Title: The effect of dietary supplements on core temperature and sweating responses in hot environmental conditions: a meta-analysis and meta-regression.

Running heading: Dietary supplements for thermoregulation in the heat.

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Abstract

Dietary supplements are widely used among individuals exposed to hot environments, but whether their consumption confers any thermoregulatory effect is unclear. Therefore, we systematically evaluated the effect of dietary supplementation on key aspects of thermoregulation (core temperature [T_{core}] and sweating responses) in the heat. Three databases were searched in April 2024. After screening, 124 peer-reviewed articles were identified for inclusion within three separate meta-analyses: (1) peak T_{core}; (2) whole-body sweat rate (WBSR); (3) local sweat rate (LSR). The moderating effect of several variables (e.g. training and heat acclimation status), known to influence thermoregulatory function, were assessed via sub-analysis and meta-regression. There was no overall effect of the differing supplement types on WBSR (p = 0.405) and LSR (p = 0.769), despite taurine significantly increasing WBSR (n = 3, Hedges' g = 0.79, p = 0.006). Peak T_{core} was significantly affected by supplement type (p = 0.011), primarily due to caffeine's *small* significant positive effect (n = 30; Hedges' g = 0.44, p < 0.001) and taurine's (n = 3, Hedges' g = -0.66, p = 0.043) and oligonol's (n = 3; Hedges' g = -0.50, p = 0.014) *medium* significant negative effects. Dietary supplements, such as amino acids (e.g. taurine), some anti-oxidants and anti-inflammatories (e.g. oligonol) conferred the greatest thermoregulatory benefits during heat exposure. Taurine ingestion in such conditions may lower heat strain, which is likely through its augmentation of thermal sweating. Conversely, caffeine intake may potentially pose the greatest risk in the heat due to its effect on T_{core}.

Key words: Dietary supplements; thermoregulation; core temperature; sweating; evaporative cooling; heat

1. Introduction

Adult humans rely on eccrine sweat production to facilitate evaporative cooling and maintain thermal balance, particularly in hot and/or humid environments (high wet-bulb globe temperature [WBGT]; (1, 2)). In hot conditions, evaporation typically represents the primary heat transfer avenue (2), which offsets heat production at rest and during exercise or occupational work (3, 4). If heat is not sufficiently dissipated from the body to the environment, positive heat storage ensues, leading to rises in core temperature (T_{core}; uncompensable heat stress) (5). If left uncorrected, heat strain can cause heat exhaustion, heat stroke and even death in extreme scenarios (6, 7). Thus, understanding factors that control thermal sweating is of great importance for the health and wellbeing of many people.

Thermoregulatory capacity is largely determined by three primary modifiable factors: metabolic heat production, vasodilation (i.e. dry heat loss) and sweating (i.e. evaporative heat loss; (1, 8, 9)). Consequently, the ability to activate thermoregulatory defenses (i.e. thermoeffectors) and to tolerate exposure to hot environmental conditions can be improved, with sweating being the primary manipulable pathway (2, 10, 11). For example, endurance training and heat acclimation regimes are capable of lowering resting T_{core}, and the oxygen cost of exercise at a given intensity, but are notable in their capacity to accelerate sweating onset and increase sweat rate, plasma volume and skin blood flow (SkBF) (10-14). In various ways, these physiological adaptations augment avenues of heat transfer, control heat production and, ultimately, aid in maintaining thermal equilibrium during heat exposure. Given the importance of thermal sweating in achieving this, further understanding of the capacity for adaptation in sweating variables in response to various interventions is required.

More recently, the notion that dietary supplementation may offer thermoregulatory benefits or, alternatively, heighten the risk of heat illness when ingested in hot conditions has been considered (15-17). There are a number of motivations for individuals to consider dietary supplementation, such as ensuring adequate intake of certain nutrients, improving health, or supporting specific physiological functions (18, 19). Approximately 50% of US adults (20) and between 15 to 41% of UK adults (21) report dietary supplement use, with only a quarter of users taking supplements that have been recommended by a healthcare professional (22). Whilst such dietary supplements are not commonly consumed for the purpose of influencing thermoregulation, they may inadvertently affect it (16). As the popularity of dietary supplements continues to rise, in a world which is likely to experience more frequent, prolonged and intense heatwaves (23), research is needed to better understand the potential thermoregulatory effects upon human health and performance. For example, the amino acid taurine, often ingested

for its anti-oxidative and anti-hypertensive effects (24, 25), has more recently been reported to increase sweating rate/loss (a key modifiable heat dissipation pathway) by approximately 13% (26) and 27% (27) as well as reducing T_{core} compared to placebo in the heat (26, 28). Furthermore, another dietary supplement, creatine, is not typically considered to help in offsetting hyperthermia, but is commonly taken to improve high-intensity exercise performance (29). However, a review of its thermoregulatory effects highlighted that supplementation may be beneficial during exercise in high ambient temperatures due to its effects on fluid balance (17). Additionally, a recent meta-analysis established that pre-exercise hyperhydration with glycerol and/or creatine supplementation decreased the rate of rise in T_{core} after constant work exercise in both thermoneutral and hot conditions, compared to placebo (15).

Other commonly used supplements, such as dietary nitrate (NO_3^-), which has a key role in blood pressure regulation and endurance exercise enhancement (30, 31), does not appear to maintain all of these effects when humans are exposed to the heat (16). This is surprising, as there is a plausible mechanistic basis for thermoregulatory enhancement following ingestion of dietary nitrate and L-arginine, as both are known to improve NO (nitric oxide) bioavailability (32, 33). Specifically, NO bioavailability could have direct and indirect effects on eccrine sweat gland and microvascular function (34, 35). Indeed, other supplements, such as anti-oxidants (i.e. polyphenols), may support thermoregulation through protection of NO against oxidative destruction, thereby improving its bioavailability (36) and enhancing or preserving peripheral vasodilation. However, given that body fluid loss, and secondary hypovolemia, is accelerated in the heat (37), the reported reductions in blood pressure following supplementation with NO donors (38) could increase the risk of acute hypotension, particularly in the post-exercising state (39).

Branched-chain amino acids (BCAAs) have been extensively researched for their potential ergogenic role amongst athletes (40), yet have several health-related applications (41) and can be supplemented to account for age-related decline in lean muscle mass (42). Whilst less commonly supplemented for such reasons among the general population (43), BCAAs and other amino acids have a wide variety of biological roles. For example, tyrosine is used to enhance cognitive function (44, 45) and BCAAs have been reported to alleviate skeletal muscle damage and soreness following exhaustive and resistance exercise (46, 47). Given that both tyrosine and BCAAs may compete for the same blood-brain-barrier transporters, coupled with their wider roles in neurotransmitter biosynthesis pathways (48-50), sufficient balance of both supplements may be important during heat exposure. In a previous meta-analysis, the use of orally administered tyrosine or BCAAs (used separately), were capable of enhancing endurance exercise performance in the heat, but there was no effect on sub-maximal or maximal T_{core}

responses (16), thereby questioning their thermoregulatory role. Whilst many of the above-mentioned supplements are used more modestly across the population (43, 51), caffeine features in the daily intake of approximately 80 to 85% of people globally (52, 53) and is a prominent dietary supplement among athletes (54). However, caffeine has been reported to increase T_{core} when ingested before or during exercise in the heat (16), but its effects in the resting state have not been evaluated meta-analytically. Given the high prevalence of caffeine consumption, mixed with the understanding of its cardiometabolic side-effects (55, 56), this perhaps places one of the greatest risks to the general population when consumed in the heat. Collectively, it is apparent that supplementing the diet with some substances, could have implications for thermoregulatory capacity, and further research is required to understand the consistency and magnitude of effects reported across the empirical literature.

Based on the evidence, to date, a systematic evaluation of the effect of all dietary supplements on the primary modifiable thermoregulatory process of sweating, and subsequent T_{core} responses, is warranted. This is necessary to provide clarity on the magnitude and consistency of the effect of supplements on thermal balance during rest and exercise. This impact has not previously been fully considered, and there remains limited official guidance on dietary supplement intake for those exposed to thermally stressful conditions, such as athletes (57-59), and military personnel (60) or, indeed, the general public (61). Given the range of effects that different supplements appear to have on T_{core}, at least in the exercising state in the heat (16), coupled with the clear lack of specific guidance on this topic, a comprehensive evaluation of the collective evidence is an important step in developing an evidence-based understanding of the benefits or risks associated with using dietary supplements in hot conditions.

The aims of the current meta-analysis were to investigate the effects of all known orally administered dietary supplements on T_{core} and sweating responses in the heat. The effect of rehydration solutions, such as electrolytes, on thermal sweating have been thoroughly evaluated (37, 62, 63) and this was not replicated here; however, a number of factors were considered as moderators of T_{core} and sweating responses, such as hydration status among participants in studies evaluating dietary supplementation in the heat (64, 65). Likewise, training and acclimatization/acclimation status (11), protocol (rest *vs* exercise) and exercise intensity were considered to potentially impact thermoregulatory sweating and T_{core} (66-68). Environmental conditions, such as WBGT (and/or heat stress index; and vapor pressure) will also influence the ability to evaporatively cool (69, 70). Therefore, to evaluate the effects of dietary supplements on thermoregulation in the heat, these factors were considered as potential moderating variables and formed part of a secondary meta-regression analysis.

2. Methods

2.1 Search strategy

All of the available literature was searched and obtained according to the PRISMA guidelines, with a predetermined search strategy (71). Medical subject heading (MeSH) terms were active during the searches. There was no limit on the status, date or language of the publication. The final Boolean searches were performed in PubMed, SPORTDiscus (EBSCO) and Scopus on 9th April 2024. The search terms used were '(dietary supplements OR dietary supplementation OR nutritional supplements OR nutritional supplementation OR supplements OR supplementation OR ergogenic OR ergogenic aids OR nutraceuticals OR amino acids OR anti-oxidants OR vitamins OR minerals OR stimulants OR herbs OR herbal) AND (heat OR temperature OR sweat OR sweating OR sweat response OR sweating response OR sudomotor OR body temperature regulation OR thermoregulation OR thermoregulatory OR heat loss OR cooling OR evaporative OR evaporation OR thermal stress OR heat stress OR hyperthermia OR hyperthermic)'. As there is no *a-priori* list of dietary supplements that effect thermal balance, no supplements were searched individually by name. Two authors (JP and MW) verified the search terms and the accuracy of the returned results. 'Other sources' were also identified, such as through social media (Twitter or 'X'), the reference lists of included papers and additional database (Google Scholar) searching using various combinations of the above search terms.

2.2 Study selection

Any duplicates were removed, and titles and abstracts were screened for inclusion by two investigators (JP and MW), in accordance with agreed inclusion criteria. The single paper retrieved which had been published in a language other than English was translated digitally using two separate translation software programs; Google Translate and DeepL Translator (DeepL GmbH, Cologne, Germany). The reference lists of the initial papers were reviewed independently by two authors (JP and MW). The remaining articles were then assessed separately (and without influence) by JP and MW against the inclusion and exclusion criteria. There was 100% agreement in study selection between the two reviewers. Papers were required to have been published in a peer-reviewed journal as original research articles with a cross-over, randomized control trial, an intervention or an independent groups design. They must also have included a control or placebo group, and participants were required to be healthy

adults (≥ 18 years). To be included in this analysis, the studies must have: (1) administered a dietary supplement (by the definition below); (2) been conducted in an ambient dry-bulb temperature of ≥ 30 °C or WBGT ≥ 20 °C or small ranges up to those temperatures in either a laboratory or field setting. A WBGT of ≥ 20 °C was considered to provide sufficient heat stress, even when dry-bulb temperature was < 30 °C (72). Of the remaining papers, 71 were removed for the reasons outlined in Figure 1, which were primarily that they included supplements that were: a drug; not orally administered; a macro-nutrient or a rehydration solution (e.g. electrolytes or a supplement with a mechanism of action considered to be directly related to hydration). Other reasons were the absence of measures of T_{core} and the sweating response, or environmental issues.

A dietary supplement was defined by adapting the IOC position statement (58) and the European Food Safety Authority statement (19) as: a non-food, non-pharmacological, food component, nutrient or non-food compound that is purposefully orally ingested in addition to the habitual diet, for its nutritional or physiological effects. This may be to maintain sufficient intake of certain nutrients, correct deficiencies, or support physiological function, including thermoregulatory responses to the heat. The supplement is not being consumed for its calorific value, its effects on hydration (the mechanism of action is not through rehydration) and is not an energy drink. Ingestion of the supplement is also recognized to be legal as per the Misuse of Drugs Act 1971 (73) and is not on the World Anti-Doping Association's prohibited substances list (74).

2.3 Data extraction and quality assessment

Data were manually extracted independently by two authors (JP and MW) and entered into a custom-designed Microsoft Excel spreadsheet. Any discrepancies were verified by a third independent reviewer. Extracted data included: (1) characteristics of the sample (sex, age, health, training and heat acclimation/acclimatization status); (2) study design; (3) supplement, dose and timing of intake; (4) fluid intake before and during exercise (i.e. hydration status); (5) environmental conditions (temperature and humidity); (6) trial type (i.e. exercise type or rest and length); (7) peak T_{core} (rectal, gastrointestinal, esophageal or tympanic); and (8) bias. Risk of bias was assessed independently by two authors (JP and MW) according to the Cochrane collaboration guidelines (75). Where details of the study were unclear, the authors of the relevant papers were contacted for specific information or to clarify the method that was used. There was 100% agreement between the investigators concerning the outcome of this quality assurance procedure, hence, it was not considered necessary to include a third independent reviewer. There were three outcome measures for this meta-analysis: (1) T_{core} reported at the end of the trial, the end of the

exercising portion of the trial or at the point of the highest thermal strain, hereafter referred to as 'peak T_{core}'; (2) whole-body sweat rate (WBSR) across the trial or exercising portion of the trial; and (3) local sweat rate (LSR) reported at the end of the trial or at the point of the highest thermal strain.

2.4 Statistical analysis

Data analysis was performed by one author (JP). Data were extracted from the qualifying papers in the form of a mean, standard deviation (SD) and sample size (*n*) for the meta-analysis. Publicly available software (WebPlotDigitizer, Version 4.3) was used to extrapolate any unreported values from the figures to mean and SD data. Where data were expressed as mean and standard error (SE or SEM) or CI, they were converted to mean and SD. Authors of the original research articles were contacted for any missing data; however, if mean data were not accessible, these articles were excluded. If standard error or CI were missing, they were imputed using the sample pooled SD from similar included studies in accordance with Cochrane guidelines (75, 76). There were 17 instances (seven in the T_{core} meta-analysis and 10 in the WBSR meta-analysis) where no dispersion data (SD, SE, SEM or CI) were provided. For selected study designs (i.e. intervention studies with pre-post supplementation), the post-intervention values were extracted as the outcome measures for the 'supplementation condition' and the pre-intervention values as the 'placebo or control condition' (75). For cross-over trials (within-subject) or independent designs, the outcome measures for the supplementation condition were considered against the placebo or control condition. Standardized mean difference (SMD) was used to compare the results between studies utilizing different protocols and measures. Peak T_{core} outcome data were reported as peak T_{core} (°C) or rate of rise (°C·h^{-1}) of T_{core}. Mean, maximum, peak and mean body temperature were also included if peak T_{core} data were not provided. Whole-body sweating response outcome data were reported as WBSR (mL·min^{-1}) and body mass change (%). Outcome data representing WBSL (i.e. body mass or sweat loss and body mass change), reported in absolute L, mL, kg or g were converted to WBSR (mL·min^{-1}) using trial length data and WBSR reported in L·h^{-1} or mL·h^{-1} were directly converted to mL·min^{-1}. LSR outcome data reported in nL·min^{-1}, were converted to mg·cm·min^{-1} and reported as such.

Three meta-analyses were conducted, one for each outcome measure. These were performed in RStudio (R Core Team; (77)) and included 135, 106 and 11 comparison groups for the peak T_{core}, WBSR and LSR meta-analyses, respectively. Not all studies reported T_{core} or a sweating response data, hence, they were excluded from the respective analyses. All data were analyzed with a random-effects model, with heterogeneity assessed using the

I^2 statistic. Outliers were detected using a function in RStudio and influence on analysis investigated. Publication bias was accounted for by funnel plots and conducting Egger's test (78). Any adjustments to the effect sizes based on this procedure are reported in the results. Hedges' *g* and 95% CIs were used to express SMD between dietary supplementation and placebo groups across studies. Sub-analysis of the different dietary supplements included were conducted for all three meta-analyses. Meta-regressions were also conducted to determine the effect of candidate moderators on peak T_{core}, WBSR and LSR outcomes, as reported in each study: training status (highly trained *vs* recreationally active); heat acclimation status (heat acclimated *vs* non-heat acclimated); hydration status (euhydrated *vs* hypohydrated); fluid ingestion during exercise (fluid ingestion *vs* no fluid ingestion); duration of trial; WBGT; trial type (exercise *vs* rest); supplement dose (where sufficient no. of studies) and duration of supplementation (where applicable). The thresholds for the magnitude of effects were < 0.2, 0.2, 0.5 and 0.8 for *trivial, small*, *medium* and *large* effects, respectively (79). Alpha (α) was set at $P \leq 0.05$ for all analyses.

3. Results

3.1 Study selection

The initial searches retrieved 39,383 articles, which were reduced to 37,907 after removal of duplicates. After further screening and removal of reviews, animal studies and other irrelevant papers, 177 articles remained. Searches of social media (Twitter or 'X'), additional databases and reference lists within the 177 papers provided 32 further papers. Of the 209 articles, 52 were removed based on their incomplete compliance with the inclusion criteria and a further 33 were removed due to having: no full-text available, duplicate data with another paper or no extractable data. This left 124 papers, of which 117, 93 and 10 papers were included in the peak T_{core}, WBSR and LSR analyses, respectively (Figure 1). Sixteen papers had more than one comparison group and, therefore, one or more additional data sets were added to the analysis for each study. As these additional comparison groups shared participants, the sample size was reduced to mitigate any unit-of-analysis error, as per the Cochrane guidelines (75). Four papers also included multiple comparison groups; however, as these did not share participants, they were included without sample size adjustment. One paper was included without addition of the duplicate peak T_{core} data.

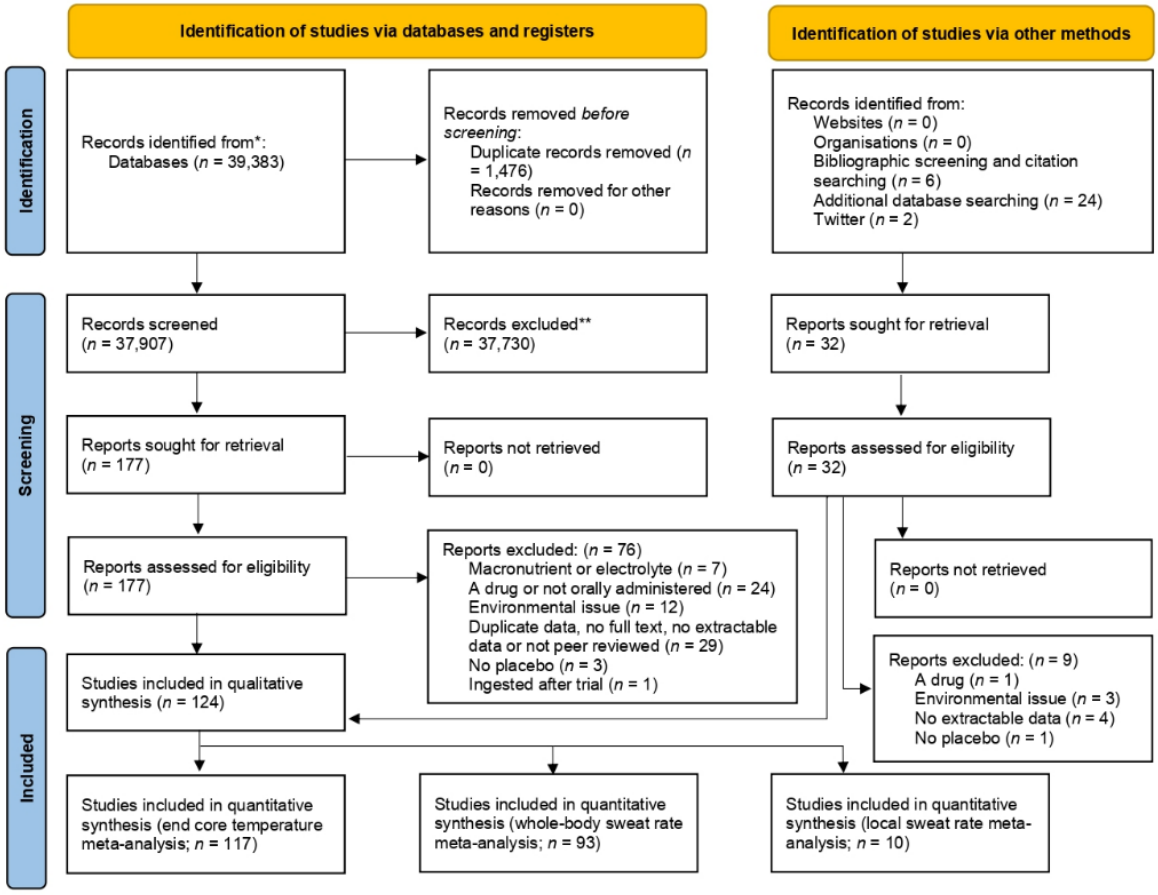


Figure 1. The process of study selection.

3.2 Study characteristics

The characteristics of the 124 included studies are summarized in Table 1. The studies included a total of 1,553 participants, comprising both males and females (males 90%; both males and females 9%; unreported 1%) of varying training (highly trained 43%; recreationally active 40%; unreported 18%) and heat acclimation statuses (heat acclimated 13%; non-heated acclimated 38%; unreported 49%). One hundred and six studies were cross-over designs, 12 studies were an independent groups design, and 6 studies were pre-to-post interventions. Thirty-nine different types of dietary supplements or supplement combinations were included in varying doses (Table 1). These were a combination of acute doses (single day; $n = 81$; 65%) and chronic administration (≥ 2 days; $n = 43$; 35%). The trial types included were exercise (90%) and rest (10%). The measures of T_{core} were rectal (62%), tympanic (10%), esophageal (9%), gastrointestinal (14%), oral (1%) and unreported (4%). The measures of body mass or sweat loss or sweat rate, representing WBSR were reported in L (7%), mL (7%), kg (17%) or g (3%),

$g \cdot m^{-2} \cdot h^{-1}$ (1%), % change (11%), $L \cdot h^{-1}$ (16%), $mL \cdot h^{-1}$ (1%) and $mL \cdot min^{-1}$ (8%) or were unreported (29%). Ambient dry-bulb temperature (mean 33.8°C; range 25 to 46.6°C), WBGT (mean 27.5°C; range 18.5 to 35.1°C) and RH% (mean 47%; range 12 to 80%) are reported herein. There were no adverse health-related events noted in any of the studies.

3.3 Meta-analysis

The results of the peak T_{core} meta-analysis (n = 135) are reported in Figure 2. Overall, the pooled analysis of all supplements revealed that there was a *trivial* non-significant positive effect on peak T_{core} compared to placebo (Hedges' g = 0.004, 95% CI -0.091 to 0.100, p = 0.930). The I^2 statistic demonstrated 20.6% heterogeneity. The results of the WBSR (n = 106) and LSR (n = 11) meta-analyses are reported in Figure 3 and Figure 4 respectively. Overall, WBSR (Hedges' g = 0.041, 95% CI -0.095 to 0.176, p = 0.559) and LSR (Hedges' g = 0.021, 95% CI -0.224 to 0.266, p = 0.869) had a *trivial* non-significant increase with dietary supplementation compared to placebo, with 1.7% and 0% heterogeneity (I^2), respectively

Table 1. Summary of studies included in the meta-analyses (n = 124).

Study	Design	Sample	Supplement, dose and timing	Temperature and relative humidity	Core temperature method	Trial type	Sweating measure
			Caffeine				
Anderson & Hickey (4)[2]	Double-blind, counter-balanced, placebo-controlled, cross-over	Moderately trained males (n = 8). Age 24 ± 3 years	Caffeine 5 mg·kg^{-1} (30 min pre-exercise)	28°C 50% RH WBGT 22.9°C	Rectal every 10 min (PCT)	60 min cycling @ 50% $\dot{V}O_{2max}$	No sweating response data reported
Beaumont & James (13)	Double-blind, randomized, repeated-measures, placebo-controlled, cross-over	Healthy, recreationally active, non-heat acclimated males (n = 8). Age 22 ± 1 years	Caffeine 6 mg·kg^{-1} (60 min pre-exercise)	30°C 50% RH WBGT 24.6°C	Gastrointestinal every 5 min (PCT)	60 min cycling @ 55% W_{max} followed by 30 min TT	Sweat rate (L). Converted to WBSR (mL·min^{-1})
Cheuvront et al. (34) A and B	Double-blind, randomized, placebo-controlled, cross-over	Healthy, physically active, moderately fit, non-heat acclimated males (n = 10). Age 23 (18-37) years	Caffeine 9 mg·kg^{-1} (timing not mentioned) A Quercetin 2000 mg (timing not mentioned) B	40°C 20-30% RH WBGT 28-30.1°C	Rectal every 5 min (PCT)	30 min cycling @ 50% $\dot{V}O_{2peak}$ followed by 15 min TT	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})
Cohen et al. (37) A and B	Double-blind, randomized, placebo-controlled, cross-over	Healthy, heat acclimatized, competitive male (n = 5) and female (n = 2) runners (n = 7). Age 33.3 ± 9.2 years	Caffeine 5 mg·kg^{-1} (60 min pre-exercise) A Caffeine 9 mg·kg^{-1} (60 min pre-exercise) B	WBGT 24-28°C	Tympanic pre and post exercise (PCT)	21 km running TT	Body mass change (%).

Del Coso et al. (49)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, heat acclimated, endurance trained males (*n* = 7). Age 27 ± 1 years.	Caffeine 6 mg·kg^{-1} (45 min pre-exercise)	36.0°C 29.0% RH WBGT 26.7°C	Rectal every 10 min (PCT)	120 min cycling @ 63% $\dot{V}O_{2max}$	Sweat loss (L). Converted to WBSR (mL·min^{-1})
Dias et al. (52)[1] A and B	Double-blind, randomized, independent design	Healthy males (*n* = 59; 20 *vs* 20 *vs* 19) Age 21.6 ± 6.9 years	Caffeine 3 mg·kg^{-1} (6 x 3 mg·kg^{-1}·d^{-1}; no timing mentioned) A Caffeine 6 mg·kg^{-1} (5 x 6 mg·kg^{-1}·d^{-1}; no timing mentioned) B	37.7°C 56.3% RH WBGT 32.4°C	Rectal (no T_{core} data reported)	90 min treadmill walking @ 5.6 km·h^{-1} with a 5% incline	Body-weight loss (kg). Converted to WBSR (mL·min^{-1})
Ely et al. (57)	Double-blind, counter-balanced, placebo-controlled, cross-over	Healthy, moderately fit, non-heat acclimated males (*n* = 10). Age 23 (range 19) years	Caffeine 9 mg·kg^{-1} (90 min pre-exercise)	40°C 25% RH WBGT 29.1°C	Rectal every 5 min (reported mean body temperature; End mean body temperature)	30 min cycling @ 50% $\dot{V}O_{2peak}$	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})
Falk et al. (58)	Double-blind, placebo-controlled, cross-over	Trained males (*n* = 7). Age 23.8 ± 2.4 years	Caffeine 5 mg·kg^{-1} (120 min pre-exercise) and 2.5 mg·kg^{-1} (30 min pre-exercise)	25°C 50% RH WBGT 20.3°C	Rectal every 15 min (PCT)	Treadmill walking @ 70-75% $\dot{V}O_{2max}$ (speed 1.56 s^{-1} with a 22-kg backpack)	Water loss (mL). Converted to WBSR (mL·min^{-1})
Ferreira et al. (62) A and B	Double-blind, randomized, placebo-controlled, cross-over	Well-trained, heat acclimated, male cyclists (*n* = 8). Age 23.9 ± 8.6 years	Caffeine 5 mg·kg^{-1} (60 min pre-exercise) A Caffeine 9 mg·kg^{-1} (60 min pre-exercise) B	30°C average, ranged from 28.5-32°C 71-78% RH WBGT 25.6-29.7°C	Tympanic pre and post exercise (PCT)	45 km cycling TT	Body mass loss (kg). Converted to WBSR (mL·min^{-1})

Fujii et al. (65)	Single-blind, randomized, placebo-controlled, cross-over	Healthy, physically active, non-heat acclimatized males (*n* = 12). Age 23 ± 2 years	Caffeine 5 mg·kg^{-1} (70 min pre-exercise)	37°C 50% RH WBGT 31°C	Esophageal continuously (T_{core} rate of rise °C/hr)	45 min cycling @ 55% $\dot{V}O_{2peak}$	Sweat loss (L). Converted to WBSR (mL·min^{-1})
Ganio et al. (74)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, trained, non-heat acclimated male cyclists (*n* = 11). Age 25 ± 6 years	Caffeine 3 mg·kg^{-1} (60 min pre-exercise)	33°C 41% RH WBGT 26.1°C	Rectal every 15 min (PCT)	90 min cycling @ 65% thermoneutral $\dot{V}O_{2max}$ followed by 15 min TT	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})
Gordon et al. (78)	Double-blind, independent design	Healthy, fit males (*n* = 10; 5 *vs* 5). Age 19.4 ± 1.5 years	Caffeine 5 mg·kg^{-1} (60 min pre-exercise)	26.7°C average, ranged from 24.5-28.9°C 41-54% RH WBGT 18.9-24.1°C	Rectal pre- and post-exercise (PCT)	120 min running	Sweat loss (kg). Converted to WBSR (mL·min^{-1})
Hanson et al. (83)[2] A and B	Single-blind, randomized, placebo-controlled, cross-over	Trained male (*n* = 6) and female (*n* = 4) endurance runners (*n* = 10). Age 26 ± 9 years	Caffeine 3 mg·kg^{-1} (60 min pre-exercise) A Caffeine 6 mg·kg^{-1} (60 min pre-exercise) B	30.6°C 50% RH WBGT 25.2°C	Gastrointestinal every 1 km (PCT)	10 km running TT	No sweating response data reported
Hunt et al. (95)[3] A and B	Double-blind, randomized, counter-balanced, placebo-controlled, cross-over	Healthy, non-heat acclimated, caffeine habituated males (*n* = 10) and females (*n* = 4; *n* = 14; A) and caffeine non-habituated males (*n* = 8) and females (*n* = 6; *n* = 14; B). Age	Caffeine 5 mg·kg^{-1} (60 min pre-exercise)	30.6°C 31% RH WBGT 22.6°C	Esophageal every 5 s (T_{core} rate of rise °C/hr)	60 min cycling @ 7 W·kg^{-1} $\dot{H}_{prod}$	WBSL (kg). Converted to WBSR (mL·min^{-1}). LSR at the back and arm (mg·min·cm^{-1}; ventilated

		27 ± 5 *vs* 23 ± 3 years					capsule technique)
John et al. (102)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, recreationally active, non-heat acclimated, non caffeine-habituated males (*n* = 12). Age 23 ± 4 years	Caffeine 5 mg·kg^{-1} (60 min pre-exercise)	35°C 40% RH WBGT 27.6°C	Rectal continuously (PCT)	Cycling @ thermoneutral GET	WBSR (mL·min^{-1}).
Kazman et al. (109)	Double-blind, randomized, placebo-controlled, cross-over	Healthy males and females (*n* = 32). Age 27 ± 8 years	Caffeine 7.5 mg·kg^{-1} (60 min pre-exercise)	40°C 40% RH WBGT 31.9°C	Rectal (no timing mentioned; PCT)	60 min treadmill walking @ 5 km·h^{-1} with 2% incline, followed by a 5 min stepping test (24 steps·min^{-1}) and 15 deep knee bends	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})
Kim & Lee (119)[1]	Randomized, cross-over	Healthy males (*n* = 9). Age 24.1 ± 3.5 years	Caffeine 3 mg·kg^{-1} (60 min pre-trial)	25°C 60% RH WBGT 21.3°C 42°C bath	No T_{core} data reported	30 min water immersion up to umbilical line	WBSL volume (mL). Converted to WBSR (mL·min^{-1})
MacNaughton et al. (144)[2]	Double-blind, counter-balanced, placebo-controlled, cross-over	Healthy males (*n* = 6). Age 22 range 19-25 years	Caffeine 5 mg·kg^{-1} (no timing mentioned)	28°C 42% RH WBGT 22°C	Rectal (no timing mentioned; PCT)	120 min resting	No sweating response data reported
Millard-Stafford et al. (158)	Double-blind, randomized, repeated-measures, placebo-	Healthy, highly trained male cyclists (*n* = 16). Age 27.5 ± 7 years	Caffeine 1.2 mg·kg^{-1} (0 min pre-exercise) and 3.5 mg·kg^{-1} (at 60 min)	28°C 60% RH WBGT 24°C	Rectal every 5 min (PCT)	120 min cycling @ alternating 15 mins of 60 and 70% $\dot{V}O_{2max}$ followed by 15 min TT	Sweat rate (mL·h^{-1}). Converted to WBSR (mL·min^{-1})

	controlled, cross-over						
Nakamura et al. (172)	Double-blind, randomized, placebo-controlled, cross-over	Trained male footballers (n = 8). Age 19.9 ± 0.3 years.	Caffeine 3 mg·kg^{-1} (60 min pre-trial)	31.7°C 63.5% RH WBGT 27.9°C	Rectal every 30 s (PCT)	2 x 43 min bouts consisting of 21 cycling intermittent sprints	Sweat volume (L). Converted to WBSR (mL·min^{-1})
Ping et al. (201)[2]	Double-blind, randomized, placebo-controlled, cross-over	Recreational, heat acclimated male runners (n = 9). Age 25.4 ± 6.9 years	Caffeine 5 mg·kg^{-1} (60 min pre-exercise)	31°C 70% RH WBGT 27.9°C	Rectal every 10 min (PCT)	Treadmill running @ 70% $\dot{V}O_{2max}$	No sweating response data reported
Pitchford et al. (202)	Double-blind, randomized, counter-balanced, placebo-controlled, cross-over	Highly trained, non-heat acclimated male cyclists (n = 9). Age range 22-42 years	Caffeine 3 mg·kg^{-1} (90 min pre-exercise)	35°C 25% RH WBGT 25.2°C	Gastrointestinal continuously (PCT)	Total work cycling TT	Body weight loss (kg). Converted to WBSR (mL·min^{-1})
Roelands et al. (213)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, trained, non-heat acclimated males (n = 8). Age 23 ± 5 years	Caffeine 6 mg·kg^{-1} (60 min pre-exercise)	30°C 50-60% RH WBGT 24.6-25.9°C	Rectal every 5 min (PCT)	60 min cycling @ 55% W_{max} followed by total work TT	Sweat rate (mL·min^{-1}).
Roti et al. (218) A and B	Double-blind, randomized, independent design	Healthy, active males (n = 59; 20 *vs* 20 *vs* 19). Age 21.6 ± 3.1 years	Caffeine 3 mg·kg^{-1} (6 x 3 mg·kg^{-1}·d^{-1}; no timing mentioned) A Caffeine 6 mg·kg^{-1} (6 x 6 mg·kg^{-1}·d^{-1}; no timing mentioned) B	37.7°C 56.3% RH WBGT 32.4°C	Rectal every 15 min (PCT)	90 min treadmill walking @ 1.56 m·s^{-1} with a 5% incline	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})

Stebbins et al. (242)[2]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, active males (*n* = 11). Age range 18-40 years	Caffeine 6 mg·kg^{-1} (0 min pre-trial and 45 min pre-exercise)	38°C 40% RH WBGT 30.2°C	Rectal periodically (Mean T_{core})	40 min resting followed by 35 min cycling @ 50% $\dot{V}O_{2max}$	No sweating response data reported
Suvi et al. (246)[1]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, physically active, non-heat acclimated males (*n* = 13) and females (*n* = 10; *n* = 23). Age 24.9 ± 4.1 *vs* 22.5 ± 2 years	Caffeine 6 mg·kg^{-1} (4 mg·kg^{-1} 60 min and 2 mg·kg^{-1} 0 min pre-exercise)	42°C 20% RH WBGT 29.5°C	Rectal every 1 min (PCT)	50 min treadmill walking @ 60% thermoneutral $\dot{V}O_{2peak}$ followed by TTE	Sweat production (mL·min^{-1})
			Creatine				
Branch et al. (23)	Double-blind, randomized, counter-balanced, placebo-controlled, cross-over	Healthy, competitive male cyclists and triathletes (*n* = 7). Age 38 ± 7 years	Creatine 100 g (5 x 20 g·d^{-1})	38°C 35% RH WBGT 29.3°C	Tympanic every 10 min (PCT)	60 min cycling @ 50% $\dot{V}O_{2max}$	Body mass loss (%)
Kern et al. (117)	Double-blind, randomized, independent design	Healthy moderately-highly active males (*n* = 20; 10 *vs* 10). *Age* 22.3 ± 3.6 years.	Creatine 335 g (5 x 21 g·d^{-1} followed by 23 x 10 g·d^{-1})	37°C 25% RH WBGT 26.7°C	Rectal every 15 min (PCT)	60 min cycling @ 60% $\dot{V}O_{2max}$	Body weight loss (%)
Kilduff et al. (118)	Double-blind, randomized, independent design	Endurance-trained, non-heat acclimated males (*n* = 21; 11 *vs* 10). Age 27 ± 5 *vs* 27 ± 4 years	Creatine 159.6 g (7 x 22.8 g·d^{-1})	30.3°C 70% RH WBGT 27.2°C	Rectal every 5 min (PCT)	Cycling @ incremental work rate at 60-90 rpm	Sweat rate (mL·min^{-1})
Mendel et al. (157)	Double-blind, independent design	Healthy, recreationally active, non-heat acclimated	Creatine 100 g (5 x 20 g·d^{-1})	39°C 26% RH	Rectal every 10 min (PCT)	40 min cycling @ 55% $\dot{V}O_{2max}$	Weight loss (kg). Converted to

		males (n = 15) and female (n = 1; n = 16 8 *vs* 8). Age 26 ± 3.6 *vs* 26 ± 1.9 years		WBGT 28.5°C			WBSR ($mL \cdot min^{-1}$)
Rosene et al. (215)[2]	Double-blind, randomized, cross-over	Regularly exercising males (n = 14). Age 21.1 ± 1.4 years.	Creatine 0.3 $g \cdot kg^{-1} \cdot d^{-1}$ (3 x 0.3 $g \cdot kg^{-1} \cdot d^{-1}$)	32.6°C 18.5% RH WBGT 22.1°C	Rectal every 5 min (PCT)	60 min treadmill running @ 60-65% $\dot{V}O_{2max}$	No sweating response data reported
Vogel et al. (261)[1]	Randomized, independent design	Healthy, recreationally active, non-heat acclimated males (n = 16; 7 *vs* 9). Age 22 ± 1 years	Creatine 100 g (5 x 20 $g \cdot d^{-1}$)	32°C 50% RH WBGT 26.5°C	T_{core} not measured	2 x 75 min exercise (4 x 10 min cycling bouts @ 30% initial sprint resistance at 60 rpm)	Body weight change (%)
Volek et al. (263)	Double-blind, randomized, independent design	Healthy males (n = 20; 10 *vs* 10). Age 23 ± 1 years	Creatine 0.3 $g \cdot kg^{-1}$)7 x 0.3 $g \cdot kg^{-1}$)	37°C 80% RH WBGT 34.8°C	Rectal every 5 min (PCT)	15 min cycling @ 70% $\dot{V}O_{2peak}$, followed by 15 min @ 60% $\dot{V}O_{2peak}$, followed by 3 x 10 s maximal sprints)	Sweat rate ($mL \cdot min^{-1}$)
Watson et al. (267)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, physically active, non-heat acclimated males (n = 12). Age 22 ± 1 years	Creatine 194 g (9 x 21.6 $g \cdot d^{-1}$)	33.5°C 41% RH WBGT 26.4°C	Rectal every 20 min (PCT)	80 min treadmill exercise (4 x 20 min sequences of 4 min resting, alternating 3 min walking, 1 min run x 3 and 4 min walk)	Sweat loss (kg). Converted to WBSR ($mL \cdot min^{-1}$)
Weiss & Powers (270)	Double-blind, randomized, counter-balanced, independent design	Healthy, aerobically trained males (n = 24; 12 *vs* 12). Age 22.9 ± 3.0 years	Creatine 125 g (5 x 25 $g \cdot d^{-1}$)	37°C %RH – not mentioned	Gastrointestinal every 10 min (PCT)	60 min cycling @ 70% age predicted maximum HR	Sweat loss (kg). Converted to WBSR ($mL \cdot min^{-1}$)

Wright et al. (278)	Single-blind, intervention	Physically active, heat acclimatized males (*n* = 10). Age 25.7 ± 4.9 years	Creatine 120 g (6 x 20 g·d^{-1})	35°C 60% RH WBGT 30.4°C	Rectal continuously (PCT)	6 x 10 s maximal cycling sprints	Sweat loss (kg). Converted to WBSR (mL·min^{-1})
			Glycerol				
Anderson et al. (5)[2]	Double-blind, randomized, placebo-controlled, cross-over	Endurance trained males (*n* = 6). Age 23.3 ± 6.6 years	Glycerol 1 g·kg^{-1} (120 min pre-exercise)	35°C 30% RH WBGT 26°C	Rectal every 15 min (PCT)	90 min cycling @ 98% L_T, followed by 15 min TT	No sweating response data reported
Coutts et al. (41)[1]	Randomized, placebo-controlled, cross-over	Well-trained heat acclimatized male (*n* = 7) and female (*n* = 3) triathletes (*n* = 10). Age 33.3 ± 7.3 years	Glycerol 1.2 g·kg^{-1} (130 min pre-exercise)	30.1-45.6°C 46.3-51.7% RH WBGT 23.9-32.9°C	No T_{core} data reported	Olympic distance triathlon	Sweat loss (%)
Desroches et al. (103)	Randomized, placebo-controlled, cross-over	Healthy, recreationally active males (*n* = 9) and females (*n* = 1; *n* = 10). Age 24 ± 4 years	Glycerol 1.4 g·kg^{-1} FFM (120, 100, 80 and 60 min pre-exercise)	30°C 50% RH WBGT 24.6°C	Gastrointestinal (no timing mentioned)	5 km treadmill running TT	Sweat loss (mL).
Dini et al. (54)[1] A and B	Randomized, independent design	High-level oarsmen (*n* = 14; 5 *vs* 5 *vs* 4). Age 26 ± 5 years	Glycerol 1 g·kg^{-1} (180 min pre-exercise) A Glycerol 1 g·kg^{-1} (1 g·kg^{-1} 180 min pre-exercise and 23 and 61 min during) B	36°C 30% RH WBGT 26.8°C	Rectal continuously (PCT)	89 min rowing	Fluid loss (mL). Converted to WBSR (mL·min^{-1})

Hillman et al. (91)	Randomized, placebo-controlled, cross-over	Healthy, non-heat acclimated trained male cyclists (n = 7). Age 28 ± 8 years	Glycerol 1.2 g·kg^{-1} (120 min pre-exercise)	35°C 40% RH WBGT 27.6°C	Rectal every 5 min (PCT)	90 min cycling TT	Body mass change (%)
Hitchins et al. (92)	Double-blind, counter-balanced, placebo-controlled, cross-over	Trained, non-heat acclimated male cyclists (n = 8). Age 27 ± 4.2 years	Glycerol 1 g·kg^{-1} (150 min pre-exercise)	33.2°C 57.8% RH WBGT 28.6°C	Rectal every 5 min (PCT)	60 min cycling (30 min @ fixed power output, followed by 30 min @ self-paced power output)	Sweat loss (%)
Kavouras et al. (107)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, endurance trained male cyclists (n = 8). Age 24 ± 3 years	Glycerol 1 g·kg^{-1} (30 min pre-exercise)	36.8°C 48.1% RH WBGT 30.5°C	Rectal every 4 min (PCT)	Cycling @ 74% $\dot{V}O_{2peak}$	Sweating (mL). Converted to WBSR (mL·min^{-1})
Latzka et al. (128)[3]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, heat acclimated males (n = 8). Age 23 ± 6 years	Glycerol 1.2 g·kg^{-1} (no timing mentioned)	34.9°C % RH (not reported) WBGT 30.3°C	Rectal and Esophageal (no timing mentioned)	120 min treadmill exercise @ 45% $\dot{V}O_{2max}$	Whole-body sweating rate (g·m^{-2}·h^{-1}). Local sweating rate of the upper arm (mg·min·cm^{-1}; ventilated capsule technique)
Lyons et al. (142)	Randomized, placebo-controlled, cross-over	Healthy, heat acclimatized males (n = 4) and females (n = 2; n = 6). Age 26.2 ± 3.7 years	Glycerol 1 g·kg^{-1} (150 min pre-exercise)	42°C 25% RH WBGT 30.6°C	Rectal every 15 min (PCT)	90 min treadmill exercise @ 60% $\dot{V}O_{2max}$	Sweat output (mL). Converted to WBSR (mL·min^{-1})
Marino et al. (146)	Double-blind, randomized, placebo-	Healthy, moderately-to-well trained males (n = 6) and females	Glycerol 1.2 g·kg^{-1} (150 min pre-exercise)	34.5°C 63.4% RH	Rectal every 5 min (PCT)	60 min cycling TT	Sweat rate (L·h^{-1}). Converted to

	controlled, cross-over	(n = 1; n = 7). Age 21.2 ± 2.4 years		WBGT 30.5°C			WBSR (mL·min^{-1})
McCullagh et al. (150)[1]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, well-trained males (n = 5) and females (n = 1; n = 6). No age provided	Glycerol 1.2 g·kg^{-1} (120 min pre-exercise)	30°C % RH (not reported) WBGT 30.3°C	No T_{core} data reported	150 min exercise (10 km treadmill running and 40 km cycling @ a set load [~177 W] followed by 5 km treadmill running TT)	Body weight loss (kg). Converted to WBSR (mL·min^{-1})
Scheadler (227)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, non-heat acclimatized, endurance trained males (n = 6). Age 27.8 ± 6 years	Glycerol 1.2 g·kg^{-1} (140 min pre-exercise)	30°C 50% RH WBGT 24.6°C	Gastrointestinal (no timing mentioned; PCT)	Set distance treadmill running @ ~83% $\dot{V}O_{2peak}$	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})
Wingo et al. (277)	Double-blind, randomized, repeated-measures, placebo-controlled, cross-over	Heat acclimatized male mountain bikers (n = 12). Age 24.5 ± 3.8 years	Glycerol 1 g·kg^{-1} (no timing mentioned)	WBGT 28.1°C	Rectal every 16 km (PCT)	48 km mountain-bicycle race	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})
			Sodium citrate				
Nelson et al. (177)	Blinded, randomized, placebo-controlled, cross-over	Healthy, non-heat acclimatized, moderately trained males (n = 12). Age 24.3 ± 4.2 years	Sodium citrate 0.2 g·kg^{-1} (100 min pre-exercise)	30.9°C 63.8% RH WBGT 27.2°C	Rectal every 5 min (PCT)	62 min cycling @ 15% below V_T (~60% $\dot{V}O_{2peak}$)	Sweat loss (L). Converted to WBSR (mL·min^{-1})
Sims et al. (238)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, non-heat acclimatized, endurance trained males (n = 8). Age 36 ± 11 years	Sodium citrate 7.72 g AND Sodium chloride 4.5 g (45 min pre-exercise)	32°C 50% RH WBGT 26.5°C	Rectal every 30 s (PCT)	Treadmill running @ 70% $\dot{V}O_{2max}$	Sweat loss rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})

Sims et al. (237)	Double-blind, randomized, counter-balanced, placebo-controlled, cross-over	Healthy, non-heat acclimatized, endurance trained females (n = 13). Age 26 ± 6 years	Sodium citrate 7.72 g AND Sodium chloride 4.5 g (20 min pre-exercise)	32°C 50% RH WBGT 26.5°C	Rectal every 1 min (PCT)	Treadmill running @ 70% $\dot{V}O_{2max}$	Sweat loss rate ($L \cdot h^{-1}$). Converted to WBSR ($mL \cdot min^{-1}$)
Suvi et al. (245)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, endurance trained males (n =20). Age 30.8 ± 5.4 years	Sodium citrate 200 $mg \cdot kg^{-1}$ (3 x 200 $mg \cdot kg^{-1} \cdot d^{-1}$; consumed the day before, the evening before and 120 min pre-exercise)	32°C 46% RH WBGT 25.9°C	Rectal every 1 min (PCT)	40 km cycling TT	Sweat production ($L \cdot h^{-1}$). Converted to WBSR ($mL \cdot min^{-1}$)
Vaher et al. (259)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, endurance trained, non-heat acclimated males (n = 16). Age 25.8 ± 4.4 years	Sodium citrate 500 $mg \cdot kg^{-1}$ (120 min pre-exercise)	32°C 50% RH WBGT 26.5°C	Rectal every 1 min (PCT)	5 km treadmill running TT	Body mass loss (kg). Converted to WBSR ($mL \cdot min^{-1}$)
			Sodium bicarbonate				
Katagiri et al. (106)[3]	Blinded, placebo-controlled, cross-over	Healthy males (n = 11). Age 23 ± 4 years	Sodium bicarbonate 300 $mg \cdot kg^{-1}$ (90 min pre-exercise)	35°C 40% RH WBGT 27.6°C	Esophageal every 1 s (PCT)	60 min cycling @ 50% $\dot{V}O_{2peak}$	Body weight loss (kg). Converted to WBSR ($mL \cdot min^{-1}$).
Katagiri et al. (105)[3]	Counter-balanced, placebo-controlled, cross-over	Healthy males (n = 13). Age 24 ± 2 years	Sodium bicarbonate 300 $mg \cdot kg^{-1}$ (95 min pre-exercise)	35°C 50% RH WBGT 29.1°C	Esophageal every 1 s (PCT)	60 min cycling @ 50% $\dot{V}O_{2peak}$	Body weight loss (%). Converted to WBSR ($mL \cdot min^{-1}$). LSR on the left forearm and chest ($mg \cdot min \cdot cm^{-1}$;

							ventilated capsule technique)
			Nitrate				
Amano et al. (2)[2,3]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, active males (n = 5) and females (n = 3; n = 8). Age 24 ± 4 years	Nitrate (NO_3^-) 8 mmol (2 x 8 mmol·d^{-1} and 8 mmol 120 min pre-exercise)	30°C 50% RH WBGT 24.6°C	Esophageal continuously (PCT)	30 min cycling @ 55% $\dot{V}O_{2max}$	LSR on the left ventral forearm and chest (mg·min·cm^{-1}; ventilated capsule technique)
Cramer et al. (42)	Intervention	Healthy males (n = 3) and females (n = 6; n = 9). Age 67 ± 5 years	Nitrate (NO_3^-) 16.8 mmol (6 x 16.8 mmol·d^{-1} and 16.8 mmol 120 min pre-trial)	42.5°C 34.2% RH WBGT 33°C	Gastrointestinal continuously (PCT)	120 min resting in a reclining chair	WBSL (kg). Converted to WBSR (mL·min^{-1})
Fowler et al. (64)[3]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, physically inactive, non-heat acclimated males (n = 11). Age 25 ± 5 years	Nitrate (NO_3^-) 9.2 mmol (5 x 9.2 mmol·d^{-1})	35°C 28% RH WBGT 25.7°C	Rectal every 1 min (PCT)	Cycling @ thermoneutral GET at 70 rpm	Body mass change (%). LSR on the chest, forearm, thigh and calf (nL·min^{-1}; ventilated capsule technique)
Kent et al. (115)[2]	Double-blind, repeated-measures, counter-balanced, placebo-controlled, cross-over	Endurance-trained male cyclists (n = 12). Age 26.6 ± 4.4 years	Nitrate (NO_3^-) 13 mmol (2 x 6.5 mmol·d^{-1} and 13 mmol 120 min pre-exercise)	35°C 48% RH WBGT 28.9°C	Gastrointestinal every 20% work rate (PCT)	Total work cycling TT	No sweat response data extractable

Kent et al. (114)	Double-blind, counter-balanced, placebo-controlled, cross-over	Endurance trained male cyclists (*n* = 12). Age 27 ± 6 years.	Nitrate (NO_3^-) 13 mmol (2 x 6.5 mmol·d^{-1} and 13 mmol 120 min pre-trial)	33.3°C 48.8% RH WBGT 27.5°C	Gastrointestinal every 5 min (PCT)	60 min cycling @ 60% $\dot{V}O_{2peak}$	Sweat loss (L). Converted to WBSR (mL·min^{-1})
Kuennen et al. (125)	Double-blind, randomized, counter-balanced, placebo-controlled, cross-over	Healthy, recreationally active males (*n* = 9). Age 24 ± 1 years	Nitrate (NO_3^-) 4.2 mmol (6 x 8.4 mmol·d^{-1}, with 4.2 mmol 2.5 h pre-trial)	41.2°C 15% RH WBGT 27.8°C	Rectal every 5 s (PCT)	45 min treadmill walking @ 4.83 km·h^{-1} with a 1.5% incline	Sweat rate (mL·min^{-1})
McQuillan et al. (155)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, well-trained endurance male cyclists (*n* = 8). Age 25 ± 8 years	Nitrate (NO_3^-) 8 mmol (2 x 8 mmol·d^{-1} and 8 mmol 90 min pre-exercise)	35°C 60% RH WBGT 30.4°C	Rectal continuously (PCT)	20 min cycling @ 40-60% PPO, followed by 4 km TT	Sweat loss (L·h^{-1}). Converted to WBSR (mL·min^{-1})
Smith et al. (239)[2]	Double-blind, randomized, counter-balanced, placebo-controlled, cross-over	Recreationally trained males (*n* = 12), Age 22 ± 4 years	Nitrate (NO_3^-) 6.2 mmol (180 min pre-exercise)	30°C 70% RH WBGT 26.9°C	Tympanic post IST (PCT)	20 x 6s cycling sprints (114s active recovery)	No sweating response data reported
			L-glutamine				
Nava et al. (175)[2]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, physically active, non-heat acclimated males (*n* = 7) and females (*n* = 4; *n* = 11). Age 28.3 ± 6.8 years	L-glutamine 0.15 g·kg^{-1} (60 min pre-exercise)	38°C 35% RH WBGT 29.3°C	Rectal (PCT)	87 min simulated fire-fighting exercise	No sweating response data reported
Ogden et al. (183)	Double-blind, randomized, counter-balanced, placebo-	Healthy, recreationally active, non-heat acclimated	L-glutamine 0.3 g·kg^{-1} FFM (60 min pre-exercise)	40.3°C 38% RH	Rectal every 10 min (PCT)	30 min treadmill running @ normothermic anaerobic LT	Sweat rate (L·h^{-1}). Converted to

	controlled, cross-over	males (n = 10). Age 29 ± 7 years		WBGT 31.8°C			WBSR ($mL \cdot min^{-1}$)
Ogden et al. (184)	Double-blind, randomized, counter-balanced, placebo-controlled, cross-over	Healthy, recreationally active, non-heat acclimated males (n = 12). Age 32 ± 6 years	L-glutamine 0.3 $g \cdot kg^{-1}$ FFM (60 min pre-exercise)	35.3°C 30.5% RH WBGT 26.3°C	Rectal every 20 min (PCT)	2 x 40 min bouts treadmill walking @ 6 $km \cdot h^{-1}$ with a 7% incline	WBSL ($L \cdot h^{-1}$). Converted to WBSR ($mL \cdot min^{-1}$)
Osborne et al. (186)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, trained, male cyclists (n = 12). Age 32 ± 6 years	L-glutamine 0.9 $g \cdot kg^{-1}$ FFM (60 min pre-exercise)	35.1°C 51% RH WBGT 29.4°C	Rectal every 2 s (Mean T_{core})	20 km cycling TT	Body mass loss (kg). Converted to WBSR ($mL \cdot min^{-1}$)
Pugh et al. (207)[2] A, B and C	Double-blind, randomized, placebo-controlled, cross-over	Healthy, recreationally active males (n = 10). Age 24 ± 4 years	L-glutamine 0.25 $g \cdot kg^{-1}$ FFM (120 min pre-exercise) A L-glutamine 0.5 $g \cdot kg^{-1}$ FFM (120 min pre-exercise) B L-glutamine 0.9 $g \cdot kg^{-1}$ FFM (120 min pre-exercise) C	30°C 40-45% RH WBGT 23.3-24°C	Rectal continuously (Mean T_{core})	60 min treadmill running @ 70% $\dot{V}O_{2max}$	No sweating response data reported
Zheng et al. (285)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, untrained males (n = 13). Age 20.2 ± 1.1 years	L-glutamine 0.6 $g \cdot kg^{-1}$ (30 min pre-exercise)	38°C 60% RH WBGT 33.2°C	Gastrointestinal continuously (PCT)	Treadmill running @ 40% $\dot{V}O_{2max}$	Body weight loss (kg). Converted to WBSR ($mL \cdot min^{-1}$)
Zuhl et al. (287)[2]	Double-blind, counter-balanced, placebo-	Healthy, endurance trained males (n = 8). Age 25 ± 4 years	L-glutamine 0.9 $g \cdot kg^{-1}$ FFM (7 x 0.9 $g \cdot kg^{-1} \cdot ffm \cdot d^{-1}$;	30°C 12-20% RH	Rectal (no timing mentioned; PCT)	60 min treadmill running @ 65-70% $\dot{V}O_{2max}$	No sweating response data reported

	controlled, cross-over		120 min pre-exercise)	WBGT 19.2-20.4°C			
Zuhl et al. (286)[2]	Double-blind, placebo-controlled, cross-over	Healthy, endurance trained males (n = 2) and females (n = 5; n = 7). Age 26 ± 4 years	L-glutamine 0.9 g·kg^{-1} FFM (120 min pre-exercise)	30°C 12-20 % RH WBGT 19.2-20.4°C	Rectal (no timing mentioned; PCT)	60 min treadmill running @ 70% $\dot{V}O_{2max}$	No sweating response data reported
			Bovine colostrum				
March et al. (145)[2]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, regularly exercising males (n = 12). Age 26 ± 6 years	Bovine colostrum 20 g (14 x 20 g·d^{-1})	30°C 60% RH WBGT 25.9°C	Rectal every 10 min (PCT)	60 min treadmill running @ 70% $\dot{V}O_{2max}$ with a 1% incline	No sweating response data reported
McKenna et al. (152)	Double-blind, randomized, counter-balanced, placebo-controlled, cross-over	Healthy, active males (n = 10). Age 20 ± 2 years	Bovine colostrum 20 g (14 x 20 g·d^{-1})	40°C 50% RH WBGT 33.5°C	Gastrointestinal every 5 min (PCT)	~46 min treadmill running @ 95% V_T	Sweat rate (mL·min^{-1})
Morrison et al. (170)[2] A and B	Double-blind, randomized, placebo-controlled, cross-over	Healthy, trained (n = 7; A) and untrained (n = 8; B; n = 15) males. Age 23 ± 4 *vs* 21 ± 2 years	Bovine colostrum 1.7 g·kg (7 x 1.7 g·kg^{-1}·d^{-1})	30°C 50% RH WBGT 24.6°C	Esophageal every 1 min (PCT)	15 min cycling @ 50% HRR, followed by 30 min treadmill running @ 80% HRR, followed by 30 min TT, followed by 15 min cycling @ 50% HRR	No sweating response data reported
			Probiotics				

Gill et al. (76)	Blinded, randomized, counter-balanced, placebo-controlled, cross-over	Healthy, endurance trained, non-heat acclimated male runners (n = 8). Age 26 ± 6 years	Probiotic L.casei 100 billion (7 x 10^{11}·d^{-1})	34°C 32% RH WBGT 25.5°C	Rectal every 10 min (Mean T_{core})	120 min treadmill running @ 60% $\dot{V}O_{2max}$	Body mass loss (%)
Shing et al. (234)	Double-blind, randomized, counter-balanced, placebo-controlled, cross-over	Healthy, trained, non-heat acclimated, male runners (n = 10). Age 27 ± 2 years	Probiotics 28 capsules (28 x 1 capsule·kg^{-1}·d^{-1} = 45 billion colony forming units)	35°C 40% RH WBGT 27.6°C	Gastrointestinal every 1 min (PCT)	Running @ 80% V_T	Body mass loss (kg). Converted to WBSR (mL·min^{-1})
			Blackcurrant extract				
Hiles et al. (90)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, recreationally active males (n = 12) and females (n = 6; n = 18). Age 27 ± 6 years	Blackcurrant extract 600 mg (7 x 600 mg·d^{-1})	34.1°C 40.8% RH WBGT 27°C	Rectal every 10 min (Mean T_{core})	60 min treadmill running @ 65% $\dot{V}O_{2max}$ with a 1% incline	Whole-body sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})
Lee et al. (129)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, recreationally active males (n = 12). Age 28 ± 6 years	Blackcurrant extract 600 mg (7 x 600 mg·d^{-1})	34.1°C 40.8% RH WBGT 27°C	Rectal every 10 min (PCT)	60 min treadmill running @ 70% $\dot{V}O_{2max}$ with a 1% incline	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})
			Tyrosine				
Coull et al. (40)	Double-blind, counter-balanced, placebo-controlled, cross-over	Recreationally active, non-heat acclimated males (n = 8). Age 23 ± 1 years	Tyrosine 150 mg·kg^{-1} (60 min pre-exercise)	40°C 30% RH WBGT 30.1°C	Rectal every 5 min (PCT)	60 min treadmill walk followed by 2.4 km TT wearing a 25 kg backpack	Sweat loss (L). Converted to WBSR (mL·min^{-1})

Kishore et al. (120)[2]	Double-blind, randomized, placebo-controlled, cross-over	Healthy males (*n* = 10). Age range 20-30 years	Tyrosine 6.5 g (90 min pre-trial)	45°C 30% RH WBGT 34.1°C	Oral temperature (Peak)	90 min resting	No sweating response data reported
Tumilty et al. (255)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, endurance exercising, non-heat acclimated males (*n* = 8). Age 32 ± 11 years	Tyrosine 150 mg·kg^{-1} (60 pre-exercise)	30°C 60% RH WBGT 25.9°C	Rectal every 10 min (PCT)	Cycling @ 68% $\dot{V}O_{2peak}$	Body mass loss (kg). Converted to WBSR (mL·min^{-1})
Tumilty et al. (254)	Double-blind, randomized, placebo-controlled, cross-over	Endurance exercising, non-heat acclimated males (*n* = 7). Age 20 (range 26) years	Tyrosine 150 mg·kg^{-1} (60 pre-exercise)	30°C 60% RH WBGT 25.9°C	Rectal every 5 min (PCT)	60 min cycling @ 57% $\dot{V}O_{2peak}$ followed by total work TT	Body mass loss rate (kg·h^{-1}). Converted to WBSR (mL·min^{-1})
Tumilty et al. (256) A, B and C	Double-blind, randomized, placebo-controlled, cross-over	Healthy, recreationally active, non-heat acclimated males (*n* = 8). Age 23 ± 4 years	Tyrosine 150 mg·kg^{-1} (timing not mentioned) A Tyrosine 300 mg·kg^{-1} (timing not mentioned) B Tyrosine 400 mg·kg^{-1} (timing not mentioned) C	30°C 60% RH WBGT 25.9°C	Rectal continuously (PCT)	60 min cycling @ 10% delta of the $\dot{V}O_2$ at GET plus 10% of the difference between GET and $\dot{V}O_{2peak}$, followed by a individualized work target TT	Body mass change (%)
Watson et al. (268)	Randomized, counter-balanced, placebo-controlled, cross-over	Physically active, trained, non-heat acclimated males (*n* = 8). Age 23 ± 3 years	Tyrosine 150 mg·kg^{-1} (120 min, 60 min and during)	30°C 50% RH WBGT 24.6°C	Rectal every 5 min (PCT)	Cycling @ 70% $\dot{V}O_{2peak}$	Sweat rate (mL·min^{-1})

BCAAs

Cheuvront et al. (33)	Placebo-controlled, cross-over	Healthy, physically active, moderately fit, heat acclimated males (n = 7). Age 21 ± 2 years	BCAAs 14 g (0 min pre- and during exercise)	40°C 20% RH WBGT 28°C	Rectal every 10 min (PCT)	60 min cycling @ 50% $\dot{V}O_{2peak}$ followed by 30 min TT	Fluid loss (%)
Macedo et al. (143)[2]	Double-blind, randomized, placebo-controlled, cross-over	Physically active males (n = 9). Age 25.4 ± 1.2 years	BCAAs 30 mg·kg^{-1} (120, 60 and 0 min pre-exercise and every 30 min during exercise)	35°C 60% RH WBGT 30.4°C	Rectal every 30 s (PCT)	Cycling @ 40% peak power at 50 rpm	No sweating response data reported
Mittleman et al. (161)	Double-blind, placebo-controlled, cross-over	Healthy, moderately trained males (n = 7) and females (n = 6; n = 13). Age 24 ± 2.9 *vs* 25.6 ± 7 years	BCAAs Females (9.4 g) and males (15.8 g; 5 mL·kg^{-1} of 5.88 g·L^{-1} (every 60 min at rest and 30 min during exercise)	34.4°C 39% RH WBGT 27°C	Esophageal every 5 min (PCT)	Cycling @ 40% $\dot{V}O_{2peak}$	Sweat loss (L). Converted to WBSR (mL·min^{-1})
Watson et al. (269)[2]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, endurance exercising, non-heat acclimated males (n = 8). Age 28.5 ± 8.2 years	BCAAs 4 x 250 mL at 12 g·L^{-1} (30 min intervals pre-exercise and 150 mL every 15 min during exercise)	30°C 38% RH WBGT 23.1°C	Rectal every 10 min (PCT)	Cycling @ 50% $\dot{V}O_{2peak}$	No sweating response data reported
			Taurine				
Page et al. (187)[3]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, non-heat acclimated males (n = 11). Age 23 ± 2 years.	Taurine 50 mg·kg^{-1} (120 min pre-exercise)	35°C 40% RH WBGT 27.6°C	Rectal every 1 min (PCT)	Cycling @ thermoneutral V_T at 80 rpm	Body mass change (g). Converted to WBSR (mL·min^{-1}). LSR on the chest, upper-arm

							thigh and calf ($nL \cdot min^{-1}$; ventilated capsule technique)
Peel et al. (192)[3]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, active, non-heat acclimated males (n = 12) and females (n = 3; n = 15). Age 27 ± 5 years	Taurine 50 $mg \cdot kg^{-1}$ (~60 min pre-exercise)	37.5 °C 34.2% RH WBGT 28.9 °C	Rectal every 5s (PCT)	45 min treadmill walking @ 200 W/m^2 $\dot{H}_{prod}$	WBSL (g; calculated from pre-post BM loss) LSR upper back (absorbent patch technique)
			GABA				
Miyazawa et al. (163)	Randomized, placebo-controlled, cross-over	Healthy, exercise trained males (n = 8). Age 22.8 ± 3.7 years	GABA 1 g (20 min pre-trial)	35°C 50% RH WBGT 29.1°C	Esophageal (no timing mentioned; PCT)	30 min semi-recumbent cycling @ 65% $\dot{V}O_{2peak}$ at 60 rpm	Sweat loss (g). Converted to WBSR ($mL \cdot min^{-1}$)
Miyazawa et al. (162)[3]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, moderately active males (n = 8). Age 23.5 ± 3.6 years	GABA 1 g (0 min pre-trial)	33°C 50% RH WBGT 27.3°C	Esophageal (no timing mentioned; PCT)	30 min resting	Sweat loss (g). Converted to WBSR ($mL \cdot min^{-1}$). LSR on the chest ($mg \cdot min \cdot cm^{-1}$; ventilated capsule technique)
			Betaine				
Armstrong et al. (6)[2]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, well-trained male runners (n = 10). Age 20 ± 2 years.	Betaine 5 g (45 min pre-exercise)	31.1°C 34.7% RH WBGT 23.6°C	Rectal periodically (PCT)	75 min treadmill running @ 65% $\dot{V}O_{2max}$ followed by TTE @ 84% $\dot{V}O_{2max}$	WBSR ($L \cdot h^{-1}$). No sweating data extractable

Willingham et al. (276)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, recreationally active males (n = 11). Age 29.1 ± 5.2 years	Betaine 50 mg·kg^{-1} (7 x 50 mg·kg^{-1}·d^{-1})	40°C 60% RH WBGT 35.1°C	Gastrointestinal every 15 min (PCT)	60 min resting	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})
			L-arginine				
Tyler et al. (258)	Double-blind, placebo-controlled, cross-over	Healthy, recreationally active, non-heat acclimated males (n = 8). Age 27 ± 6 years	L-arginine 10 g (30 min pre-trial)	35°C 50% RH WBGT 29.1°C	Rectal every 5 min (PCT)	90 min resting, followed by 30 min cycling @ 60% W_{max}, followed by 30 min resting	Body mass loss (kg). Converted to WBSR (mL·min^{-1})
			Ascorbic acid				
Carrillo et al. (27)[2]	Double-blind, randomized, independent design	Healthy, aerobically fit males (n = 8) and females (n = 4; n = 12; 6 *vs* 6). Age 23.4 ± 4.6 years.	Ascorbic acid (vitamin C) 1500 mg (9 x 1500 mg·d^{-1} and 8 mmol 120 min pre-exercise)	34.8°C 13% RH WBGT 22.8°C	Rectal pre and post exercise (PCT)	180 min cycling @ 55% $\dot{V}O_{2max}$	No sweating response data extractable
Kotze et al. (123) A and B	Placebo-controlled, independent design	Non-heat acclimated, males (n = 13; 4 *vs* 5 *vs* 4). Age 23 ± 3 *vs* 24 ± 2 *vs* 20 ± 2.9 years	Ascorbic acid (vitamin C) 250 mg (180-240 min pre-exercise) A Ascorbic acid (vitamin C) 500 mg (180-240 min pre-exercise) B	33.9°C %RH (did not mention)	Rectal every 60 min (PCT)	240 min block stepping @ 35 W workload	Sweat output (kg). Converted to WBSR (mL·min^{-1})
			Vitamin E				

Keong et al. (116)[2]	Double-blind, randomized, placebo-controlled, cross-over	Recreational, heat acclimated male athletes (*n* = 18). Age 24.9 ± 1.4 years	Vitamin E No dose stated (6 weeks)	31°C 70% RH WBGT 27.9°C	Rectal every 10 min (PCT)	Treadmill running @ 70% $\dot{V}O_{2max}$	No sweating response data reported
			Eurycoma longifolia Jack				
Muhamad et al. (171)	Double-blind, randomized, placebo-controlled, cross-over	Healthy, male recreational athletes (*n* = 12). Age 23.3 ± 3.7 years	Eurycoma longifolia Jack 150 mg (7 x 150 mg·d^{-1} and 150 mg 60 min pre-exercise)	31°C 70% RH WBGT 27.9°C	Tympanic every 10 min (PCT)	60 min treadmill running @ 60% $\dot{V}O_{2max}$ followed by 20 min TT	Sweat rate (L·h^{-1}). Converted to SR (mL·min^{-1})
			Oligonol				
Lee & Shin (132)[2,3]	Placebo-controlled, cross-over	Healthy males (*n* = 19). Age 23.7 ± 2.3 years	Oligonol 200 mg (7 x 200 mg)	26°C 60% RH WBGT 22.2°C 42°C bath	Tympanic (no timing mentioned; PCT)	30 min half body water immersion	LSR on the chest, back, abdomen and thigh (mg·min·cm^{-1}; ventilated capsule technique)
Lee et al. (131)[1]	Placebo-controlled, cross-over	Healthy males (*n* = 19). Age 23.7 ± 2.3 years	Oligonol 200 mg (7 x 200 mg)	26°C 60% RH WBGT 22.2°C 42°C bath	Tympanic (no timing mentioned; PCT)	30 min half body water immersion	WBSL volume (mL·30 min). Converted to WBSR (mL·min^{-1})
Shin et al. (232)[2]	Randomized, placebo-controlled, cross-over	Healthy males (*n* = 13). Age 21.8 ± 2.3 years.	Oligonol 100 mg (30 min pre-trial)	26°C 60% RH	Tympanic (no timing mentioned; PCT)	30 min lower leg water immersion	No sweating response data reported

				WBGT 22.2°C 43°C bath			
Shin et al. (233)[2]	Double-blind, randomized, placebo-controlled, cross-over	Healthy males (*n* = 17). Age 21.6 ± 2.1 years	Oligonol 100 mg (60 min pre-trial)	26°C 60% RH WBGT 22.2°C 42°C bath	Tympanic (no timing mentioned; PCT)	30 min half body water immersion	No sweating response data reported
			Polyphenols				
Trinity et al. (253)[2]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, well-trained male cyclists (*n* = 12). Age 26.8 ± 5 years	Polyphenols 3600-ppm (7 x 3600-ppm·d^{-1})	31.5°C 55% RH WBGT 26.7°C	Rectal continuously (PCT)	20 min cycling @ 40, 50, 60 and 70% followed by 30 min cycling @ 5% above L_T, followed by 10 min TT @ 90% $\dot{V}O_{2max}$	Body mass loss (kg). Converted to WBSR (mL·min^{-1})
			Curcumin				
Szymanski et al. (249)	Double-blind, counter-balanced, placebo-controlled, cross-over	Healthy, recreationally active, non-heat acclimated males (*n* = 6) and females (*n* = 2; *n* = 8). Age 19 ± 1 years	Curcumin 300 mg (3 x 500 mg·d^{-1}, with 300 mg 60 min pre-exercise)	37°C 25% RH WBGT 26.7°C	Esophageal every 5 min (PCT)	60 min treadmill running @ 65% $\dot{V}O_{2max}$	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})
			Quercetin				
Kuennen et al. (124)	Double-blind, counter-balanced, placebo-controlled, cross-over	Healthy, non-heat acclimated, physically active males (*n* = 8). Age 28 ± 4.8 years	Quercetin 2000 mg·d^{-1} (with breakfast)	46.6°C 21% RH WBGT 33.3°C	Rectal continuously (PCT)	45 min treadmill running @ 50% $\dot{V}O_{2max}$	WBSR (mL·min^{-1})

Menthol							
Bray et al. (24)	Double-blind, randomized, cross-over	Healthy, moderately trained, non-heat acclimated males (*n* = 5) and females (*n* = 5; *n* = 10). Age 23 ± 5 years	Menthol drink 85 mL (0.01% menthol; 0 min pre-exercise, every 10 min during and 1 min pre-TT)	35°C 54% RH WBGT 29.7°C	Rectal every 20 s (PCT)	40 min @ 50% $\dot{V}O_{2max}$, followed by 15 min TT	WBSL (kg). Converted to WBSR ($mL \cdot min^{-1}$)
Riera et al. (211)[2]	Randomized, placebo-controlled, cross-over	Healthy, heat acclimated, trained male cyclists and triathletes (*n* = 12). Age 42 ± 13 years	Menthol aroma 190 mL (0.5 g/L; 0.01% menthol; 15 and 0 min pre-trial and every 5 km)	30.7°C 78% RH WBGT 28.6°C	Gastrointestinal pre, post and every 5 km (PCT)	20 km cycling TT	No sweating response data reported
Vogel et al. (262)[2]	Double-blind, randomized, placebo-controlled, cross-over	Healthy, non-heat acclimated, endurance trained male (*n* = 8) and female (*n* = 6) runners (*n* = 14). Age 31 ± 6 years	Menthol gel 16 g (0.5% menthol; 5 min pre-exercise and 50 and 40 min mid-trial)	33°C 49% RH WBGT 27.2°C	Gastrointestinal every 10 min (PCT)	40 min treadmill running @ 60% HR_{max} at $\dot{V}O_{2max}$, followed by 20 min TT with a 1% incline	Body mass loss (kg). Converted to WBSR ($mL \cdot min^{-1}$)
Folic acid							
Gagnon et al. (73)[3]	Intervention	Healthy males (*n* = 3) and females (*n* = 6; *n* = 9). Age 68 ± 3 years	Folic acid 5 mg (42 x 5 $mg \cdot d^{-1}$)	42°C 30-70% RH WBGT 31.7-38.3°C	Esophageal continuously (PCT)	100 min resting	WBSL (kg). Converted to WBSR ($mL \cdot min^{-1}$). LSR on the forearm ($mg \cdot min \cdot cm^{-1}$; ventilated capsule technique)

Beta-glucan							
Zabriskie et al. (282)	Double-blind, randomized, counter-balanced, placebo-controlled. cross-over	Healthy, recreationally active males (n = 16) and females (n = 15; n = 31). Age 29.6 ± 6.7 *vs* 30.1 ± 8.9 years	Beta-glucan 250 mg (11 x 250 mg·d^{-1})	37.2°C 45.2% RH WBGT 30.3°C	Gastrointestinal every 10 min (PCT)	60 min treadmill walking @ 55% $\dot{V}O_{2peak}$	Body weight loss (kg). Converted to WBSR (mL·min^{-1})
Ginseng							
Ping et al. (200)[2]	Double-blind, randomized, placebo-controlled, cross-over	Recreational, heat acclimated male runners (n = 9). Age 25.4 ± 6.9 years	Ginseng 200 mg (60 min pre-exercise)	31°C 70% RH WBGT 27.9°C	Rectal every 10 min (PCT)	Treadmill running @ 70% $\dot{V}O_{2max}$	No sweating response data reported
Catechin							
Nishimura et al. (180)[2,3]	Placebo-controlled, cross-over	Healthy males (n =8). Age 26 ± 8 years	Catechin 121 mg/100 mL (4 mL·kg^{-1} 3 x (0, 30 and 60 min during)	35°C 75% RH WBGT 32.3°C 40°C bath	Tympanic (no timing mentioned; PCT)	90 min lower leg water immersion	LSR on the upper arm (mg·min·cm^{-1}; ventilated capsule technique)
Effective microorganism X							
Taylor et al. (251)[2]	Double-blind, randomized, cross-over	Males (n = 6). Age 22.0 ± 1.3 years	Effective microorganism X 70 mL (7 x 70 mL·d^{-1})	34.7°C 51.7% RH WBGT 29°C	Rectal every 5 min (PCT)	20 x 10 s IST @ maximal running velocity, with 80 s active recover @ 35% $\dot{V}O_{2max}$	No sweating response data reported
α-KG and 5-HMF							

Klarod et al. (121)	Randomized, placebo-controlled, cross-over	Healthy, regularly active males (n = 7). Age 2.7 ± 2.6 years	α-KG 4.8 g AND 5-HMF 60 mg (48 h pre-trial)	33°C 40% RH WBGT 26°C	Tympanic pre and post exercise (PCT)	Treadmill running @ 1 km·h·min^{-1} increases	No sweating response data reported
			Thermo Speed Extreme				
Pokora et al. (204)[2]	Double-blind, randomized, placebo-controlled, cross-over	Healthy males (n = 12) and females (n = 13; n = 25). Age 23 ± 1.3 years	Thermo Speed Extreme (green tea extract 5.1 mg·kg^{-1}, synephrine 0.3 mg·kg^{-1} and caffeine 3 mg·kg^{-1}; 0 min pre-trial)	26°C 56% RH WBGT 21.8°C	Tympanic periodically (PCT)	6 h resting	No sweating response data reported
			Whey protein				
Snipe et al. (240)	Randomized, cross-over	Healthy non heat acclimatized, endurance trained male (n = 6) and female (n = 5) runners (n = 11). Age 31 ± 5 years	Whey protein hydrolysate 15 g (0 min pre-exercise and every 20 min during)	35.5°C 27% RH WBGT 25.9°C	Rectal every 10 mins (PCT)	120 min treadmill running @ 60% $\dot{V}O_{2max}$	Body mass loss (%)
			Amino acids				
Costa et al. (39) A and B	Double-blind, randomized, counter-balanced, placebo-controlled, cross-over	Non-heat acclimated, endurance running trained males (n = 20; 10 *vs* 10). Age 32 ± 8 years	Amino acid beverage VS001 474 mL·d^{-1} (7 x 474 mL·d^{-1}; 237 mL 0 min pre-exercise and every 20 min during) A	34.6°C 38% RH WBGT 27.1°C	Rectal (no timing mentioned; PCT)	120 min treadmill running @ 60% $\dot{V}O_{2max}$	Body mass loss (%)

			Amino acid beverage VS006 474 mL·d^{-1} (7 x 474 mL·d^{-1}; 237 mL 0 min pre-exercise and every 20 min during) B				
Mixed supplements							
Bandyopadhyay et al. (10)[2]	Double-blind, randomized, placebo-controlled, cross-over	Recreational, heat acclimated male runners (n = 9). Age 25.4 ± 6.9 years	Caffeine 5 mg·kg^{-1} AND Ginseng 200 mg (60 min pre-exercise)	31°C 70% RH WBGT 27.9°C	Rectal every 10 min (PCT)	Treadmill running @ 70% $\dot{V}O_{2max}$	No sweating response data reported
Yu et al. (281)[2] A, B and C	Single-blind, randomized, placebo-controlled, cross-over	Healthy, non caffeine-habituated students (n = 12). Age 23.8 ± 2.4 years	Caffeine 5 mg·kg^{-1} (60 min pre-exercise) A Taurine 50 mg·kg^{-1} (60 min pre-exercise) B Taurine 5 mg·kg^{-1} AND Caffeine 50 mg·kg^{-1} (60 min pre-exercise) C	35°C 65% RH WBGT 31.1°C	Tympanic every 3 min (PCT)	Cycling @ thermoneutral V_T at 80 rpm	No sweating response data reported
Easton et al. (55) A, B[2] and C	Double-blind, randomized, intervention	Healthy, endurance trained males (n = 23; 12 [creatine and glycerol; creatine) *vs* 11 [glycerol]). Age 31 ± 7 years	Glycerol 1 g·kg^{-1} (6 x 1 g·d^{-1} and 1 g 5 h pre-trial) A Creatine	30°C 70% RH WBGT 26.9°C	Rectal every 5 min (PCT)	40 min cycling @ 63% WR_{max} followed by 16.1 km TT	Sweat rate (L·h^{-1}). Converted to WBSR (mL·min^{-1})

			120 g (6 x 20 g·d^{-1} and 10 g 5 h pre-trial) B Creatine 120 g (6 x 20 g·d^{-1} and 10 g 5 h pre-trial) AND Glycerol 1 g·kg^{-1} (6 x 1 g·d^{-1} and 1 g 5 h pre-trial) C				
Beis et al. (14)	Intervention	Healthy males (*n* = 14). Age 27 ± 8 years	Creatine 10 g, Glycerol 1 g·kg^{-1} AND Glucose 75 g (6 x creatine 10 g·d^{-1}, glycerol 1 g·kg^{-1} and glucose 75 g·d^{-1} and 5 h pre-exercise)	35.1°C 69.4% RH WBGT 31.8°C	Gastrointestinal every 5 min (PCT)	30 min treadmill running @ 60% $\dot{V}O_{2max}$, with a 1% incline	Sweat loss (L). Converted to WBSR (mL·min^{-1})
Polyviou et al. (205) A and B	Double-blind, randomized, intervention	Healthy, endurance trained males (*n* = 18; 9 *vs* 9). Age 31.5 ± 9 years	Creatine 20 g, Glycerol 2 mg AND Glucose 150 g (7 x creatine 20 g·d^{-1}, glycerol 2 mg·kg^{-1}·d^{-1} and glucose 150 g·d^{-1}) A Creatine 20 g, Glycerol 2 mg, Glucose	30°C 70% RH WBGT 26.9°C	No method mentioned, measured every 5 min (PCT)	40 min cycling @ pre-determined work rate, followed by 16.1 km TT	Sweat loss (mL). Converted to WBSR (mL·min^{-1})

	100 g AND Alpha lipoic acid 1000 mg (7 x creatine 20 g·d^{-1}, glycerol 2 mg·kg^{-1}·d^{-1}, glucose 100 g·d^{-1} and alpha lipoic acid 1000 mg) B	

TT time-trial, *TTE* time-to-exhaustion, *IST* intermittent-sprint-test, *PPO* peak power output, *PCT* peak core temperature, T_{core} core temperature, *RH* relative humidity, *WBGT* wet-bulb globe temperature, $\dot{V}O_{2max}$ maximal oxygen uptake, $\dot{V}O_{2peak}$ peak oxygen uptake, W_{max} watt maximum, WR_{max} work rate maximum, $\dot{H}_{prod}$ heat production, *PPO* peak power output, *HR* heart rate, L_T lactate threshold, *GET* gas exchange threshold, V_T ventilatory threshold, *rpm* revolution per minute, *WBSR* whole-body sweat rate, *WBSL* whole-body sweat loss, *LSR* local sweat rate, *FFM* fat free mass, *BCAAs* branched-chain amino acids, *GABA* gamma-aminobutyric acid, α-KG alpha-ketoglutaric acid, 5-HMF 5-hydroxymethylfurfural, [1] not included in peak core temperature analysis, [2] not included in the sweating response analysis, [3] included in local sweat rate analysis. Data are reported as mean ± SD. The table is a reflection of the studies, as reported by the authors of the original article.

1

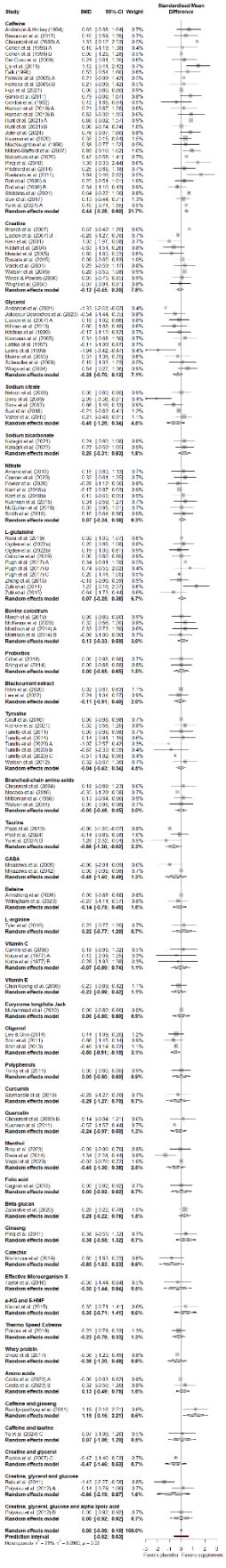
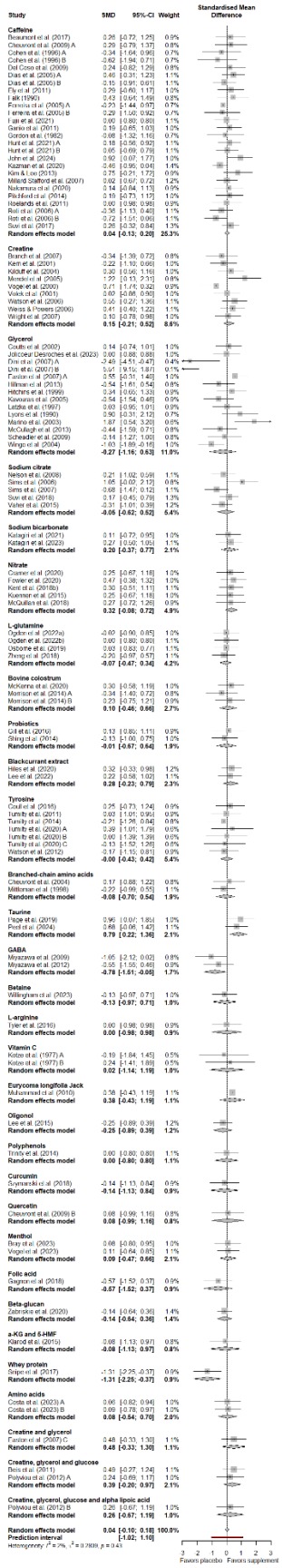


Figure 2. Effect of dietary supplementation on peak core temperature.



4

5 **Figure 3.** Effect of dietary supplementation on whole-body sweat rate.

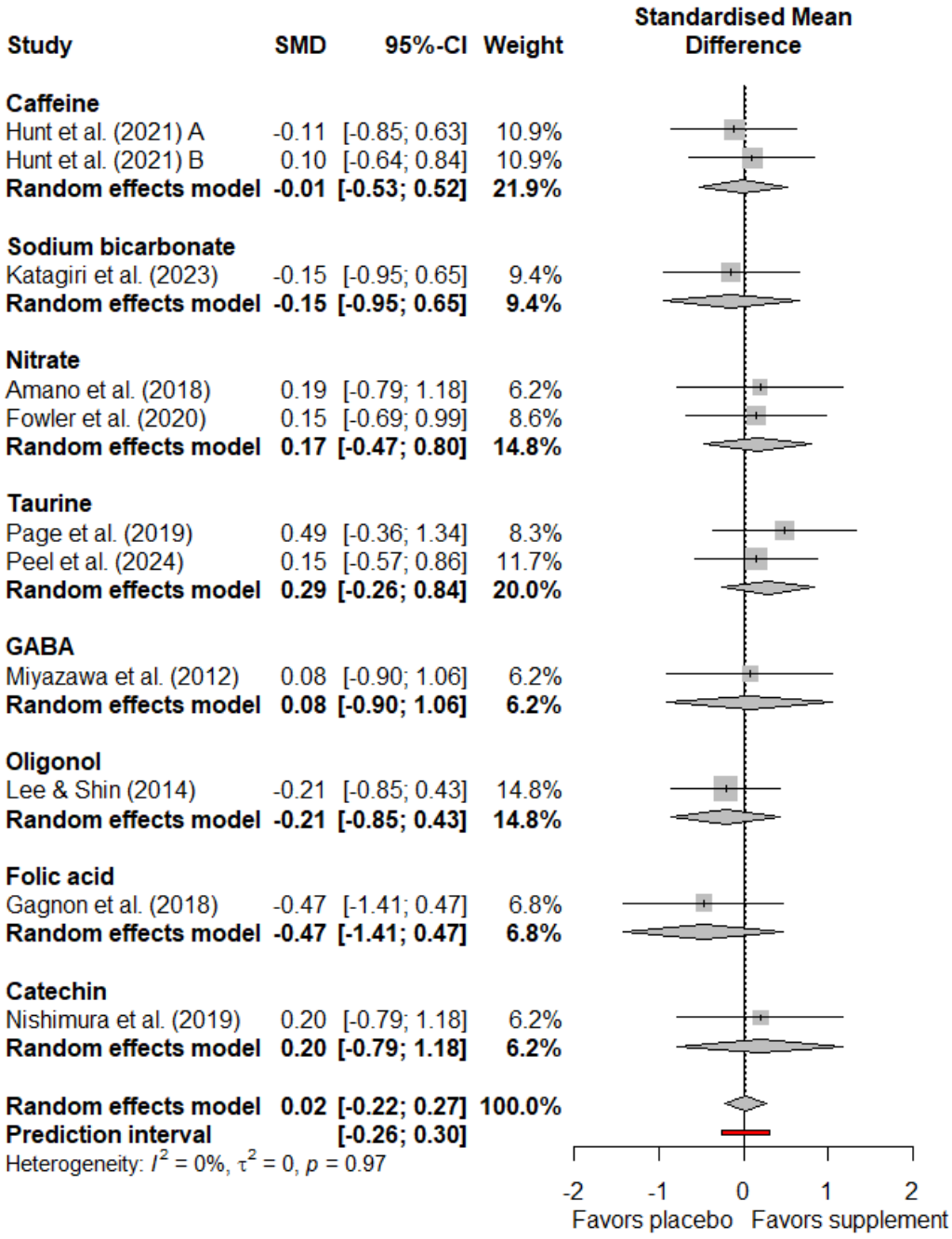


Figure 4. Effect of dietary supplementation on local sweat rate.

3.4 Sub-group analysis

3.4.1 Peak core temperature

Sub-group analysis demonstrated a significant overall pooled effect of the different dietary supplement categories on peak T_{core} (p = 0.015). However, the following supplements all demonstrated non-significant *trivial* effects on peak T_{core}: creatine (Hedges' g = -0.12, 95% CI -0.453 to 0.203, p = 0.456), nitrate (Hedges' g = 0.07, 95% CI -0.237 to 0.381, p = 0.648), L-glutamine (Hedges' g = 0.07, 95% CI -0.246 to 0.384, p = 0.667), bovine colostrum (Hedges' g = 0.13, 95% CI -0.327 to 0.588, p = 0.575), probiotics (Hedges' g = 0.00, 95% CI -0.653 to 0.653, p = 1.000), blackcurrant extract (Hedges' g = -0.11, 95% CI -0.461 to 0.453, p = 0.986), tyrosine (Hedges' g = -0.04, 95% CI -0.427 to 0.345, p = 0.835), BCAAs (Hedges' g = -0.004, 95% CI -0.327 to 0.588, p = 0.575), betaine (Hedges' g = -0.14, 95% CI -0.749 to 0.464, p = 0.646), vitamin C (Hedges' g = -0.07, 95% CI -0.891 to 0.743, p = 0.859), Eurycoma longifolia Jack (Hedges' g = 0.00, 95% CI -0.800 to 0.800, p = 1.000), polyphenols (Hedges' g = 0.00, 95% CI -0.800 to 0.800, p = 1.000), folic acid (Hedges' g = 0.00, 95% CI -0.924 to 0.924, p = 1.000), amino acids (Hedges' g = 0.13, 95% CI -0.492 to 0.753, p = 0.681), combined caffeine and taurine (Hedges' g = 0.07, 95% CI -1.063 to 1.200, p = 0.906) and combined creatine, glycerol, glucose and alpha lipoic acid (Hedges' g = 0.00, 95% CI -0.924 to 0.924, p = 1.000).

There were a number of caffeine-based supplements that increased T_{core}, with isolated caffeine (Hedges' g = 0.44, 95% CI 0.275 to 0.603, p < 0.001) having a *small* significant positive effect and combined caffeine and ginseng demonstrating a *large* significant positive effect (Hedges' g = 1.19, 95% CI 0.163 to 2.208, p = 0.023). L-arginine (Hedges' g = 0.22, 95% CI -0.765 to 1.203, p = 0.663), sodium bicarbonate (Hedges' g = 0.26, 95% CI -0.309 to 0.829, p = 0.370), beta-glucan (Hedges' g = 0.28, 95% CI -0.217 to 0.784, p = 0.268), ginseng (Hedges' g = 0.38, 95% CI -0.554 to 1.316, p = 0.424) and combined alpha-ketoglutaric acid (α-KG) and 5-hydroxymethylfurfural (5-HMF; Hedges' g = 0.35, 95% CI -0.709 to 1.408, p = 0.518) had *small* non-significant positive effects. Glycerol (Hedges' g = -0.28, 95% CI -0.700 to 0.130, p = 0.179), sodium citrate (Hedges' g = -0.46, 95% CI -1.261 to 0.341, p = 0.261), GABA (Hedges' g = -0.46, 95% CI -1.401 to 0.480, p = 0.337), vitamin E (Hedges' g = -0.23, 95% CI -0.889 to 0.423, p = 0.487), curcumin (Hedges' g = -0.28, 95% CI -1.268 to 0.704, p = 0.575), quercetin (Hedges' g = -0.24, 95% CI -0.973 to 0.496, p = 0.524), menthol (Hedges' g = -0.46, 95% CI -1.299 to 0.380, p = 0.283), Thermo Speed Extreme (Hedges' g = -0.23, 95% CI -0.785 to 0.327, p = 0.420), Effective microorganism X (Hedges' g = -0.30, 95% CI -1.441 to 0.841, p = 0.606), whey protein (Hedges' g = -0.36, 95% CI -1.201 to 0.486, p = 0.407) and combined creatine and glycerol (Hedges' g = -0.47, 95% CI -1.460 to 0.530, p = 0.359) had *small* non-significant negative effects.

There were some medium-to-large effects of supplementation on peak T_{core}, such as oligonol (Hedges' g = -0.50, 95% CI -0.907 to -0.101, p = 0.014) and taurine (Hedges' g = -0.66, 95% CI -1.296 to 0.022, p = 0.043), which

had a *medium* significant negative effect, and combined creatine, glycerol and glucose (Hedges' g = -0.66, 95% CI -2.187 to 0.873, p = 0.400) had *medium* non-significant effects. Catechin (Hedges' g = -0.80, 95% CI -1.825 to 0.235, p = 0.130) had *large* non-significant negative effects on peak T_{core}.

3.4.2 Whole-body sweat rate

Sub-group analysis demonstrated a non-significant overall pooled effect of the different supplement categories on WBSR (p = 0.434). Caffeine (Hedges' g = 0.04, 95% CI -0.129 to 0.203, p = 0.660), creatine (Hedges' g = 0.15, 95% CI -0.208 to 0.517, p = 0.403), sodium citrate (Hedges' g = -0.05, 95% CI -0.616 to 0.525, p = 0.875), L-glutamine (Hedges' g = -0.07, 95% CI -0.473 to 0.337, p = 0.742), bovine colostrum (Hedges' g = 0.10, 95% CI -0.457 to 0.659, p = 0.723), probiotics (Hedges' g = -0.01, 95% CI -0.666 to 0.642, p = 0.972), tyrosine (Hedges' g = -0.001, 95% CI -0.426 to 0.423, p = 0.995), BCAAs (Hedges' g = -0.08, 95% CI -0.703 to 0.540, p = 0.797), betaine (Hedges' g = -0.13, 95% CI -0.967 to 0.706, p = 0.760), L-arginine (Hedges' g = 0.00, 95% CI -0.980 to 0.980, p = 1.000), vitamin C (Hedges' g = 0.02, 95% CI -1.141 to 1.191, p = 0.967), polyphenols (Hedges' g = 0.00, 95% CI -0.800 to 0.800, p = 1.000), curcumin (Hedges' g = -0.14, 95% CI -1.126 to 0.838, p = 0.774), quercetin (Hedges' g = 0.08, 95% CI -0.992 to 1.156, p = 0.881), menthol (Hedges' g = 0.09, 95% CI -0.473 to 0.660, p = 0.746), beta-glucan (Hedges' g = -0.14, 95% CI -0.635 to 0.362, p = 0.591), amino acids (Hedges' g = 0.08, 95% CI -0.544 to 0.965, p = 0.877) and combined α-KG and 5-HMF (Hedges' g = -0.08, 95% CI -1.131 to 0.965, p = 0.877) all had *trivial* non-significant effects.

For WBSR, nitrate (Hedges' g = 0.32, 95% CI -0.083 to 0.716, p = 0.120), blackcurrant extract (Hedges' g = 0.28, 95% CI -0.227 to 0.791, p = 0.277), Eurycoma longifolia Jack (Hedges' g = 0.38, 95% CI -0.429 to 1.188, p = 0.358), sodium bicarbonate (Hedges' g = 0.20, 95% CI -0.368 to 0.768, p = 0.490), combined creatine and glycerol (Hedges' g = 0.48, 95% CI -0.332 to 1.296, p = 0.246), combined creatine, glycerol and glucose (Hedges' g = 0.39, 95% CI -0.195-0.975, p = 0.192) and combined creatine, glycerol, glucose and alpha lipoic acid (Hedges' g = 0.26, 95% CI -0.671 to 1.187, p = 0.586) had *small* non-significant positive effects. Glycerol (Hedges' g = -0.27, 95% CI -1.163 to 0.632, p = 0.562) and oligonol (Hedges' g = -0.25, 95% CI -0.886 to 0.392, p = 0.448) had a *small* non-significant negative effect.

There were a number of medium-to-large effects on WBSR, including GABA (Hedges' g = -0.78, 95% CI -1.514 to -0.053, p = 0.036), which had a *medium* significant negative effect and folic acid (Hedges' g = -0.57, 95% CI -1.523 to 0.373, p = 0.235), which had a *medium* non-significant negative effect. Taurine (Hedges' g = 0.79, 95%

CI 0.225 to 1.363, p = 0.006) had a *medium* significant positive effect and whey protein (Hedges' g = -1.31, 95% CI -2.248 to -0.371, p = 0.006) had a *large* non-significant negative effect.

3.4.3 Local sweat rate

Sub-group analysis demonstrated a non-significant effect of the different supplement categories on LSR (p = 0.886). Caffeine (Hedges' g = -0.005, 95% CI -0.529 to 0.519, p = 0.985), GABA (Hedges' g = 0.08, 95% CI -0.905 to 1.056, p = 0.880), nitrate (Hedges' g = 0.17, 95% CI -0.471 to 0.804, p = 0.608) and sodium bicarbonate (Hedges' g = -0.15, 95% CI -0.950 to 0.653, p = 0.717) had *trivial* non-significant effects. Catechin (Hedges' g = 0.20, 95% CI -0.787 to 1.180, p = 0.695), and taurine (Hedges' g = 0.29, 95% CI -0.261 to 0.835, p = 0.305) had *medium* non-significant positive effects. Oligonol (Hedges' g = -0.21, 95% CI -0.849 to 0.427, p = 0.517) and folic acid (Hedges' g = -0.47, 95% CI -1.414 to 0.467, p = 0.323) also had *medium* non-significant effects but decreased the local sweating response.

3.5 Meta-regression

Across the three meta-analyses, there were no significant moderating effects. The effect of several moderating variables on WBSR and LSR could not be assessed due to either an insufficient number of studies included in the analysis (supplement dose) or a lack of variation within the moderating variables in the included studies (e.g. training, heat acclimation and hydration status).

88 **Table 2.** Meta-regression of potential moderating variables of the peak core temperature, whole-body sweat rate and local sweat rate meta-analyses.

Moderator	Peak core temperature	Whole-body sweat rate	Local sweat rate
Training status	β = -0.019, p = 0.854 (n = 115)	β = -0.129, p = 0.416 (n = 89)	____
Heat acclimation status	β = 0.092, p = 0.617 (n = 71)	β = -0.440, p = 0.090 (n = 65)	____
Hydration status	β = -0.190, p = 0.764 (n = 105)	β = -0.126, p = 0.876 (n = 84)	____
Fluid ingestion during the trial	β = -0.018, p = 0.889 (n = 89)	β = -0.152, p = 0.416 (n = 73)	β = 0.078, p = 0.835 (n = 6)
Wet-bulb globe temperature	β = -0.008, p = 0.596 (n = 134)	β = -0.011, p = 0.655 (n = 105)	β = -0.003, p = 0.929 (n = 11)
Trial type	β = -0.249, p = 0.128 (n = 135)	β = -0.138, p = 0.640 (n = 106)	β = -0.238, p = 0.367 (n = 11)
Trial length	β = 0.001, p = 0.645 (n = 134)	β = -0.002, p = 0.202 (n = 105)	β = -0.002, p = 0.669 (n = 11)
Dosing duration	β = -0.005, p = 0.531 (n = 135)	β = -0.003, p = 0.844 (n = 106)	β = -0.014, p = 0.261 (n = 11)
Caffeine dose	β = 0.037, p = 0.465 (n = 30)	β = -0.065, p = 0.170 (n = 26)	____
Creatine dose	β = 0.057, p = 0.551 (n = 10)	β = 0.077, p = 0.448 (n = 9)	____

Glycerol dose	β = -0.340, p = 0.837 (n = 11)	β = -2.958, p = 0.124 (n = 14)	____
Sodium citrate dose	β = 2.157, p = 0.225 (n = 5)	β = -0.181, p = 0.911 (n = 5)	____
Nitrate dose	β = -0.006, p = 0.895 (n = 8)	β = -0.002, p = 0.967 (n = 5)	____
Glutamine dose	β = 0.015, p = 0.980 (n = 10)	β = -0.085, p = 0.919 (n = 4)	____
Tyrosine dose	β = -0.003, p = 0.183 (n = 8)	β = -0.001, p = 0.865 (n = 7)	____
Bovine colostrum dose	β = -0.001, p = 0.911 (n = 4)	____	____
BCAA dose	β = 0.045, p = 0.389 (n = 4)	____	____

89

3.6 Risk of bias

The studies included had a generally 'low' or 'unclear' risk of bias, with only 14 studies stating randomization procedures (26-28, 80-90) and three studies with pre-post intervention designs not randomizing or blinding (91-93). Allocation concealment was 'high' in three studies (91-93); Figure 5). A number of outliers were detected in the peak T_{core} meta-analysis (91, 94-103), owing to the large effects that were elicited by some supplements on peak T_{core} responses, but Egger's test showed that there was no publication bias ($p = 0.427$). Several outliers were detected in the WBSR meta-analysis (104-107); however, Egger's test indicated no publication bias ($p = 0.358$), and influence analysis demonstrated no outcome changes when these were removed. No outliers or publication bias ($p = 0.638$) were detected in the LSR meta-analysis (Figure 6).

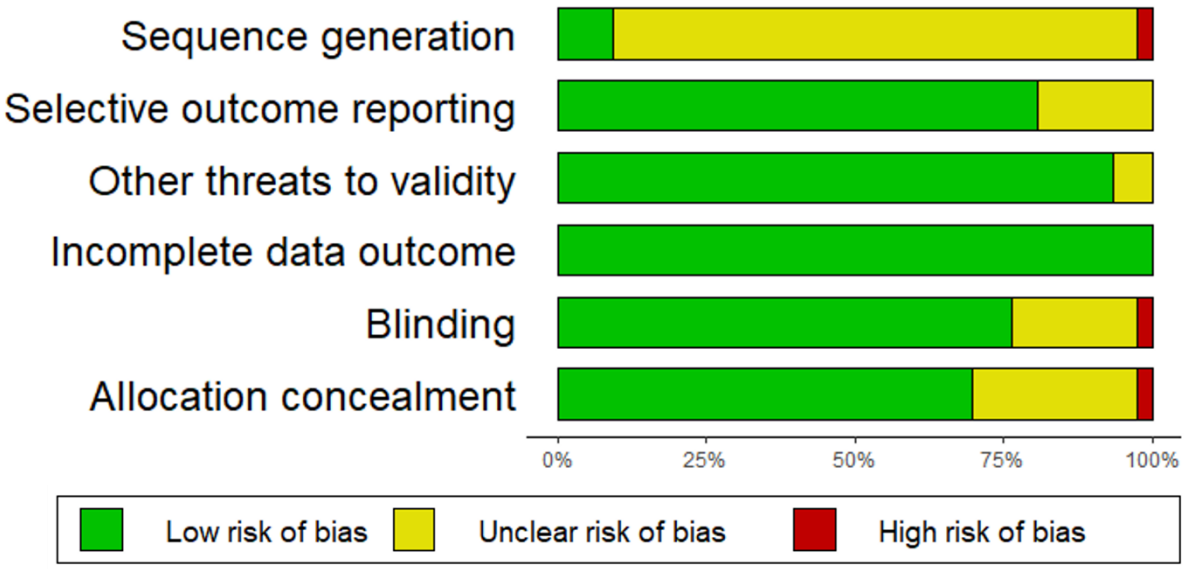


Figure 5. Risk of bias.

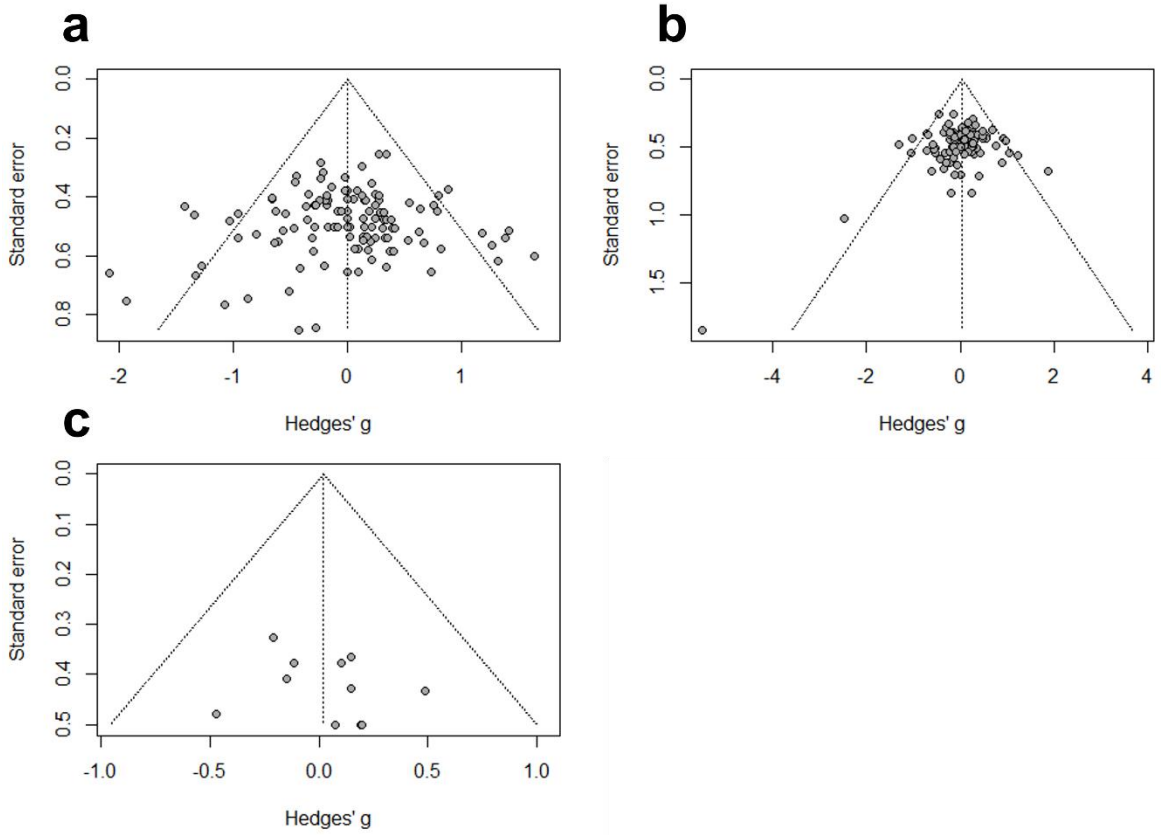


Figure 6. Publication bias for (a) peak core temperature, (b) whole-body sweat rate and (c) local sweat rate.

4. Discussion

The main findings of the current meta-analyses were that, overall, pooled analysis of all dietary supplements demonstrated no effect on peak T_{core} in the heat (Figure 2). However, there were differences between supplements, with caffeine, taurine and oligonol significantly affecting peak T_{core} responses, but to varying degrees and directions. Caffeine supplementation appeared to induce a thermogenic effect, while other supplements, such as taurine and oligonol lowered T_{core} responses compared to placebo. This is consistent with our previous meta-analytical findings on the thermal effects of caffeine and taurine during exercise in the heat (16), but this work has now expanded the evidence to a wider pool of supplements, across both resting and exercising conditions. Further, the additional analyses of sweating responses revealed that, collectively, dietary supplements may increase WBSR (Figure 3) but have limited effects on LSR, which is likely to be due to the smaller number of studies included in the analysis (Figure 4). Despite this, there was variation across supplements regarding their effects on sweating, with taurine demonstrating the greatest increases in WBSR and LSR, and others such as oligonol and folic acid,

reducing these responses. In the heat, sweating is the primary heat loss avenue, and as such, is responsible for limiting thermal gain (i.e. T_{core} increases). The findings herein, which indicate that dietary supplements may influence these aspects of thermoregulation, have implications for individuals exposed to hot environmental conditions. Further, as demonstrated by the meta-regression analysis (Table 2), there were also no moderating effects of training and heat acclimation status, hydration status, fluid ingestion during the trial and WBGT on the supplements' capacity to alter T_{core} and sweating responses. Thus, the effects reported are unlikely to be altered by other modifiable factors.

4.1 Nitrate, L-arginine and folic acid

In regard to WBSR and LSR, the current analysis revealed a *small* and *trivial*, non-significant positive effect of nitrate, which is a supplement well-established to improve NO bioavailability (32, 108). It is theorized that NO may contribute to eccrine sweat gland function, as local inhibition of NO synthase - NO's precursor – with N^G-nitro-L-arginine methyl ester (L-NAME), has been shown to attenuate sweat rate during moderate exercise in the heat (35, 109), though not all studies provide support for this (110). Further, NO also appears to have a role in regulating cutaneous vasodilation (111-113). Interestingly, numerous studies, in isolation, reported no significant increases in sweating (80, 92, 114-117), which equated to a *small* non-significant effect based on the collective evidence of the current meta-analysis. Therefore, the degree to which nitrate supplementation augments the sweating response is likely to be insufficient to elicit substantial thermoregulatory benefits. This is supported by the findings of the peak T_{core} analysis herein, where increases in sweating did not translate to reductions in T_{core}. These findings, in combination, therefore, question whether nitrate supplementation has the capacity to aid thermal balance in hot environmental conditions. In line with this, supplementation with other precursors to NO, specifically L-arginine and folic acid, demonstrated no significant thermoregulatory improvements, as peak T_{core} was not lower and sweat rate was not increased following their supplementation. Together, these results suggest that supplementation strategies aiming to increase NO bioavailability fail to enhance the sweating responses, and thus, opportunity to evaporatively cool when used in a hot environment. Interestingly, many of these studies also demonstrated no greater cutaneous blood flow or dry heat transfer capacity, thereby questioning any thermoregulatory advantage of nitrate or NO donors in the heat (80, 93, 118). Consequently, supplementation with ~4.2 to 16.8 mmol dietary nitrate, 10 g L-arginine or 5 mg folic acid cannot currently be recommended during heat exposure to improve thermal balance, but do not appear to have any deleterious effects.

147

148 **4.2 Caffeine**

149 The peak T_{core} analysis demonstrated that caffeine and caffeine in combination with ginseng had *small* and *large*
150 significant positive effects, respectively. Substantial rises in T_{core} can cause heat strain and, ultimately, lead to heat
151 exhaustion and heat stroke if not sufficiently controlled (6, 7). This is particularly the case during heat exposure,
152 or exercise in hot conditions, when avenues of dry heat dissipation are reduced due to a smaller temperature
153 gradient between the ambient air and skin's surface (69, 119). There is evidence that caffeine supplementation
154 increases $\dot{V}O_2$ and, consequently, heat production at comparable exercise intensities compared to placebo (96,
155 120), potentially explaining this observed T_{core} rise. Indeed, the $\dot{V}O_2$ response to exercise has been reported to be
156 increased by 3% to 15% following caffeine supplementation in the heat (98, 99, 121, 122), although others have
157 demonstrated negligible differences (95, 123, 124). These results could be attributed to the methodological
158 differences between studies, as noted by John et al. (83), which calls for improved standardization of laboratory
159 procedures in studies relating to thermoregulation and caffeine supplementation. In addition to the current results,
160 regarding T_{core}, WBSR and LSR were not increased with caffeine supplementation. Given the capacity of sweating
161 to help dissipate excess metabolic heat through evaporative cooling, these *negligible* effects would place greater
162 demand upon dry heat transfer. However, it appears that caffeine-mediated reductions in cutaneous blood flow,
163 owing to vasoconstriction of the skin microvasculature, would preclude this possibility (82, 125). Thus, greater
164 heat production, coupled with reduced SkBF and no increase in sweat production, explains why heat retention
165 would ensue and the observed rises in T_{core} reported herein. Indeed, the previous meta-analytical findings support
166 this observation and have been corroborated further by a recent meta-analysis, which demonstrated a $0.1°C \cdot h^{-1}$
167 greater T_{core} rate of rise following caffeine supplementation (126). Interestingly, combined caffeine and taurine
168 only had a *trivial* effect on peak T_{core}, theoretically due to taurine's thermolytic effect negating the additional heat
169 production elicited by caffeine. However, without $\dot{V}O_2$ data and corroboration of these findings, this remains
170 speculative. Overall, these results suggest that caffeine has an undesirable (i.e. heat gaining) effect on thermal
171 balance and questions its use in hot environmental conditions. Therefore, acute caffeine intake of between 3 to 9
172 $mg \cdot kg^{-1}$ prior to exercise, or at rest during heat exposure, should potentially be avoided due to its thermogenic
173 effect in such conditions. While caffeine intake has not been directly linked to heat illness cases, substances that
174 elevate T_{core} could result in an increased risk of heat related illnesses (127, 128).

175

176 **4.3 Taurine**

177 The current evaluation of sweating responses revealed that taurine had a *medium*, significant effect on peak T_{core}
178 and WBSR, as well as a *small,* non-significant positive effect on LSR. These studies suggest that ingestion of
179 taurine prior to exercise in the heat augmented the sweating response by hastening sweat onset (26) and increasing
180 sweat rate (26, 27). Theoretically, this would improve thermal balance, due to enhanced latent heat transfer and
181 reduced heat storage, delaying rises in T_{core} (1, 5). While this indicates that taurine can exert a beneficial
182 thermoregulatory effect, these findings require replication, including further insight into its mechanisms of action,
183 which are poorly understood. More thorough elucidation of taurine's effects on sweating and the consequential
184 impact on heat transfer and heat tolerance is necessary, alongside investigation of these mechanisms. However,
185 based on these studies, acute intake of 50 $mg \cdot kg^{-1}$ of taurine prior to exercise in the heat induces an earlier sweating
186 onset, greater sweating rate and lower T_{core} responses and may offer a strategy to improve thermoregulatory
187 capacity.

188

189 **4.4 Tyrosine, BCAAs and GABA**

190 Tyrosine and BCAAs demonstrated no significant effect on peak T_{core} or WBSR. Despite these amino acids
191 previously being reported to provide some of the greatest performance effects of any supplements during exercise
192 in the heat (16), they do not appear to confer thermoregulatory benefits. The ability to reduce central fatigue is
193 often ascribed to these supplements to explain their erogenicity in such conditions (129-132), but no apparent link
194 to temperature regulation was found in this meta-analysis. However, tyrosine is an essential substrate for tyrosine
195 hydroxylase, which is involved in axonal catecholamine synthesis (particularly norepinephrine; (133)). Thus,
196 sufficient tyrosine availability is required to maintain catecholamine levels and facilitate sympathetic
197 vasoconstrictive effects on the subcutaneous vasculature (134). This has been reported to attenuate the rate of
198 cold-induced decline in T_{core} among those likely to have tyrosine deficiency (134), but there were no similar effects
199 reported across studies conducted in the heat. Interestingly, another amino acid, GABA, has some potential to
200 offer thermoregulatory benefits, with the peak T_{core} analysis revealing a *small*, yet non-significant thermolytic
201 effect. While one of the two studies that supplemented GABA demonstrated null peak T_{core} effects, there was a
202 slower rate of rise in T_{core} across the 30-min exercising period (135). GABA is a widely distributed
203 neurotransmitter within the central nervous system, where it acts in the hypothalamus to regulate internal body
204 temperature (136-138). Exogenous supplementation in humans is thought to increase GABA's availability in the

hypothalamus (139) and, thereby, influence temperature regulation (135). The hypothalamus contains cold-sensitive neurons, which have a role in controlling heat production upon detection of local and peripheral temperature changes (140, 141). In the animal model, suppression of these neurons appears to occur following GABA administration, leading to lowered T_{core} responses in the heat (142). Indeed, the two original research articles included in the current meta-analysis (135, 143) observed reductions in metabolic heat production, which could in part explain the effects on T_{core} in the GABA supplementation conditions. Additionally, GABA attenuates activity of the sympathetic nervous system (144, 145), which would likely suppress epinephrine and norepinephrine release (146), as observed by Miyazawa et al. (143). Reductions in catecholamines have been associated with slower rises in T_{core} during hyperthermic exercise (147), which is supported by the findings herein. Considering these effects on heat production, it is unsurprising that there was also a *large*, significant reduction in WBSR and a *trivial* effect on LSR, as it is a known driver of the thermal sweating response (5, 66, 68). Therefore, while GABA appears to reduce one avenue of heat dissipation (i.e. evaporative cooling), it has created a greater heat storage capacity, which would delay the onset of hyperthermic symptoms during heat stress and may be effective during short duration exercise in the heat. Based on the two studies herein, the administration of 1 g of GABA directly prior to heat exposure (rest or exercise) appears to provide a beneficial effect on thermal balance through a reduction in heat gain. However, acute tyrosine and BCAA intake would not be a useful supplement in hot environmental conditions, due to the null impacts on thermoregulation.

4.5 Glycerol and creatine

The peak T_{core} analysis herein revealed *small*, non-significant negative effects for glycerol and combined creatine and glycerol supplementation. *Medium*, non-significant negative effects were observed for combined creatine, glycerol and glucose and *trivial*, non-significant effects for creatine and combined creatine, glycerol, glucose and alpha lipoic acid. While these results demonstrate that glycerol supplementation had a *small*-to-*medium* effect on peak T_{core}, the variation across studies decreased the certainty of these findings, rendering them non-significant. When ingested, glycerol provides osmotic pressure in the plasma and intra- and extra-cellular water compartments – where concentrations are evenly distributed – and thereby increase their water content (15, 148, 149). Creatine acts similarly, as its transport into cells (primarily skeletal muscle) increases total body water through expansion of intra- and extracellular water compartments, with even fluid distribution (150-152). This increase to total body water and plasma volume expansion induces ‘hyperhydration’ and affords excess fluid to compensate for sweat

losses (153, 154), alongside providing greater availability to sweat glands to facilitate sweat production (155). This would likely improve thermoregulatory capacity, through increased evaporative cooling, but also because additional total body water enhances the specific heat carrying capacity of the tissues and blood (156-158). Here, it can help transfer heat from the core to the periphery to be dissipated (159-161).

Creatine had a *trivial*, non-significant positive effect on WBSR, and combined creatine and glycerol, combined creatine and glycerol with the addition of glucose and combined creatine and glycerol with the addition of glucose and alpha lipoic acid had *small*, non-significant positive effects. The role of glycerol combined with creatine was, therefore, also partially effective in promoting a sweating response but, as with the peak T_{core} responses, the effects were inconsistent across studies, which increased the uncertainty of the *small* effects. Surprisingly, glycerol alone had a *small*, non-significant negative effect on WBSR. Though, this was largely influenced by two glycerol supplementation conditions from the same study, where much larger fluid losses in the placebo group were reported (104). Collectively, it appears that these supplements may be capable of lowering T_{core} and enhancing sweating responses compared to placebo, with the combination of creatine and glycerol potentially providing the greatest thermoregulatory benefit. However, with the large inconsistencies between studies and non-significant findings this is far from established, and further work is required to understand the heterogeneity of responses. For WBSR this could be dose related, as for glycerol, Dini et al. B (104) provided the highest glycerol dose (3 $g \cdot kg^{-1}$) and observed a large, negative effect on WBSR. Theoretically, glycerol ingestion of a large quantity may surpass concentrations that can be absorbed into the intra- and extra-cellular fluid, further elevating plasma concentrations and increasing osmotic pressure. This may prevent fluid being drawn from the plasma to the sweat glands, thereby decreasing sweat rate. Without further investigation into the effect of glycerol dose on the sweating response, more specifically, this remains speculative. Indeed, despite the outcome from this single study, the moderating effect of glycerol dose on WBSR was not significant. Overall, these findings demonstrate that lower doses of glycerol (1 to 1.4 $g \cdot kg^{-1}$), alone or in combination with 20 to 25 $g \cdot d^{-1}$ of creatine for between 3 to 9 days, appear to aid thermal balance during exercising heat stress, through hyperhydration. Additional investigation into whether this supplementation strategy would provide similar benefits during passive heating is also warranted. Higher doses of glycerol (e.g. 3 $g \cdot kg^{-1}$), however, may reduce this capacity due to lower sweat rates, though a greater understanding is necessary before providing definitive recommendations.

4.6 Sodium citrate and sodium bicarbonate

As supplements often ingested prior to high-intensity exercise to improve blood buffering capacity, both sodium citrate and sodium bicarbonate have also been reported to increase plasma osmolality and plasma volume (162). This could feasibly help with thermoregulation in the same manner as creatine or glycerol loading; indeed, ingestion of sodium citrate had a *small*, yet non-significant negative effect on peak T_{core}, which was similar to the previous supplements detailed above. However, this was not coupled with a greater WBSR. Conversely, sodium bicarbonate had a *small*, non-significant positive effect on T_{core}. In these two studies, the placebo group ingested sodium chloride to match the sodium content of the two conditions, as they were investigating the buffering capacity of the supplement and not its effects on fluid balance (162-164). Therefore, it is likely that any potential osmotic effects that could theoretically have aided thermoregulation, would be indistinguishable from the effects in the placebo condition. In support of this, there was a *small*, non-significant positive effect on WBSR and no effect on LSR. To establish whether sodium bicarbonate's effects on fluid balance can aid thermoregulatory function in hot environmental conditions, studies would need to be conducted with a placebo group that does not contain any sodium. It appears that sodium citrate can potentially improve thermoregulatory capacity in the heat, though this was inconsistent across studies. Any thermolytic effect is likely due to its effects on plasma volume, as expansion was observed across all studies included in the analysis, but to a larger degree in the studies which demonstrated lower T_{core} responses. As there was no greater WBSR associated with the lower T_{core} response, a greater heat carrying capacity of the blood may be responsible for these observed effects (156, 158). However, further research is required to corroborate these findings and establish whether sodium bicarbonate can elicit the same benefits. Therefore, based on the studies included in this analysis, there is evidence to suggest that acute sodium citrate ingestion of ~100 to 600 $mg \cdot kg^{-1}$ can improve thermoregulatory capacity during exercise in the heat, but more research is needed to establish these effects at rest and with sodium bicarbonate supplementation.

4.7 Betaine

Betaine is an amino acid, which acts as both an osmolyte, to assist with cell volume regulation, and as a methyl group donor to convert homocysteine to methionine (165). It can be supplemented to reduce high plasma concentrations of homocysteine (166) or to improve endurance and resistance exercise performance (167). Due to its osmotic role, it has mechanistic potential to aid fluid balance and thermoregulation during exposure to heat stress (168). However, both the current peak T_{core} and WBSR analyses demonstrated no effects. In addition to the measured variables in the current meta-analysis, one of the included studies observed plasma volume expansion

across the study in response to betaine supplementation (169); however, the other did not (168). Together, these results question whether betaine is efficacious for fluid balance when ingested prior to exercise in the heat. There is also some evidence to suggest that betaine may attenuate thermal cellular stress in a similar manner to heat shock proteins (170, 171) and in animal models, it has repeatedly been demonstrated to reduce T_{core} when chronically supplemented (172-174). Therefore, betaine may have the capacity to improve heat tolerability, and considering the limited and equivocal evidence in humans, this supplement requires further investigation.

4.8 Anti-oxidants and anti-inflammatories

In the current meta-analysis, lower peak T_{core} responses for several supplements with known anti-oxidative and anti-inflammatory properties were found. Oligonol and catechin, had a *medium*, significant and a *large*, non-significant negative effect on peak T_{core}, respectively. Furthermore, *small*, non-significant negative effects were observed for curcumin, vitamin E and Effective microorganism X (an anti-oxidant mixture) and *trivial*, non-significant negative effects for blackcurrant extract. The anti-inflammatory role of oligonol, catechins, curcumin, vitamin E, Effective microorganism X is most likely responsible for the lowered T_{core} responses compared to placebo, where endogenous pyrogenic cytokines (175) may be attenuated. Indeed, oligonol supplementation lowered circulating levels of the pyrogenic cytokines, such as interleukins IL1-β and IL-6 (176), along with reductions in serum prostaglandin E_2, a known intermediary in the development of fever (177, 178). The cytokine response can be acutely lowered with anti-inflammatory substances (179), theoretically leading to decreased thermal gain (180), explaining why the rate of rise in T_{core} was reduced, despite no greater WBSR or LSR. However, not all of these studies observed reductions in pro-inflammatory cytokines (84, 181), despite attenuated increases in T_{core}. All trials investigating oligonol and catechin – which had the greatest effects – induced heat strain via hot water immersion of the lower body at rest. This is a rapid means by which to facilitate heat gain, as water is highly conductive (182), yet it partially attenuates other avenues of heat dissipation, such as evaporation (1). It is possible that an immersive protocol induced greater thermal strain and production of pyrogenic cytokines, meaning that T_{core} responses were more readily identified between conditions. However, the rise in T_{core} within these trials was less than would be expected, only reaching an average of 37.52°C across all trials; although this was with tympanic measurement, which may explain the relatively low T_{core} values. Another explanation for lower peak T_{core} responses is increased heat dissipation; however, sweating was only greater following catechin and blackcurrant supplementation and these effects were non-significant. While this may partly explain the improved

thermal balance, in this instance, it appears likely that reductions in endogenous pyrogenic cytokines have an important role to play in the efficacy of many of the anti-inflammatory supplements. Nevertheless, only oligonol has demonstrated significant impacts on aspects of thermoregulation and, therefore, further investigation of these supplements and mechanisms is required to provide definitive answers.

An additional role of anti-oxidants is to improve cellular oxidative capacity and, therefore, redox status (183). These effects could be directly extended to sudomotor function, based on the reported relationships between systemic markers of lipid peroxidation and sweat production (184). However, further research is needed to explore this possibility, owing to the failure of local anti-oxidant infusion to acutely alter the local sweating response during exercise-heat stress (185), which questions the likelihood that anti-oxidants play a major role in thermoregulatory sweating. Indeed, a greater sweating response was not observed for the majority of these supplements. A component of catechin, epicatchin, has been associated with greater cutaneous blood flow during heat exposure through improved NO signaling (186, 187). The results were non-significant, but if substantiated, the observed augmented sweating response may be due to the associated enhancement of skin blood demonstrated in response to catechin supplementation (188). In combination, these would improve evaporative and dry heat transfer, explaining the lower T_{core} response. Similarly, there is evidence that anthocyanins, a key component of blackcurrants promotes production of NO, through augmented NO synthase activity (189). Furthermore, Eurycoma longifolia Jack – another supplement with an anti-oxidative function – had a *medium*, positive non-significant effect on WBSR, yet no significant change in peak T_{core}. Neither of these two latter studies measured or estimated SkBF, or characterized other indices of vascular function and, therefore, it can only be speculated that any potential greater WBSR observed – albeit non-significant – is in response to the aforementioned mechanisms.

Interestingly, beta-glucan and ginseng, other supplements with anti-inflammatory properties, had *small*, non-significant positive effects on peak T_{core}, and beta-glucan also had no effect on WBSR. While other endogenous pyrogens were significantly reduced immediately post-exercise in the beta-glucan condition compared to placebo, there was a transient elevation of macrophage inflammatory protein 1β, which may provide a potential explanation for these findings. However, without further investigation into beta-glucans' thermoregulatory effects during heat exposure, any mechanistic explanations remain speculative. Ginseng is a herb with many bioactive ingredients, which has been demonstrated to increase body temperature in the animal model, and may also partially explain this thermogenic effect (190).

Other anti-oxidants; vitamin C and polyphenols had no observable effects on peak T_{core} or WBSR. Quercetin and combined α-KG and 5-HMF also had no effect on WBSR, but a *small*, non-significant negative and a *small*, non-significant positive effect on peak T_{core} was observed, respectively. It has been theorized that quercetin, a well characterized anti-oxidant, is capable of inhibiting (via ROS scavenging) the necessary molecular signaling events required to acquire the acclimated phenotype, by reducing the heat-shock factor or hypoxia-inducible factor response to heat exposure (191). Acutely, anti-oxidant intake would improve redox balance and potentially aid heat tolerance, but if supplemented chronically or alongside heat exposure may blunt adaptations (191, 192). A similar argument can be posed for supplements with anti-inflammatory properties (193). Indeed, a greater number of studies demonstrated beneficial peak T_{core} and sweating responses (e.g. catechin, oligonol, quercetin), when supplemented acutely (1 day), but there is no clear consensus on dosing length and supplement efficacy within the current analysis. Nevertheless, based on the required time-course of these cellular adaptations, this mechanism could partially explain the lack of difference between anti-oxidants consumed over longer periods (≥ 7 days) and placebo supplements in the current meta-analysis. Across the anti-oxidant and anti-inflammatory supplements in the current meta-analysis, 10 of the 19 supplements were consumed repeatedly across 3 to 42 days, which means that any potential thermoregulatory effects may have been masked. In summary, the use of anti-oxidants results in variable responses in the heat, which could be partly explained by their multi-ingredient composition, or dosing period. It is important that the specific mechanisms by which these variable effects occur should be investigated, especially if chronic administration of anti-oxidants and anti-inflammatories may reduce adaptation to heat exposure and exacerbate heat illness. Indeed, many of these supplements are more likely to be ingested by people who require anti-oxidative or anti-inflammatory agents, such as older or clinical populations, who are also more vulnerable to heat stress (194, 195) and are also less likely to tolerate increases in T_{core} (i.e. ginseng). Such individuals could benefit from reductions in T_{core} and dietary supplements that may induce this (i.e. oligonol and catechin), assuming that there are no other apparent side-effects.

The current analysis suggests that 100 to 200 mg oligonol ingested approximately 30 to 60 min pre-heat exposure has a beneficial effect on thermal balance, by reducing heat gain. Although further investigation into oligonol's efficacy during exercising heat stress is necessary to further elucidate its effects on thermoregulatory capacity. Catechin appears to have a similar effect, though corroboration of this finding is required, as only one study has been conducted thus far. There is also tentative evidence that prolonged intake of 800 mg curcumin, vitamin E, 70 mL Effective microorganism X (3, 42 and 7 days, respectively), may reduce T_{core} responses and 600 mg blackcurrant extract and 150 mg Eurycoma longifolia Jack may improve sweat rate during exercise in the heat.

However, these results were non-significant and based on only one (curcumin, vitamin E, Effective microorganism X and Eurycoma longifolia Jack) or two studies (blackcurrant extract), so these results are not conclusive. Further research is required to establish these anti-inflammatory supplements' efficacy during heat exposure and their effects on endogenous pyrogenic cytokines. Additional investigation into their effects when ingested acutely, at rest and during more ecological valid conditions is warranted before more definitive thermoregulatory effects can be established. Similarly, the potential thermogenic effects of 200 mg ginseng, 250 mg beta-glucan and combined 4.8 g α-KG and 60 mg 5-HMF require additional examination, as their intake cannot currently be recommended based on the results herein. Further, ingestion of 250 to 1500 mg vitamin C and polyphenols does not appear to influence thermoregulatory responses (T_{core} or sweat rate) during exercising heat stress and, therefore, while intake is unlikely to facilitate improved thermal balance, it is also unlikely to have detrimental performance or heath consequences. However, establishing these effects following acute doses may reveal further impacts on thermoregulatory capacity.

4.9 L-glutamine, bovine colostrum, probiotics, whey protein and amino acids

L-glutamine, bovine colostrum and probiotic supplementation all had no effects on peak T_{core} and WBSR, suggesting that they confer no thermoregulatory benefit in the heat. These supplements, along with curcumin, are often ingested prior to exercise in hot environmental conditions, with the aim of maintaining gastrointestinal (GI) barrier integrity and reducing symptoms of GI dysfunction. Gastrointestinal injury and changes to epithelial permeability are relatively common during exercising heat stress (196), which consequently, leads to translocation of endotoxins and bacterial lipopolysaccharides into the central circulation, causing systemic endotoxemia (197). The subsequent release of pro-inflammatory cytokines can, in turn, cause cytokemia and additional elevations in T_{core} (197-199). However, evidence for these supplements' efficacy is equivocal, along with their function as ergogenic aids in the heat. Favorable effects of supplementation with whey protein (106) and an amino acid beverage have been demonstrated on GI permeability during exercising heat stress, where there was a *small*, non-significant negative, and a *trivial* effect on peak T_{core} , respectively. Whey protein supplementation also induced a *large*, significant negative effect on WBSR. In this study the whey protein condition had a lower circulatory endotoxin concentration post-exercise compared with placebo (106), which theoretically may explain any T_{core} differences. The large inhibitory effect on sweating was unexpected, but given the lower T_{core} – and likely heat production –, the drive for sweating would be reduced (67). The only other supplement to display any potential

improvements to thermoregulatory capacity is curcumin – as detailed previously – which is more likely to be due to its aforementioned anti-inflammatory role. Probiotics and bovine colostrum supplementation did not reduce circulating endotoxin or cytokine concentrations in the studies within which these were measured (200-203) and only one study which supplemented L-glutamine demonstrated reductions in endotoxins and TNF-α (204). These supplements may be less effective at preventing GI injury in the heat, due to greater redistribution of blood flow from the gut (GI ischemia) to the peripheral vasculature (205) and, consequently, have no influence of T_{core} responses. Indeed, only a few studies identified improvements to GI barrier integrity (85, 103, 204, 206) and largely attributed this improvement to upregulation of heat shock protein 70, which inhibits inflammation (103, 204, 207). Therefore, the long-term use of probiotics (7 to 28 days) and ~20 to 140 g bovine colostrum (7 to 14 days) and acute use of 0.15 to 0.9 $g \cdot kg^{-1}$ L-glutamine to maintain GI barrier integrity in hot environmental conditions appears to provide no thermoregulatory advantage. Whilst supplements targeting the GI tract during heat stress are an area of ongoing interest, further research is required to establish other efficacious alternatives. Indeed, an acute dose of whey protein (15 g) may provide an effective option (106), but without replication of these results, this cannot be definitively stated.

4.10 Menthol and Thermo Speed Extreme

The oral supplementation of menthol non-significantly lowered peak T_{core}. This reduction was unanticipated but the variability across studies explains the non-significant effect. Menthol is typically considered to be a non-thermal cooling agent (208), which evokes the perception of cooling via transduction of the TRPM8 receptors in the oral cavity (209-212) and possibly the viscera (213), without directly affecting thermal balance according to current literature (214-216). However, current findings were heavily influenced by a single study's results, where T_{core} was estimated by tympanic measurement (100), which can be less reliable if the correct procedures are not adhered to. Therefore, there is some doubt over these results. As discussed in Barwood and colleagues' expert-led consensus article (208), there are some reports of menthol causing vaso-reactivity in the skin's subcutaneous vasculature when applied externally, but no consensus was reached on any form of menthol administration and thermoregulatory effects. Therefore, replication of this single study may be required to confirm whether acute menthol ingestion can mechanistically affect temperature regulation. Additionally, there was no effect on WBSR, which supports the current consensus (208). Thermo Speed Extreme is another supplement which did not affect peak T_{core} and given that this supplement contains ingredients such as caffeine (217), this finding is somewhat

unexpected. It is possible that the tympanic measures used within this study were insufficiently sensitive to detect T_{core} changes. However, significantly greater chest T_{sk} was observed at certain time-points across the trial, which could enhance dry heat dissipation to the environment, particularly as the ambient air was much cooler (26.2°C) than average T_{sk} across participants (34°C). The ingredient piperine could be responsible for this likely enhancement of cutaneous vasodilation, as *in-vitro* studies suggest it may have vaso-modulating effects (218). This could explain the tendency towards lower T_{core} values, despite the thermogenic nature of the supplement. It should be stated that this supplement would, therefore, not be appropriate for use in ambient temperatures that exceed T_{sk}, where skin surface to ambient air temperature gradients, and dry heat transfer capacity are reduced.

4.11 Moderating effects

No candidate moderators, such as training and heat acclimation status, hydration status and fluid ingestion during the trial, affected peak T_{core} or sweating responses to dietary supplementation. For hydration status, this is likely due to the majority of papers stipulating the inclusion of hydrated participants. However, there was more variation in the training (highly trained; 43% *vs* recreationally active; 39%) and heat acclimation (acclimated; 14% *vs* non-acclimated; 36%) status of participants and whether fluid was ingested during the trials (ingested; 46% *vs* not ingested; 22%), yet no moderating effects were found. Nevertheless, it would be useful for future studies to consider investigating the efficacy of dietary supplements on thermoregulation among participants of different training and heat acclimation statuses, given the effect of these processes on sweating and T_{core} responses (11). Some supplements, such as sodium citrate, nitrate, L-glutamine and tyrosine, have only been used to assess thermoregulatory responses in non-acclimated participants, which limits the wider application of these to potential end-users. Whether this would augment or negate any effects seen from these supplements is of particular interest and important to establish for individuals in competitive sport, military and occupational settings. In addition, all other meta-regressions (WBGT, trial type and length and supplementation period) did not moderate the effect of dietary supplementation on peak T_{core} or sweating. There is a large range of supplements included within the current meta-analyses, each with differing underpinning mechanisms and nuances in their efficacy. It is, therefore, unsurprising that there are no consistent moderating factors.

While these trial moderators had no significant effects in the present analysis, they still require further investigation, particularly within the most efficacious supplements included here. For example, acute supplementation and the use of exercise was most common, with no variation within certain supplement

categories. The effect of chronic supplementation of certain supplements, such as various anti-oxidants, glycerol, taurine, and other amino acids (e.g. L-glutamine), on T_{core} and sweating responses in the heat is almost completely unknown. Taurine has been shown to elicit various physiological effects following chronic supplementation, which may be advantageous during heat exposure, such as enhanced vascular function (25) and an improved endurance trained phenotype (219-221). All studies investigating the effects of L-glutamine on GI barrier integrity in the heat have supplemented acutely and it is possible that a chronic dose may be more efficacious. Indeed, long-term administration (2 months) has demonstrated beneficial effects on GI permeability in patients with Crohn's disease (222). Longer term glycerol intake has previously elicited hyperhydration for up to 49 hours (223), but whether it can be maintained over a greater period of time is currently unknown. Further research into this, alongside potential side effects (e.g. hyponatremia) would help establish whether glycerol supplementation can provide long-term beneficial effects on thermal tolerance. Additionally, as detailed above, the chronic and acute effects of various anti-oxidants and anti-inflammatory supplements in the heat requires investigation. Furthermore, establishing the efficacy of these supplements during differing trial types with differing physiological demands is necessary to be able to provide practical advice and application to athletes, workers and the general population. The meta-regression of WBGT demonstrated no effect, but ambient vapor pressure does have an established impact on avenues of heat dissipation (69). For example, supplements which augment thermal sweating (e.g. taurine) will likely be most effective in dry environments where any sweat produced can be evaporated, thereby providing a cooling effect. Depending on the mechanistic actions of certain supplements, beneficial thermoregulatory effects, this could have a large impact on their efficacy and ability to help individuals maintain thermal equilibrium. Investigation of these above factors is important, particularly amongst the most efficacious of the supplements examined within these meta-analyses.

4.12 Limitations

Within these meta-analyses, several supplements were taken in combination, such as creatine and glycerol (91, 224, 225), caffeine and ginseng (94), caffeine and taurine (28), combined α-KG and 5-HMF (226), whey protein (106), amino acid beverage (227), Effective microorgansim X (228) and Thermo Speed Extreme (217). However, as only a few studies employed a co-ingestion strategy, there is limited information on the thermoregulatory outcomes when using this approach across a wide range of different supplements. Herein, the combined effect of creatine and glycerol was beneficial for thermal balance, while the co-ingestion of caffeine and ginseng further

exacerbated caffeine's thermogenic effect. As such, the former could be recommended to improve fluid balance in the heat; however, the latter may pose a greater heat stress risk and potentially should be avoided in hot conditions. This is perhaps unsurprising given that caffeine alone causes an increase in T_{core}. Considering these differing findings and the indication that co-ingestion potentially influences the thermoregulatory responses to these supplements, greater clarity across supplement types regarding these effects is certainly warranted. Indeed, athletes and military personnel often combine dietary supplements (229, 230), which may increase the risk of heat stress if a harmful combination is unwittingly ingested. Therefore, further research regarding the effect of dietary supplement co-ingestion on thermoregulatory responses during heat exposure is necessary and represents a key gap in the literature and a further lack of specific supplementation guidance for potential users.

5. Conclusion

In summary, for the first time, the effects of various dietary supplements on T_{core} and sweating responses in the heat have been evaluated. The amino acids taurine and GABA, alongside whey protein, lowered peak T_{core}, indicating an improvement to thermal balance. While GABA and whey protein negatively impacted WBSR, taurine increased the sweating response, demonstrating an enhancement to thermoregulatory capacity, albeit from a single study. However, other amino acids, such as tyrosine and BCAAs appeared to have no meaningful effect on thermoregulation. Various supplements with anti-oxidative and anti-inflammatory properties (e.g. oligonol, catechin, curcumin, vitamin E and quercetin) provided beneficial effects on peak T_{core}, which may in-part be explained through improved redox balance and attenuation of endogenous pyrogenic cytokines. Nevertheless, not all of these supplements improved thermal balance, highlighting the need for additional research in this area. A number of supplements (e.g. glycerol, creatine, sodium citrate and betaine), which appear to induce hyperhydration and/or expand plasma volume, non-significantly lowered T_{core} responses. Mechanistically, this may be through increasing heat carrying capacity and/or improving fluid availability to the sweat gland, as some supplements (e.g. combined glycerol and creatine) also demonstrated an effect on sudomotor function. However, T_{core} and sweat rate findings were inconsistent across studies and supplement types, rendering the results non-significant overall. Many other supplements such as nitrate, L-arginine, folic acid (taken for their effects on NO bioavailability) and L-glutamine, bovine colostrum and probiotics (taken for their effects on GI barrier integrity) did not appear to provide any thermoregulatory benefit in the heat. Peak T_{core} was greater following caffeine and combined caffeine and ginseng supplementation, without any increases in sweating responses. Consequently,

caffeine when ingested during heat exposure appears to be thermogenic and, therefore, may have potential negative health implications. Several other supplements, such as ginseng, beta-glucan and combined α-KG and 5-HMF also demonstrated *small* thermogenic effects, though these results were non-significant.

Although additional investigation is certainly required, some supplements have demonstrated the potential to improve thermoregulatory capacity in the heat. However, it appears that others have null or even deleterious effects on thermal balance when ingested in such conditions. These findings suggest that certain supplements, such as caffeine, should possibly be avoided in hot conditions and others, such as taurine, may elicit a thermoregulatory benefit. This has potential implications for those ingesting dietary supplements for their health and/or performance effects during periods of heat exposure. Indeed, official guidance documents for the general population, athletes and military personnel could also be updated to reflect the varying effects different dietary supplements appear to have on thermoregulation, detailing which to avoid and which may be advantageous in hot conditions. Additional investigation into many of these supplements is required to corroborate findings and provide greater understanding of their effects. Specifically, future research should focus on the thermolytic effects of various supplements such as taurine, GABA, oligonol and catechin in varying conditions, alongside further mechanistic insight into these responses.

Grants

No funding was provided to support this manuscript.

Disclosures

The authors, JP, MW, MM, SH, RN and LK have no conflicts of interest directly relevant to its contents.

Author contributions

JP and MW conceived and designed research, performed the searches, screening of manuscripts and study quality scoring. JP performed the data analysis and prepared figures. All authors (JP, MW, MM, SH, VN and LK) assisted with data interpretation, drafting, editing and revising of the manuscript, as well as reading and approving the final version of the manuscript.

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