.001$, $p = 0.977$, $\eta p^2 < 0.001$), heart rate

($F(1, 9) = 1.45$, $p = 0.259$, $\eta p^2 = 0.139$), $\dot{V}O_2$ ($F(1, 9) = 0.004$, $p = 0.953$, $\eta p^2 < 0.001$), or RER ($F(1, 9) = 0.06$, $p = 0.817$, $\eta p^2 = 0.006$). No significant main effects of time were observed for blood lactate ($F(1.37, 12.33) = 0.61$, $p = 0.500$, $\eta p^2 = 0.063$), blood glucose ($F(2.30, 20.66) = 2.00$, $p = 0.156$, $\eta p^2 = 0.182$), $\dot{V}O_2$ ($F(1.35, 12.12) = 0.60$, $p = 0.500$, $\eta p^2 = 0.063$), or RER ($F(1.67, 15.05) = 1.05$, $p = 0.361$, $\eta p^2 = 0.105$). However, a significant main effect of time was observed for heart rate ($F(1.54, 13.82) = 20.54$, $p < 0.001$, $\eta p^2 = 0.695$). Bonferroni-adjusted pairwise comparisons revealed that heart rate was significantly higher at 30 min ($p = 0.018$), 45 min ($p = 0.003$), and 60 min ($p = 0.005$) compared with 15 min. Heart rate was also significantly higher at 45 min than at 30 min ($p = 0.039$). No statistically significant differences were detected between 30 and 60 min ($p = 0.056$) or between 45 and 60 min ($p = 0.495$). No significant condition × time interactions were observed for blood lactate ($F(3, 27) = 0.503$, $p = 0.684$, $\eta p^2 = 0.053$), blood glucose ($F(2.11, 19.02) = 0.852$, $p = 0.448$, $\eta p^2 = 0.086$), heart rate ($F(1.14, 10.27) = 0.23$, $p = 0.675$, $\eta p^2 = 0.025$), $\dot{V}O_2$ ($F(1.14, 10.30) = 1.70$, $p = 0.224$, $\eta p^2 = 0.159$), or RER ($F(1.55, 13.95) = 1.18$, $p = 0.323$, $\eta p^2 = 0.116$). Greenhouse–Geisser corrections were applied to the main effect of time and the condition × time interaction where violations of sphericity were detected.

Table 5. Physiological and metabolic responses during submaximal exercise in the *Sideritis* (SID) and placebo (PLA) conditions ($n = 10$; mean ± SD).

Variable	Condition	Pre	15 min	30 min	45 min	60 min
Blood lactate (mmol/L)	SID	1.57 ± 0.54	2.60 ± 1.23	2.85 ± 0.92	2.68 ± 1.38	2.97 ± 1.30
	PLA	1.61 ± 0.46	2.95 ± 1.53	3.69 ± 1.69	3.40 ± 2.00	3.16 ± 1.30
Blood glucose (mmol/L)	SID	5.37 ± 0.74	4.96 ± 0.81	4.83 ± 0.77	5.25 ± 0.83	5.06 ± 0.49
	PLA	5.16 ± 0.60	4.76 ± 0.63	4.93 ± 0.40	5.18 ± 0.76	5.18 ± 0.93
Heart rate (beats/min)	SID	88.9 ± 24.1	165.9 ± 11.0 ^{a}	175.0 ± 8.0 ^{b}	178.8 ± 6.5 ^{c}	180.4 ± 5.3 ^{bc}
	PLA	79.5 ± 14.6	159.4 ± 22.7 ^{a}	168.0 ± 18.5 ^{b}	173.4 ± 12.5 ^{c}	175.7 ± 11.1 ^{bc}
VO_2 ($mL \cdot kg^{-1} \cdot min^{-1}$)	SID	—	32.9 ± 5.6	33.3 ± 6.4	33.2 ± 6.2	34.9 ± 4.3
	PLA	—	33.3 ± 3.8	33.9 ± 3.3	33.9 ± 3.4	33.2 ± 2.9
RER	SID	—	0.92 ± 0.04	0.92 ± 0.04	0.92 ± 0.04	0.90 ± 0.04
	PLA	—	0.93 ± 0.04	0.93 ± 0.05	0.90 ± 0.05	0.92 ± 0.10

Pre, pre-exercise; VO_2, oxygen uptake; RER, respiratory exchange ratio. A dash indicates that no pre-exercise value was available. Different superscript letters indicate statistically significant differences between time points (Bonferroni-adjusted $p < 0.05$). Post hoc comparisons were performed for the main effect of time, averaged across supplementation conditions (SID and PLA).

4. Discussion

The principal finding of the present study was that acute ingestion of 950 mg of SidTea+ *Sideritis scardica* extract was associated with significantly longer TEX during high-intensity running following 60 min of submaximal exercise. Mean TEX was 98 s longer under SID than PLA (95% CI: 20–176 s), corresponding to a 42.8% difference between condition means. The standardized effect size was $d^z = 0.90$ (95% CI: 0.14–1.63). The relatively wide confidence intervals indicate considerable uncertainty regarding the magnitude of the observed effect, with the true mean difference potentially ranging from small to substantial. Importantly, these findings reflect performance in a laboratory-based TEX test conducted at 90–95% $\dot{V}O_2$max following 60 min of running at 70–75% $\dot{V}O_2$max in an overnight-fasted state and should not be interpreted as an equivalent improvement in race time, distance covered, or competitive performance. No statistically significant differences between conditions were detected for HR, $\dot{V}O_2$, RER, blood lactate, or blood glucose. Thus, the observed increase in exercise tolerance was not accompanied by statistically detectable differences in the

measured cardiorespiratory or metabolic responses. These findings should be considered preliminary given the small sample size and exploratory nature of the study.

In the present study, no statistically significant between-condition difference in $\dot{V}O_2$ was detected. This finding was expected to some extent, since the submaximal phase was performed at a fixed relative intensity and oxygen uptake is mainly determined by exercise intensity, cardiorespiratory fitness and exercise economy [26]. Consistent with previous findings involving other plant-derived supplements, improvements in exercise tolerance may occur without statistically significant changes in $\dot{V}O_2$ during constant-intensity exercise. For example, Deley et al. reported a significant increase in time to exhaustion following acute grape and apple polyphenol supplementation, without statistically significant between-condition differences in mean or maximal $\dot{V}O_2$ [27]. It could be argued, therefore, that the greater TEX under SID was not due to a measurable reduction in the oxygen cost of running. No statistically significant difference in heart rate responses was detected between conditions. HR is largely affected by exercise intensity, training status and environmental conditions [28,29]. Thus, a single dose of *Sideritis scardica* would not necessarily be expected to alter HR during exercise performed at the same relative workload. Similar mean HR does not establish similar cardiovascular stress. The values observed in the present study are consistent with the expected reliance on carbohydrate metabolism during exercise performed at 70–75% $\dot{V}O_2$max [30,31]. No statistically significant between-condition difference in RER was detected during submaximal exercise, providing no clear evidence of altered whole-body substrate utilization following acute SID supplementation. However, the absence of statistically significant differences in RER and $\dot{V}O_2$ does not exclude potential changes in substrate oxidation or cardiorespiratory demand. Therefore, the physiological mechanisms underlying the subsequent improvement in TEX remain uncertain. Blood glucose was not statistically different between the two conditions. During exercise, blood glucose is regulated by the balance between hepatic glucose production and skeletal muscle glucose uptake, under the influence of several hormonal factors [32]. Maintenance of blood glucose during prolonged submaximal exercise has also been demonstrated in a previous study from our laboratory using a comparable exercise protocol [33]. It is therefore possible that any effect of *Sideritis scardica* on glucose metabolism was insufficient to alter circulating glucose concentrations in these young, physically active participants. Mean submaximal blood lactate was 0.53 mmol·L^{-1} lower following SID than PLA (mean paired difference: −0.53 mmol·L^{-1}; 95% CI: −1.12 to 0.07 mmol·L^{-1}; $p = 0.076$). However, the confidence interval included zero, and the difference was not statistically significant. This finding does not establish an effect of supplementation on lactate metabolism, and the present measurements cannot distinguish changes in lactate production from changes in clearance [34]. Whether this response contributed to the subsequent improvement in TEX remains uncertain. An additional methodological consideration is that post-exhaustion blood samples were collected after different exercise durations in the SID and PLA conditions, owing to differences in time to exhaustion. Therefore, post-exhaustion blood lactate and glucose concentrations were not measured after equivalent exercise exposure, which may have influenced the observed responses and complicates their direct comparison between supplementation conditions. Given the small sample size, the non-significant difference in submaximal blood lactate, and the absence of differences in RER or blood lactate at exhaustion, a potential metabolic contribution to the observed TEX response remains uncertain. Interestingly, the improvement in TEX following SID supplementation was not accompanied by significant differences in the measured cardiorespiratory or metabolic responses between conditions. These findings suggest that the observed performance improvement occurred without detectable alterations in HR, VO_2, RER, blood lactate, or blood glucose under the present experimental conditions. However, given the relatively small sample size, subtle physiological

or metabolic effects cannot be excluded. Furthermore, the absence of significant differences in these variables does not establish the involvement of alternative mechanisms. Potential central or perceptual contributions to the observed performance response therefore remain speculative and warrant direct investigation in future studies.

In contrast to the physiological and metabolic variables, for which no statistically significant between-condition differences were detected, TEX was significantly greater following SID ingestion. Although SID supplementation was associated with longer TEX, the relatively wide 95% confidence interval for the mean paired difference (20–176 s) indicates considerable uncertainty regarding the magnitude of the effect. Furthermore, improved TEX under controlled laboratory conditions does not necessarily translate into enhanced competitive endurance performance. The absence of statistically significant differences in the measured physiological variables should not be interpreted as evidence of physiological equivalence between conditions.

The mechanisms underlying this improvement cannot be established from the present data but may involve pathways related to fatigue perception or central nervous system function that were not directly assessed. Exercise-induced oxidative stress has been proposed as one of the mechanisms contributing to the development of fatigue during prolonged exercise, although reactive oxygen species also play an essential role in cellular signalling and training adaptation [22]. Therefore, any potential antioxidant-mediated ergogenic effect of *Sideritis scardica* should be interpreted within this broader physiological context. Several bioactive constituents of *Sideritis scardica*, including flavonoids and phenylethanoid glycosides, have been reported to exert neuromodulatory effects. Verbascoside, a phenylethanoid glycoside found in *Sideritis* species [13–15], has been shown to prolong time to exhaustion in rats during treadmill exercise at a dose of 10 $mg \cdot kg^{-1}$, potentially through modulation of central serotonergic pathways [35]. Whether verbascoside is present in SidTea+ in relevant amounts is unknown, because individual constituents were not quantified [23], and these animal data cannot be extrapolated directly to the present findings in humans. These findings raise the possibility that SID enhanced exercise tolerance by influencing perceived exertion, arousal, or central motor drive rather than peripheral metabolic responses. However, this interpretation remains speculative because ratings of perceived exertion and neurophysiological variables were not assessed.

A complementary mechanism may involve vascular or cerebrovascular responses. Polyphenol-rich extracts can influence endothelial function and nitric oxide-related pathways, while *Sideritis* supplementation has been associated with alterations in cerebral blood flow and cognitive performance in humans [24]. Such effects could potentially contribute to improved tolerance during high-intensity exercise without producing detectable changes in the peripheral physiological or metabolic variables measured in the present study. Nevertheless, endothelial function, cerebral oxygenation, and cerebral blood flow were not assessed, precluding conclusions regarding their contribution to the observed increase in TEX.

Collectively, central, antioxidant, and cerebrovascular pathways represent plausible hypotheses rather than demonstrated mechanisms underlying the observed TEX response, as the relevant physiological and biochemical mediators were not directly assessed. Future studies incorporating perceptual, neurophysiological, and cerebrovascular measurements are therefore required to clarify the mechanisms underlying the potential acute ergogenic effects of *Sideritis scardica*.

Limitations

Several limitations should be considered when interpreting these findings. The sample size was small and predominantly female, limiting the generalizability of the results and the ability to examine potential sex-specific responses. With only two men, sex-specific

efficacy analyses would not be reliable. Furthermore, habitual physical activity was not formally quantified using a standardized assessment, limiting the precision with which participants' training status can be characterized. In addition, the absence of symptoms in five volunteers over 48 h supports only limited acute tolerability and cannot establish broader safety. Although the crossover design reduced between-participant variability, the improvement in TEX should be confirmed in a larger independent sample. The study was not based on an a priori sample size calculation. With ten paired observations, a two-sided α of 0.05, and 80% statistical power, the design was sensitive primarily to large, standardized effects (Cohen's $d^z \approx 1.0$), corresponding to approximately 108 s based on the observed standard deviation of the paired TEX differences. Therefore, the estimated treatment effect of 98 s (95% CI: 20.2–175.8 s) is imprecise and may overestimate the underlying effect. Furthermore, the nonsignificant secondary outcomes cannot exclude potentially meaningful physiological effects.

Two participants withdrew after the first treatment period. Although their first-period data were successfully collected, these observations were excluded from the complete-case analysis. Dietary intake was self-recorded and did not differ significantly between conditions, but mean energy and carbohydrate intake were higher before the SID trial; as the study was not designed to establish equivalence, residual dietary differences cannot be excluded. Furthermore, only a single acute dose of SidTea+ was investigated; consequently, dose–response relationships and the effects of repeated supplementation cannot be determined. In addition, ratings of perceived exertion and measures of cerebral oxygenation, endothelial function, oxidative stress, inflammation, and neuromuscular function were not assessed. Consequently, the mechanisms underlying the observed improvement in exercise tolerance cannot be determined from the present data.

The timing of supplementation represents an additional limitation, as pharmacokinetic data for SidTea+ are unavailable. Although previous human studies have reported acute physiological effects and systemic absorption of metabolites following *Sideritis scardica* consumption, the circulating concentrations of its bioactive constituents were not assessed in the present study. Consequently, the optimal supplementation-to-exercise interval and the mechanisms underlying the observed TEX response remain uncertain. An additional limitation concerns the registration of multiple primary outcomes without a prospectively specified statistical testing hierarchy or multiplicity-adjustment strategy. Although TEX represented the principal performance outcome of interest, it was one of nine registered primary outcomes. Consequently, the statistically significant improvement in TEX (unadjusted $p = 0.019$) should be interpreted as exploratory and hypothesis-generating rather than definitive confirmatory evidence of an ergogenic effect. Although standardized verbal encouragement by the same investigator and double-blinding of supplement allocation were methodological strengths, these procedures cannot eliminate ordinary test-to-test variability or potential expectancy effects on the volitional TEX outcome, particularly because blinding success was not formally assessed.

Another limitation concerns the reliability of the TEX assessment. Although treadmill workloads, familiarization, and verbal encouragement were standardized, no independent test–retest reliability assessment of TEX was performed. Therefore, the contribution of day-to-day variability to the observed performance differences remains uncertain. Published studies examining the test–retest reliability of treadmill running time-to-exhaustion protocols have reported coefficients of variation ranging from approximately 9% to 16%, depending on exercise intensity and test duration [36,37]. Using 15% of the placebo mean TEX as a provisional, reliability-informed smallest effect size of interest corresponds to approximately 34 s. Although the observed mean improvement of 98 s exceeded this threshold, its 95% confidence interval (20.2–175.8 s) included effects both below and substantially above

it. Thus, the present findings do not establish with sufficient precision that the underlying treatment effect exceeds this provisional threshold. Importantly, the proposed threshold is not a validated smallest worthwhile effect for the present protocol, for which independent test–retest reliability data are unavailable.

Given the small sample size, the magnitude and reproducibility of the ergogenic effect should be interpreted cautiously. Two participants withdrew after the first treatment period, and their available observations were excluded from the complete-case analysis, potentially introducing selection bias and reducing statistical precision. Finally, menstrual cycle information was not collected, and menstrual cycle phase was not standardized across experimental trials, which may have introduced variability in physiological responses and exercise performance, potentially influencing the observed results. Future studies should incorporate larger and more sex-balanced samples, multiple supplementation doses, and perceptual, neurophysiological, vascular, and biochemical measurements.

5. Conclusions

Acute ingestion of 950 mg of SidTea+ *Sideritis scardica* extract was associated with longer TEX during high-intensity running following prolonged submaximal exercise in a small sample of physically active adults. No statistically significant differences were detected in the measured cardiorespiratory or metabolic responses during submaximal exercise. Although these preliminary findings suggest a potential beneficial effect on exercise tolerance, they do not establish improved competitive athletic performance or identify the underlying physiological mechanisms. Given the small sample size and the absence of a prespecified multiplicity-adjustment strategy, these findings should be considered preliminary and require confirmation in larger, adequately powered trials with prospectively defined primary outcomes. Further studies incorporating sport-specific performance assessments are warranted to confirm these findings and to investigate the mechanisms underlying this effect, including potential perceptual, central nervous system, and cerebrovascular pathways.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Internal Ethics Committee of the Department of Physical Education and Sport Science, University of Thessaly (protocol no. 2604; 8 October 2025).

Informed Consent Statement: Written informed consent was obtained from all participants involved in the study.

Data Availability Statement: The data presented in this study are available from the corresponding author upon reasonable request.

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