

Review

Effects of Tart Cherry (*Prunus cerasus*) Supplementation on Overall Sleep Quality, Melatonin, and Inflammatory Biomarkers: A Systematic Review and Meta-Analysis

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Abstract

Poor sleep and insomnia are prevalent and carry substantial health and societal costs. Tart cherry (*Prunus cerasus*) contains polyphenols and melatonin and has been proposed as a dietary strategy to support sleep. This systematic review and meta-analysis synthesised evidence from randomised controlled trials (RCTs) evaluating the effects of tart cherry supplementation on sleep quality and biomarkers linked to inflammatory and melatonin-related pathways. PubMed, Scopus, and Web of Science were searched from inception to January 2026, alongside clinical trial registries. Eligible studies were human RCTs in adults (≥ 18 years) comparing tart cherry (juice, concentrate, powder, or capsules) with placebo or control. Sleep quality was the primary outcome with melatonin and inflammatory biomarkers extracted as secondary outcomes where available. Two reviewers screened records and assessed risk of bias using risk-of-bias tool for randomised trials (RoB 2.0) and certainty of evidence using Grading of Recommendations Assessment, Development and Evaluation (GRADE). Random-effects meta-analyses were conducted using Hedges' g as the standardised mean difference. Ten RCTs involving 294 enrolled or randomised participants were included.



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The studies were published between 2010 and 2024. Interventions ranged from short protocols to 12 weeks and used juice-based products or capsules. Across all trials, tart cherry produced a small, non-significant improvement in overall sleep quality compared with placebo (Hedges' $g = 0.064$; 95% CI -0.147 to 0.275; $P = 0.552$). In participants with insomnia (two trials), tart cherry significantly improved sleep quality (Hedges' $g = 0.732$; 95% CI 0.051 to 1.412; $P = 0.035$). No significant effects were observed for melatonin or inflammatory biomarkers. Reported compliance was high (mean $95.76 \pm 3.48\%$), and adverse events were infrequent. Overall risk-of-bias judgements ranged from some concerns to high. Certainty was very low for overall sleep quality in mixed populations and for inflammatory biomarkers, and low for the insomnia subgroup and melatonin. Tart cherry supplementation did not significantly improve pooled sleep quality across mixed adult populations. A benefit was observed in two small insomnia trials, but this finding was based on low-certainty evidence and should be considered preliminary. Larger, rigorously designed RCTs with standardised sleep outcomes and mechanistic biomarkers are required.

Keywords

Tart cherry supplementation; sleep quality; insomnia; systematic review and meta-analysis; melatonin; inflammatory biomarkers

1. Introduction

Sleep is a core biological process that supports health and day-to-day functioning. It occupies around one third of the human lifespan and contributes to cognitive performance, mood regulation, immune competence, and memory consolidation [1-3]. Normal sleep architecture comprises sequential stages ranging from lighter sleep through to rapid eye movement (REM) sleep [4]. When sleep is insufficient or disrupted, these restorative processes are compromised, and the consequences extend beyond fatigue, with links reported to cardiometabolic and vascular morbidity including cardiovascular disorders, obesity, hypertension, and type 2 diabetes [5, 6]. At a population level, sleep problems are common and costly [7], and insufficient or poor-quality sleep has been associated directly or indirectly with all ten leading causes of death in the United States [8-15]. Notably, many of these outcomes are also characterised by chronic low-grade inflammation [16-18].

Pharmacological treatment for insomnia includes non-prescription antihistamines and melatonin, prescription hypnotics, and selected antidepressant, anticonvulsant and antipsychotic agents [19]. These treatments can cause next-day sedation, cognitive and psychomotor impairment, dizziness and gastrointestinal symptoms [20-25]. Longer-acting hypnotics may also increase falls and driving risk, particularly in older adults [23-26]. Some off-label agents carry additional condition-specific risks [27, 28]. These limitations, together with international variation in access to exogenous melatonin, have increased interest in lower-burden dietary strategies for sleep.

Mechanistic work provides a plausible basis for the broad health impacts of poor sleep, particularly through immune and circadian pathways. Sleep supports normal immune function, and altered sleep has been associated with dysregulation of inflammatory cytokines and acute phase proteins, including interleukin 6 (IL-6), interleukin 8 (IL-8), interleukin 10 (IL-10), tumour necrosis

factor alpha (TNF- α), and C-reactive protein (CRP) [29, 30]. This inflammatory disruption may also perpetuate sleep disturbance via circadian misalignment of inflammatory signalling, reinforcing the problem it helps to create [29]. Melatonin (N-acetyl-5-methoxytryptamine), a key mediator of circadian regulation, is synthesised by the pineal gland predominantly at night and released into the circulation in response to the light-dark cycle, thereby signalling darkness and promoting sleep propensity [31]. Endogenous secretion is sensitive to environmental light and can influence nocturnal core temperature, thereby facilitating sleep onset and maintenance [32]. Consistent with this, a positive relationship between higher melatonin levels and total sleep time has been observed in healthy young individuals [33]. However, the therapeutic evidence for exogenous melatonin in insomnia is mixed, whereas its use in circadian rhythm disturbance, such as that induced by travel across time zones, is more consistently supported [34]. Moreover, access to exogenous melatonin varies internationally, with over-the-counter availability in some countries and prescription-only status in others, increasing interest in dietary sources of melatonin as a potentially accessible alternative.

Given the central role of inflammation and melatonin, attention has increasingly turned to dietary approaches that might influence these pathways. Nutrition may contribute to sleep regulation through several mechanisms, including effects on inflammatory signalling and on substrates involved in neurotransmitter and melatonin synthesis [35, 36]. Dietary intake has been linked to sleep quality through anti-inflammatory mechanisms [37, 38], and specific components such as anti-inflammatory agents, melatonin enhancing foods, and dietary sources of tryptophan and serotonin have been proposed as potentially sleep supportive [39]. Nonetheless, implementing and sustaining broad dietary change can be challenging, particularly when interventions require long term adherence [40]. This has fuelled interest in more pragmatic nutritional strategies, including supplementation, that could offer a targeted means of influencing sleep related biology.

In a survey of Canadian adults, almost one in five respondents reported using an herbal or natural remedy to improve sleep, compared with 12% using prescription medication and 8% using over-the-counter medication [41]. A range of dietary supplements are promoted for sleep, including nitrates, melatonin, magnesium, zinc, vitamin D, and L-theanine, although trial evidence varies across compounds and outcomes [42]. Recent systematic reviews have further examined the relationship between diet and sleep. Arab *et al.* [43] reported that Mediterranean, high-quality and empirically derived healthy dietary patterns were associated with lower odds of insomnia symptoms, although the certainty of evidence was very low. More recently, Mei *et al.* [44] synthesised 28 RCTs of dietary supplement interventions. They reported modest improvements in sleep quality, sleep efficiency, total sleep time, sleep latency and wake after sleep onset. However, effects varied by intervention and outcome. Among individual supplements, melatonin and magnesium have been relatively well studied, with the strongest overall evidence typically reported for melatonin [31], despite practical constraints on access in some settings.

Tart cherry (*Prunus cerasus*) is a temperate fruit tree in the Rosaceae family. The Montmorency cultivar is a French amarelle cultivar with an approximately 400-year history and is now the predominant sour-cherry cultivar grown in the United States. Because of its acidic flavour, the fruit has traditionally been consumed in processed forms, including juice, preserves and baked products, rather than eaten fresh [45]. Tart cherries have emerged as a promising candidate because of their phytochemical profile, which is rich in anthocyanins, flavanols and phenolic acids [46-48], and because they also contain melatonin [49]. On this basis, tart cherry supplementation has been

proposed as a means of targeting pathways implicated in poor sleep, including oxidative stress, inflammation and circadian regulation through increased melatonin. Randomised trials have also shown tart cherry-related reductions in inflammation and oxidative stress across several chronic conditions, including cardiovascular disease [50], certain cancers [51], metabolic syndrome [52], dyslipidaemia [53, 54], hypertension [55], and inflammatory bowel disease [56]. A growing body of randomised trials has evaluated tart cherry supplementation specifically for sleep, typically assessing sleep quality and sleep parameters alongside biomarkers related to inflammation and melatonin. Barforoush *et al.* [57] subsequently reviewed seven interventional studies. They identified possible improvements in selected sleep, melatonin, inflammatory and oxidative-stress outcomes. However, the evidence remained limited and heterogeneous because intervention dose, duration and participant characteristics varied.

Although Barforoush *et al.* [57] recently presented the evidence concerning tart cherry supplementation and sleep, their systematic review did not undertake a meta-analysis. No meta-analysis has therefore yet quantified the pooled effects of tart cherry supplementation on sleep quality and related biochemical outcomes. A systematic and meta-analytic synthesis of this literature is timely and necessary to determine the overall efficacy of these interventions. The present meta-analysis aims to critically evaluate and quantify the effects of tart cherry supplementation on sleep quality and biochemical outcomes. By integrating the available evidence, this review seeks to provide a comprehensive understanding of the potential role of tart cherry supplementation in sleep-quality management and to inform future research and clinical practice.

2. Materials and Methods

This systematic review and meta-analysis was conducted and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, including the checklist, flow diagram, and accompanying Explanation and Elaboration document [58]. In addition, the Cochrane Handbook for Systematic Reviews of Interventions was consulted to inform the methodological approach [59]. This systematic review and meta-analysis was also registered prospectively via a database of systematic reviews in health-related research (CRD420251229156).

2.1 Eligibility Criteria

Experimental studies limited to randomised controlled trials (parallel or crossover designs) assessing the effects of tart cherry or its derivatives (e.g., juice, freeze-dried powder, capsules), delivered as dietary supplementation in food or beverage form, were included. Eligible comparators were placebo, no intervention, or usual/standard care. The only inclusion criteria requirement was for participants to be aged 18 years or older. To be included, trials had to report at least one measure of sleep quality or sleep duration, assessed using subjective instruments (e.g., validated questionnaires) or objective measures (e.g., actigraphy or polysomnography). Melatonin concentrations and inflammatory biomarkers were extracted but were not mandatory for inclusion. Studies were restricted to English-language, full-text, peer-reviewed articles involving human participants, and conducted in any setting (e.g., clinical, community, or free-living), with no restrictions on intervention dose, duration, or follow-up. Non-randomised studies, observational designs, case reports, reviews, protocols, animal or in vitro studies, and grey literature without full data were excluded. Our main outcome was overall sleep quality assessed subjectively or using

objective measures such as actigraphy. Where outcomes were measured but not reported, authors were contacted, and data requested.

2.2 Search Strategy

Electronic databases from inception to January 2026 were searched, including PubMed, Scopus, and Web of Science. The search strategy incorporated terms related to tart cherry (*Prunus cerasus*) and sleep outcomes, including: 'Prunus', 'Prunus cerasus', 'Montmorency', 'tart cherry', 'sour cherry', 'cherry juice', 'cherry extract', 'cherries', 'sleep', 'insomnia', 'sleep quality', 'sleep duration', 'sleep efficiency', 'sleep onset latency', 'restless sleep', and 'sleep disturbance'. The full search strategies for each database are provided in the Supplementary Material 1. To ensure completeness, we also searched ClinicalTrials.gov, the World Health Organization (WHO) International Clinical Trials Registry Platform, and the International Standard Randomised Controlled Trial Number Registry. Forward and backward citation tracking was performed for the included articles. All searches were conducted by the same author (JKS), and duplicates were removed. Screening of titles and abstracts was undertaken independently by two review authors (JKS and LMB). Owing to the relatively small number of studies identified, all records were examined by both reviewers, with complete agreement reached ($\kappa = 1.00$). An independent reviewer was available to resolve discrepancies, although this was ultimately not required.

2.3 Data Extraction

Data extraction and recording were guided by the Cochrane Data Collection Form for Interventional Studies [59]. Data from the included studies were extracted using a standardised form developed for this review. Extracted study characteristics included author, publication year, country, study setting and trial design. Participant data included eligibility criteria, total and group-level sample sizes, age, sex and body mass index (BMI). We also extracted withdrawals or dropouts, adverse events, adherence and blinding efficacy. Intervention data included formulation, composition and duration. Sleep-quality, melatonin and inflammatory-biomarker outcomes were extracted for possible meta-analysis. One review author (JKS) independently extracted all relevant data, which were checked for accuracy and completeness by a second author (LMB). Any disagreements were to be resolved through discussion with a third independent reviewer. In cases of missing or unclear data, attempts were made to contact the corresponding author(s) by email on at least two occasions to obtain the relevant information. If no response was received, the available data were used, and any assumptions or imputed values were clearly documented in the review. For descriptive reporting, primary and secondary outcomes were recorded according to the designation used by each included trial. These study-level designations are distinct from the outcome hierarchy of the present review, in which overall sleep quality was the primary outcome and melatonin and inflammatory biomarkers were secondary outcomes.

2.4 Data Synthesis and Analysis

All outcomes were continuous. Mean changes from baseline to the trial endpoint and their corresponding standard deviations (SDs) were used to calculate Hedges' *g*. Effect estimates were reported as standardised mean differences (SMDs) with 95% confidence intervals (CIs). Statistical

significance was set at $P \leq 0.05$. Hedges' g was selected as the SMD to account for small sample bias, which is particularly relevant in meta-analyses with a limited number of studies [60]. Hedges' g was interpreted as: <0.20 (trivial), $0.20-0.49$ (small), $0.50-0.79$ (moderate), and ≥ 0.80 (large) [61]. Where necessary, outcome direction was harmonised so that effect sizes were interpretable on a common scale. For sleep outcomes scored such that higher values indicate improved sleep quality, scores were coded so that positive Hedges' g values reflect improvement in sleep. For melatonin, an increase was considered favourable; positive Hedges' g values therefore indicated improvement. Inflammatory biomarkers were retained in their natural direction, so negative values indicated reductions. Where the mean and SD change from baseline to end point were not reported, but baseline and final means and SD were available, SD change was calculated using the following equation in accordance with the Cochrane Handbook [59]:

$$SD_{change} = \sqrt{SD_{baseline}^2 + SD_{final}^2 - (2 \times correlation\ coefficient \times SD_{baseline} \times SD_{final})}$$

A correlation coefficient of $r = 0.5$ was used for these calculations, consistent with prior meta-analyses where exact correlation values were not reported [62], providing a conservative estimate of variance. For crossover trials, only data from the first phase (pre-cross-over) were used to treat the trial as a parallel-group study, and the mean change and SD were calculated similarly, as recommended by Elbourne *et al.* [63], to avoid carryover effects.

Where a study included more than one eligible tart cherry intervention arm, comparisons were handled in accordance with Cochrane guidance to avoid unit-of-analysis errors. If intervention arms had distinct placebo groups, each intervention-placebo comparison was entered separately. If a shared placebo group would otherwise have been counted twice, the placebo group was split evenly across comparisons. A random-effects meta-analysis was performed using the Paule-Mandel estimator for between-study variance (τ^2), given the small number of included studies and the expected clinical and methodological heterogeneity between interventions and outcomes. The Paule-Mandel method provides more accurate estimation of τ^2 and robust confidence intervals in small-sample meta-analyses [64]. Publication bias was assessed using funnel plots and Egger's test. Egger's test was employed (for analyses involving ≥ 3 studies) as it allows formal statistical evaluation of small-study effects in meta-analyses of continuous outcomes [65] (Supplementary Material 2). Visual inspection of funnel plots complemented the statistical assessment.

Statistical heterogeneity was assessed using the I^2 statistic. In line with conventional guidance, values of 0-40% were considered potentially unimportant, 30-60% as indicating moderate heterogeneity, 50-90% as substantial heterogeneity, and 75-100% as considerable heterogeneity [66]. Sensitivity analyses were conducted (for analyses involving ≥ 3 studies) by sequentially omitting individual studies to evaluate their influence on the overall effect estimate (Supplementary Material 2). A subgroup analysis was undertaken for trials recruiting participants with clinically defined insomnia (as defined by study eligibility criteria), given the potential for differential responsiveness in populations with established sleep pathology. No further subgroup analyses were conducted because the number of studies contributing to each outcome and candidate subgroup was insufficient to support reliable stratified estimates. Clinical and methodological heterogeneity was anticipated because populations ranged from athletes and healthy adults to people with insomnia, and interventions differed in formulation, dose and duration. Random-effects models were therefore used. This heterogeneity limits the generalisability of the pooled overall effect.

2.5 Certainty of Evidence

The certainty of evidence was independently assessed by two review authors (JKS and LMB) using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach [67]. Studies were evaluated across these key domains to assign an overall certainty rating of high, moderate, low, or very low [67, 68].

2.6 Risk of Bias

The internal validity, rigour and overall quality of included studies were independently assessed by two review authors (JKS and LMB) using the revised Cochrane Risk of Bias tool for randomised trials (RoB 2.0) [69]. The RoB 2.0 tool evaluates five key domains: the randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of reported results. Each domain was judged as having a low risk of bias, some concerns or a high risk of bias, in accordance with RoB 2.0. Overall judgements were derived using the RoB 2.0 algorithm. Disagreements were resolved through discussion between the two reviewers, with a third independent reviewer available if consensus could not be reached [59, 69].

3. Results

3.1 Search Results

The study selection process is illustrated in the PRISMA flow diagram (Figure 1). The systematic search, covering publications from database inception to January 2026, identified 480 records (PubMed $N = 56$, Scopus $N = 151$, Web of Science $N = 273$), with no additional records identified through other methods ($N = 0$). After removal of duplicates ($N = 95$), 385 records remained for screening. Title/abstract screening and eligibility assessment resulted in the exclusion of 375 records for the following reasons: study design ($N = 60$), non-human studies ($N = 83$), cherry but not tart cherry intervention ($N = 13$), and irrelevant topic/no tart cherry intervention ($N = 219$). Ultimately, 10 studies met the inclusion criteria and were retained for qualitative synthesis, all of which were also eligible for inclusion in the meta-analysis ($N = 10$).

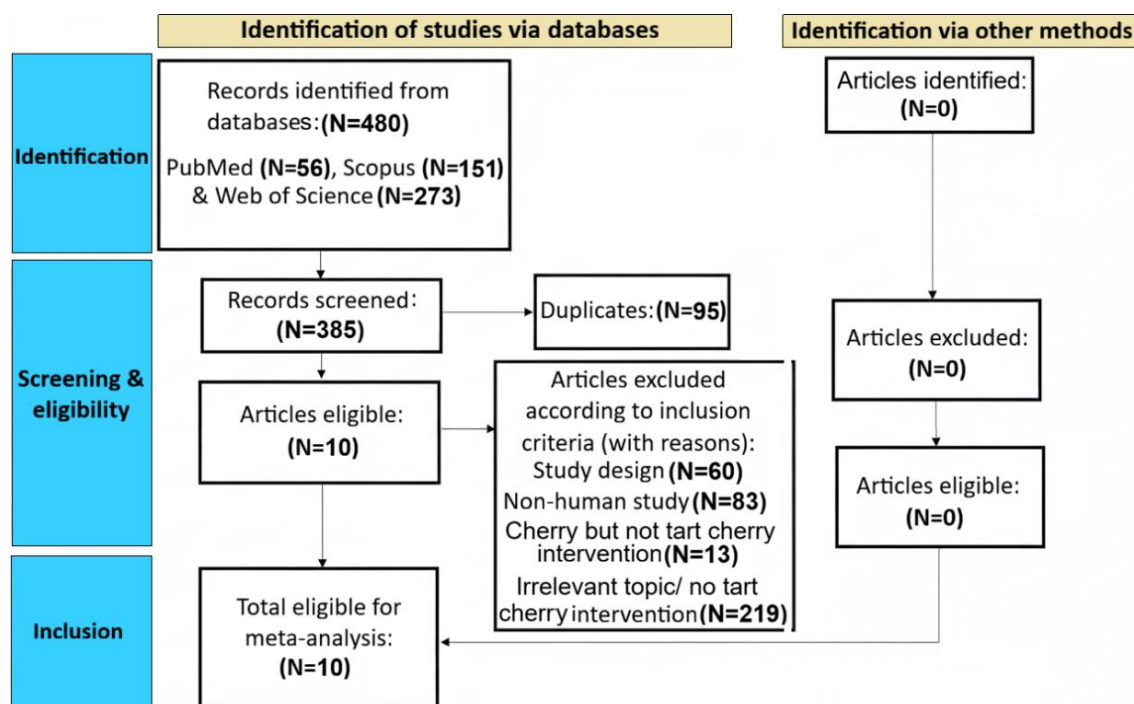


Figure 1 PRISMA-style flow diagram of study selection. Note. Numbers refer to records unless otherwise stated. *N*, number of records or studies; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Standard deviation (SD) change data were requested from one study and were provided by the authors. Where SD change values were still required but not reported in the published paper, SDs for change scores were calculated in accordance with the Cochrane Handbook.

3.2 Characteristics of Included Studies

Details of the included studies are summarised in Table 1, Table 2, Table 3. Table 1 outlines the study design, participant demographics, and diagnostic criteria. Table 2 presents the intervention and comparator formulations, polyphenol or anthocyanin content, blinding, and compliance details. Table 3 summarises the primary and secondary outcomes, along with key findings reported by each study.

Table 1 Characteristics of included studies.

Author	Year	Country	Study design	Total N	Participant population and eligibility criteria	Length of intervention
Sinclair <i>et al.</i> [53]	2022	UK	Randomised parallel double-blind placebo controlled	30	Aged 18-65 years, non-smoker, BMI < 30 kg/m ² , able to provide informed consent and not pregnant. Exclusion criteria included diabetes or other metabolic disease, uncontrolled hypertension, allergy to cherries or blueberries, habitual cherry or blueberry consumption, regular medication use and antioxidant supplementation.	20-days
Pigeon <i>et al.</i> [70]	2010	USA	Randomised cross-over double-blind placebo-controlled	16	≥65 years with insomnia but otherwise healthy, active, medically stable, not taking hypnotic or sedating medications. Typical bedtime between 9:00-12:00 a.m., sleep problems > 3 nights/week for ≥6 months, meeting research diagnostic criteria for primary insomnia, Insomnia Severity Index ≥ 10, and ≥30 minutes of either sleep-onset latency or wake after sleep onset.	2-weeks
Tucker <i>et al.</i> [71]	2024	USA	Randomised cross-over placebo-controlled	34	Aged 18-50 years, BMI ≥ 25.0 kg/m ² and sleep issues. Sleep issues were identified by a PSQI score ≥ 5 and/or an Insomnia Severity Index score ≥ 8.	2-weeks
Hillman <i>et al.</i> [72]	2022	USA	Randomised parallel double-blind placebo controlled	70	Aged 18-50 years, not pregnant, not diabetic, no unresolved infections or diseases, nonsmokers, free from prescribed anti-inflammatory and corticosteroid use for at least 2 months and no antibiotics for >12 months.	30-days
Losso <i>et al.</i> [73]	2018	USA	Placebo-controlled, double blind, balanced, crossover design	11	Male or female, age ≥ 50 years, chronic insomnia, usual bedtime 9 p.m. and midnight.	14-days

Sinclair <i>et al.</i> [74]	2022	UK	Randomised parallel double-blind placebo controlled	24	Capacity to give informed consent, aged over 18 years, recreationally active and suffering from mild to moderate patellofemoral pain.	6-weeks
Kimble <i>et al.</i> [75]	2022	UK	Randomised parallel double-blind placebo controlled	56	Low intake of fruit and vegetable (<5 servings/d) and low levels of physical activity (≤ 4 h/week of moderate-vigorous activity) and ≥ 1 additional risk factor for type II diabetes. No history of cardiometabolic disease, uncontrolled hypertension, gastrointestinal diseases, changes in dietary/physical activity patterns within 3 months, excessive alcohol intake, or a BMI ≥ 40 kg/m ²	3-months
Morehen <i>et al.</i> [76]	2021	UK	Single-blind randomised cross-over design	11	Male academy-level professional rugby-league players from one Super League club; formal eligibility criteria beyond squad membership were not explicitly reported.	7-days
Howatson <i>et al.</i> [77]	2012	UK	Randomised cross-over double-blind placebo-controlled	20	Physically active, participating in moderate physical exercise for at least 150 min/week.	7-days
Chung <i>et al.</i> [78]	2022	Korea	Randomised parallel double-blind placebo controlled	22	Elite female field hockey players with >6 years of experience and no injuries for >6 months.	48 h

Note. Participant descriptions and eligibility criteria reproduce the information reported by each trial; where formal eligibility criteria were not reported, this is stated. BMI, body mass index; d, day; h, hour; *N*, number enrolled or randomised; PSQI, Pittsburgh Sleep Quality Index; UK, United Kingdom; USA, United States of America.

Table 2 Intervention and comparator details, blinding/compliance, and adverse events.

Author	Sex placebo	N baseline placebo	Placebo dietary information	Blinding efficacy	Sex tart cherry	Adverse event tart cherry	Compliance tart cherry	Tart cherry intervention	Tart cherry dietary information
Sinclair <i>et al.</i> [53]	M = 8 & F = 7	15	30 mL placebo concentrate = 80 kcal, carbohydrates 20 g of which sugars: 0 g, protein: 0 g, and Fibre 0 g, 0 mg/mL of anthocyanins.	52% correctly identified their designated trial arm, the chi-squared test was non-significant, indicating that an effective blinding strategy was adopted.	M = 8 & F = 7	1	95.0 ± 3.0%	30 mL tart cherry consumed twice daily, diluted with 100 mL of water.	30 mL dose of cherry concentrate (Energy: 80 kcal, carbohydrates: 19 g of which sugars: 15 g, protein: 1.10 g, fibre: 1 g) approximately 9.12 mg/mL of anthocyanins and 6.63 total phenolics/mL (expressed as gallic acid equivalents).
Pigeon <i>et al.</i> [70]	NR	16	NR	NR		NR	NR	2 × 8 oz bottles (approximately 240 mL each) of tart cherry juice mixed with apple juice daily	NR
Tucker <i>et al.</i> [71]	M = 9 & F = 25	34	NR	NR		NR	NR	500 mg 100% tart cherry powder in the form of two pills one hour before bedtime	NR

Hillman <i>et al.</i> [72] (Capsules)	M = 4 & F = 8	19	1.8 kcal and 0.4 g carbohydrate (0 g fibre) no polyphenols or anthocyanins.	NR	M = 4 & F = 8	0	94%	2 × 500 mg freeze dried tart cherry capsules	1.7 kcal, 0.4 g carbohydrate, and 0.2 g fibre, and contained 760 mg total polyphenols and 330 mg total anthocyanins.
Hillman <i>et al.</i> [72] (Juice)	M = 5 & F = 5	18	68 kcal, 17 g carbohydrate, 0 g fibre) no polyphenols or anthocyanins	NR	M = 5 & F = 5	0	100%	2 × 8 oz bottles of tart cherry (approximately 240 mL each) juice daily	77 kcal and 18 g carbohydrate (0 g fibre) and contained 793 mg total polyphenols and 227 mg total anthocyanins
Losso <i>et al.</i> [73]	M = 3 & F = 5	8	NR	NR		0	NR	240 mL tart cherry juice consumed twice per day in the morning and 1 to 2 hours before bedtime.	Major compounds in cherry juice (content, µg/mL): Procyanidin B-2 451.56, cyanidin-3-O-glucosylrutinoside 123.33, cyanidin-3-O-rutinoside 20.26, and cyanidin-3-O-glucoside 3.51.
Sinclair <i>et al.</i> [74]	M = 8 & F = 4	12	30 mL placebo concentrate = 80 kcal, carbohydrates 20 g of which sugars: 0 g, protein: 0 g, and Fibre 0 g, 0 mg/mL of anthocyanins.	N = 13 correctly identified their designated trial arm, the chi-squared test was non-significant, indicating that an effective blinding strategy was adopted.	M = 9 & F = 3	0	91.55 ± 6.67%	30 mL tart cherry juice consumed twice daily, diluted with 100 mL of water.	30 mL dose of cherry concentrate (Energy: 80 kcal, carbohydrates: 19 g of which sugars: 15 g, protein: 1.10 g, fibre: 1 g) approximately 9.12 mg/mL of anthocyanins and 6.63 total phenolics/mL (expressed as gallic acid equivalents).

Kimble <i>et al.</i> [75]	M = 8 & F = 17	28	204 kcal, 51 g carbohydrate, 0.0 g protein, and 0.0 g fat, and TPC was 21.5 mg (SD = 2.3).	N & %'s not reported. But blinding efficacy was reported and successful blinding efficacy concluded.	M = 8 & F = 17	0	94.0 ± 15.0% (across both placebo and tart cherry)	30 mL tart cherry consumed twice daily, diluted with 240 mL of water.	204 kcal, 50 g carbohydrate, 2.2 g protein, and 0.0 g fat. Total anthocyanin content was 22.2 mg (SD = 6.7), TPC was 195.5 mg (SD = 13.1).
Morehen <i>et al.</i> [76]	M = 11	11	Matched for energy and carbohydrate content with the tart cherry; 100 kcal, 25 g carbohydrate, 0 g fat, 0 g protein	NR		0	100%	Two 30 mL servings mixed with 100 mL water.	Per 30 mL: 102 kcal, 25 g carbohydrate, 0 g fat, 1 g protein, 320 mg anthocyanins.
Howatson <i>et al.</i> [77]	M = 10 & F = 10	20	NR	NR		NR	NR	30 mL tart cherry consumed twice daily, diluted with 200 mL of water.	Melatonin concentration was 1.42 µg·mL ⁻¹ , equating to ~42.6 µg per 30 mL serving and ~85.2 µg·day ⁻¹ . (Total anthocyanin content = 9.12 mg·mL ⁻¹), vitamin A as β-carotene (22.64 IU·mL ⁻¹), and vitamin C as ascorbic acid (0.324 mg·mL ⁻¹).
Chung <i>et al.</i> [78]	F = 11	11	NR	NR	F = 11	NR	NR	200 mL 5 times in a 48 h period. 30 mL serving diluted with water to make a 200 mL beverage.	A total of 213 ± 41 µg/g anthocyanins.

Note. In crossover trials, the same participants contributed to both placebo/control and tart cherry conditions. Where data were identical across conditions, values are shown once only in the placebo/control column and are not repeated in the tart cherry column. Black-shaded cells indicate that a separate tart cherry value is not applicable because the same participants contributed to both conditions in a crossover trial and the corresponding value is reported in the placebo/control column. For Hillman *et al.* [72], baseline sample sizes represent the numbers randomised, whereas the sex distributions represent participants with complete sleep-record data. F, female; h, hour; IU, international unit; kcal, kilocalorie; M, male; mg, milligram; mL, millilitre; N, number of participants; NR, not reported; SD, standard deviation; TPC, total phenolic content; µg, microgram.

Table 3 Study-designated outcomes and main findings of the 10 randomised controlled trials evaluating tart cherry supplementation for sleep quality, melatonin and inflammatory biomarkers.

Author	Primary outcome	Secondary outcomes	Main Findings (Summary)
Sinclair <i>et al.</i> [53]	Systolic blood pressure	Anthropometrics; energy expenditure and substrate oxidation; haematological indices; diastolic BP and resting heart rate; psychological wellbeing; sleep efficacy (PSQI, Epworth Sleepiness Scale, Insomnia Severity Index)	In this three-arm trial (tart cherry vs blueberry vs placebo), tart cherry juice did not improve sleep efficacy, with no meaningful between-group changes in PSQI, insomnia severity, or daytime sleepiness. Cardiometabolic outcomes showed no improvement in systolic blood pressure; selected benefits were observed for other arms and outcomes (for example lipid changes with blueberry), rather than a clear sleep-related effect of tart cherry.
Pigeon <i>et al.</i> [70]	Insomnia severity and sleep continuity assessed by sleep diary (sleep onset latency, wake after sleep onset, total sleep time, sleep efficiency) and Insomnia Severity Index	Additional sleep diary indices across the intervention periods	Tart cherry juice blend was associated with pre to post improvements across sleep variables, and when compared with placebo it produced a significant reduction in insomnia severity and minutes awake after sleep onset. Between-group effects were not evident for sleep onset latency, total sleep time, or sleep efficiency.
Tucker <i>et al.</i> [71]	Objective sleep outcomes (Z-machine EEG; plus wearable-derived sleep variables); subjective sleep quality and insomnia symptoms (PSQI, Sleep Quality Scale, Insomnia Severity Index)	Inflammatory biomarkers CRP, TNF- α , IL-6, IL-8, IL-10, Interleukin 17A	A commonly used dose of Montmorency tart cherry powder for 14 days did not improve objective or subjective sleep outcomes, and did not alter inflammatory markers compared with placebo in adults with overweight or obesity and self-reported sleep issues.

Hillman <i>et al.</i> [72]	Sleep time and sleep quality from daily self-reported sleep records	Body composition; cellular health indices; blood pressure	Over 30 days, tart cherry (juice or capsules) did not improve sleep time or sleep quality vs placebo, although sleep outcomes increased over time in both groups. Blood pressure and most body composition and cellular health outcomes were unchanged, with limited isolated differences that did not suggest a consistent intervention effect.
Losso <i>et al.</i> [73]	Objective sleep assessed by polysomnography; insomnia-related questionnaires including PSQI	Mechanistic biomarkers (kynurenine:tryptophan ratio, PGE ₂ , IDO-related measures); <i>in vitro</i> assessment of IDO inhibition; cherry phytochemical profiling	Tart cherry juice increased polysomnography-measured sleep time and improved PSQI-derived sleep efficiency, with limited changes across other questionnaires. Mechanistically, tart cherry was associated with reductions in kynurenine:tryptophan ratio and PGE ₂ , and procyanidin B-2 inhibited IDO activity in vitro, supporting a plausible pathway linking tart cherry intake to sleep improvement in insomnia.
Sinclair <i>et al.</i> [74]	Patellofemoral pain symptoms (KOOS-PF); knee biomechanics	Sleep quality PSQI; psychological wellbeing (COOP WONCA); blood biomarkers (CRP, uric acid, tumour necrosis factor alpha (TNF- α), creatinine, total antioxidant capacity)	Tart cherry concentrate for 6 weeks did not improve sleep quality (PSQI) vs placebo. KOOS-PF improved in the placebo group rather than the tart cherry group, with no meaningful benefit of tart cherry on pain outcomes. Biomarkers and biomechanical outcomes did not indicate a clear advantage for tart cherry.
Kimble <i>et al.</i> [75]	Cognitive function and attention (computerised task battery); mood ratings (visual analogue scales)	Cerebral blood flow (near-infrared spectroscopy); subjective sleep quality (PSQI and related sleep components); health status; plasma metabolomics	Montmorency tart cherry improved aspects of sustained attention and subjective alertness, but did not improve global sleep quality (PSQI) compared with placebo. Reported sleep parameters showed no clear intervention-related improvement in sleep quality over 3 months.

Morehen <i>et al.</i> [76]	Recovery and inflammation following rugby league match-play (IL-6, IL-8, IL-10); muscle soreness; muscle function	Self-reported sleep, fatigue, mood, stress (visual analogue scales)	Tart cherry juice did not improve self-reported sleep and did not attenuate post-match inflammatory cytokine responses or recovery markers relative to placebo. Both groups showed expected post-match changes, but between-group differences were not evident.
Howatson <i>et al.</i> [77]	Urinary melatonin levels	Sleep quality assessed by actigraphy (time in bed, total sleep time, sleep efficiency)	Tart cherry concentrate increased urinary melatonin and improved actigraphy-derived sleep outcomes, including time in bed, total sleep time, and sleep efficiency, compared with placebo. Timing of the melatonin rhythm was not meaningfully altered, but overall melatonin exposure increased alongside improved sleep continuity.
Chung <i>et al.</i> [78]	Sleep quality after intermittent exhaustion exercise assessed by actigraphy (sleep continuity variables including time in bed, wake after sleep onset, movement index)	Melatonin and cortisol responses	Short-term tart cherry juice intake over 48 hours improved actigraphy-derived sleep outcomes, including time in bed and wake after sleep onset, compared with placebo. Melatonin and cortisol did not differ between groups, so improvements in sleep were not accompanied by detectable changes in these hormones.

Note. Primary and secondary outcomes are the designations used by the original trials and do not represent the outcome hierarchy of the present review. BP, blood pressure; COOP/WONCA, Dartmouth Cooperative Information Project/World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians functional health assessment charts; CRP, C-reactive protein; EEG, electroencephalography; IDO, indoleamine 2,3-dioxygenase; IL, interleukin; KOOS-PF, Knee injury and Osteoarthritis Outcome Score patellofemoral subscale; PGE₂, prostaglandin E₂; PSQI, Pittsburgh Sleep Quality Index; RCT, randomised controlled trial; TNF- α , tumour necrosis factor alpha.

All ten trials were single-centre, randomised controlled studies published between 2010 and 2024, and conducted in the USA [70-73], UK [53, 74-77] or Korea [78]. Study designs comprised both parallel-group [53, 72, 74, 75, 78], and crossover designs [70, 71, 73, 76, 77]. All trials adopted placebo-controlled methodology and were of double-blind trial designs with the exception of Tucker *et al.* [71] and Morehen *et al.* [76]. Hillman *et al.* [72] comprised two independent placebo-controlled comparisons (capsules and juice, each with a preparation-matched placebo) and was therefore included as two comparisons in the meta-analysis.

A total of 294 participants were enrolled across the studies, with individual sample sizes ranging from 11 to 70 participants. Participant inclusion criteria varied substantially across trials, reflecting the breadth of populations in which tart cherry supplementation has been evaluated. Studies recruited adults ranging from younger recreationally active participants to older adults with clinically defined insomnia. Several trials enrolled adults aged 18-50 years with self-reported sleep difficulties. These were typically defined using validated thresholds, including a Pittsburgh Sleep Quality Index (PSQI) score of at least 5 and/or an Insomnia Severity Index score of at least 8 [71]. Broader eligibility requirements included non-smoking status and the absence of pregnancy or chronic disease [72]. Other studies targeted specific cohorts, including recreationally active adults with mild to moderate patellofemoral pain [74], elite female field hockey players with sustained training history and no recent injuries [78], and male academy level professional rugby league players [76]. Where reported, additional eligibility criteria addressed body composition and lifestyle factors. These included BMI thresholds [53, 71] and habitual physical activity requirements [77]. One trial also required low fruit and vegetable intake, low physical activity and at least one additional risk factor for type 2 diabetes [75].

More stringent diagnostic criteria were applied in trials designed specifically for insomnia. In older adults, eligibility included age at least 65 years, chronicity and frequency of symptoms, defined sleep schedule characteristics, and threshold scores on validated insomnia measures, alongside requirements for medical stability and the avoidance of hypnotic or sedating medications [70]. Similarly, chronic insomnia in adults aged 50 years and older was specified in another trial, with usual bedtime parameters used to support a stable sleep routine [73]. Across studies, exclusions sought to reduce potential confounding from comorbid disease, concurrent medication or supplement use, and major lifestyle differences. Examples included diabetes or other metabolic disease, uncontrolled hypertension, unresolved infection, and prescribed anti-inflammatory agent or corticosteroid use [53, 72]. Habitual cherry or blueberry consumption, regular medication or antioxidant supplement use, excessive alcohol intake, and recent substantial changes in diet or physical activity were also restricted [53, 75]. Cherry allergy was a separate exclusion criterion for participant safety [53].

3.3 Tart Cherry Interventions

3.3.1 Supplement Details

The interventions tested were administered in a variety of preparations and dosing schedules. Sinclair *et al.* [53, 74] provided 30 mL tart cherry concentrate twice daily, diluted with 100 mL water. Each 30 mL dose supplied 80 kcal, 19 g carbohydrate (15 g sugars), 1.10 g protein and 1 g fibre. It contained approximately 9.12 mg/mL anthocyanins and 6.63 mg gallic acid equivalents/mL total phenolic content. Pigeon *et al.* [70] administered two 8-oz bottles (approximately 240 mL each) of

tart cherry juice daily, mixed with apple juice (composition not reported). Tucker *et al.* [71] used a capsule formulation, providing 500 mg of 100% tart cherry powder as two pills taken one hour before bedtime (composition not reported). Chung *et al.* [78] delivered five 200 mL servings over 48 hours. Each serving contained 30 mL tart cherry concentrate diluted with water to a final volume of 200 mL. The product contained 213 ± 41 µg/g anthocyanins.

Hillman *et al.* [72] evaluated encapsulated and juice-based preparations. The capsule regimen comprised two 500 mg freeze-dried tart cherry capsules. These provided 1.7 kcal, 0.4 g carbohydrate and 0.2 g fibre, with 760 mg total polyphenols and 330 mg total anthocyanins. The juice regimen comprised two 8-oz bottles (approximately 240 mL each) of tart cherry juice daily. These provided 77 kcal, 18 g carbohydrate and 0 g fibre, with 793 mg total polyphenols and 227 mg total anthocyanins. Kimble *et al.* [75] provided 30 mL tart cherry concentrate twice daily, diluted with 240 mL water. The reported daily intake was 204 kcal, 50 g carbohydrate, 2.2 g protein and 0 g fat. Total anthocyanin content was 22.2 mg (SD = 6.7), and total phenolic content (TPC) was 195.5 mg (SD = 13.1). Morehen *et al.* [76] administered two 30 mL servings of tart cherry concentrate per day, with each serving mixed with 100 mL water. Each 30 mL serving of tart cherry provided 102 kcal, 25 g carbohydrate, 0 g fat, 1 g protein, and 320 mg anthocyanins. Losso *et al.* [73] supplied 240 mL tart cherry juice twice daily (morning and 1-2 hours pre-bedtime) and reported key constituents including procyanidin B2 (451.56 µg/mL), cyanidin-3-O-glucosylrutinoside (123.33 µg/mL), cyanidin-3-O-rutinoside (20.26 µg/mL), and cyanidin-3-O-glucoside (3.51 µg/mL). Finally, Howatson *et al.* [77] provided 30 mL tart cherry concentrate twice daily, diluted with 200 mL water, reporting a melatonin content of 1.42 µg/mL (≈ 42.6 µg per 30 mL serving; ≈ 85.2 µg/day), alongside total anthocyanins of 9.12 mg/mL, vitamin A as β -carotene (22.64 IU/mL), and vitamin C as ascorbic acid (0.324 mg/mL).

3.3.2 Intervention Adherence

Adherence was defined as the proportion of prescribed doses consumed. Reported adherence with the interventions was high (mean = $95.76 \pm 3.48\%$). Across the five studies that provided compliance data [53, 72, 74-76], two trials reported perfect adherence (100%) to tart cherry juice [72, 76], and the other trials reported high compliance ($>90\%$) with both tart cherry juice and capsules. The remaining studies [70, 71, 73, 77, 78], did not report compliance data.

3.3.3 Withdrawals/Dropouts and Adverse Events

Withdrawals and adverse events were inconsistently reported across the included studies. Sinclair *et al.* [74] reported one withdrawal and no adverse events, whereas Sinclair *et al.* [53] reported one withdrawal and one adverse event in the tart cherry arm; the nature of the adverse event was not reported. Chung *et al.* [78] reported one dropout in the intervention group but did not report any adverse event data. Hillman *et al.* [72] recorded withdrawals in both intervention formats, one dropout in the capsule arm and two dropouts in the juice arm, with no adverse events reported for either tart cherry preparation. Kimble *et al.* [75] reported that three participants in each trial arm did not complete the study. One participant in the tart cherry arm withdrew because of gastrointestinal discomfort and bloating. Losso *et al.* [73] randomised 11 participants, but three were excluded after polysomnography identified sleep apnoea, leaving eight participants with insomnia. These exclusions were not attributable to either crossover condition. Losso *et al.* [73] did

not report any adverse events. Meanwhile, Morehen *et al.* [76] reported no withdrawals and no adverse events in the intervention group.

3.4 Control/Placebo Groups

3.4.1 Placebo Details

Placebo preparations generally matched the active interventions in volume, administration time and sensory characteristics, although their exact dietary compositions were inconsistently reported. Sinclair *et al.* [74] and Sinclair *et al.* [53] used an unflavoured maltodextrin-based concentrate formulated to match the tart cherry concentrate, with red and black food colouring and cherry flavour drops. Participants consumed 30 mL twice daily, diluted with 100 mL water. Each 30 mL placebo dose provided 80 kcal and 20 g carbohydrate with 0 g sugars, 0 g protein, and 0 g fibre, and contained 0 mg/mL anthocyanins. Pigeon *et al.* [70] provided two 8 oz bottles (approximately 240 mL each) daily prepared from unsweetened black cherry Kool Aid mix combined with water, colouring, a clouding agent, and sucrose, matched to the tart cherry juice for colour, sugar, and final soluble solids content, but did not report dietary composition. Tucker *et al.* [71] administered a 460 mg corn starch placebo as two pills one hour before bedtime, with no compositional details reported. Chung *et al.* [78] delivered 200 mL beverages five times over 48 hours, mixed with water and vinegar to achieve a colour and taste similar to tart cherry concentrate diluted in water, but placebo dietary information was not reported.

Hillman *et al.* [72] employed preparation specific placebos. For the capsule condition, participants received two coloured 460 mg cornstarch capsules that provided 1.8 kcal and 0.4 g carbohydrate, with 0 g fibre, and did not contain detectable polyphenols or anthocyanins. For the tart cherry juice preparation, participants consumed two 8 oz bottles (approximately 240 mL each) per day at least 8 hours apart, providing 68 kcal, 17 g carbohydrate, and 0 g fibre, again with no polyphenols or anthocyanins. Kimble *et al.* [75] provided 30 mL of an unsweetened black-cherry-flavoured Kool-Aid placebo containing dextrose, fructose, lemon juice and artificial food colouring. It was diluted in 240 mL water and consumed twice daily. The placebo was reported to provide 204 kcal, 51 g carbohydrate, 0 g protein, and 0 g fat, with TPC of 21.5 mg (SD = 2.3). Morehen *et al.* [76] used two 30 mL servings of a commercially available fruit cordial mixed with 100 mL water and maltodextrin, matched for energy and carbohydrate content with tart cherry, providing 100 kcal, 25 g carbohydrate, 0 g fat, and 0 g protein. Losso *et al.* [73] provided a placebo drink 240 mL twice daily composed of vapor distilled water with fructose, dextrose, and lemon powder, formulated to match the appearance and flavour of cherry juice, but did not report dietary composition. Howatson *et al.* [77] administered 30 mL twice daily diluted with 200 mL water using a mixed fruit cordial containing less than 5% fruit, with no placebo dietary information reported.

3.4.2 Placebo Adherence

Reported compliance with the placebo conditions was high (mean = 96.51 ± 3.98%). Across the five studies that provided compliance data [53, 72, 74-76] one trial reported 100% adherence to both placebo capsules and juice [72]. Four trials [53, 74-76] reported placebo adherence above 90%, with both placebo juice and capsules. Meanwhile, the remaining studies [70, 71, 73, 77, 78] did not report placebo adherence.

3.4.3 Withdrawals/Dropouts and Adverse Events

Withdrawals and adverse events were also inconsistently reported across the placebo groups. Sinclair *et al.* [74] and Sinclair *et al.* [53] reported no withdrawals and no adverse events in the placebo arm. Chung *et al.* [78] documented two dropouts in the placebo group but did not report adverse event data. Hillman *et al.* [72] reported withdrawals/dropouts in both comparator formats, with five withdrawals in the placebo capsule arm and four withdrawals in the placebo juice arm, and no adverse events recorded for either arm. Kimble *et al.* [75] reported that three participants in each trial arm did not complete the study. One participant in the tart cherry arm withdrew because of gastrointestinal discomfort and bloating. Losso *et al.* [73] randomised 11 participants, but three were excluded after polysomnography identified sleep apnoea, leaving eight participants with insomnia. These exclusions were not attributable to either crossover condition. Losso *et al.* [73] did not report any adverse events. Morehen *et al.* [76] reported no withdrawals and no adverse events in the placebo group.

3.4.4 Blinding Efficacy

Blinding efficacy was formally assessed only by Sinclair *et al.* [74] and Sinclair *et al.* [53], where 54% and 52% of participants correctly identified the trial arm to which they were assigned. Both trials examined blinding efficacy statistically and concluded that a suitable blinding strategy was adopted. Kimble *et al.* [75] did not report quantitative information regarding their blinding but concluded that a successful blinding strategy was adopted.

3.5 Findings by Outcome

3.5.1 Overall Sleep Quality

Across the ten studies, sleep was assessed using the PSQI [53, 73, 74], Z-machine electroencephalography (EEG) [71], self-reported sleep records [72], actigraphy [77, 78], a visual analogue scale [76], and the Insomnia Severity Index [70]. Data from six studies included in the meta-analysis produced an effect estimate favouring tart cherry. The pooled meta-analysis demonstrated a non-significant improvement in sleep quality following tart cherry supplementation compared with placebo (Hedges' $g = 0.064$; 95% CI -0.147 to 0.275; $P = 0.552$), with substantial heterogeneity ($I^2 = 63.7\%$) (Figure 2a). Egger's test was non-significant ($P = 0.330$).

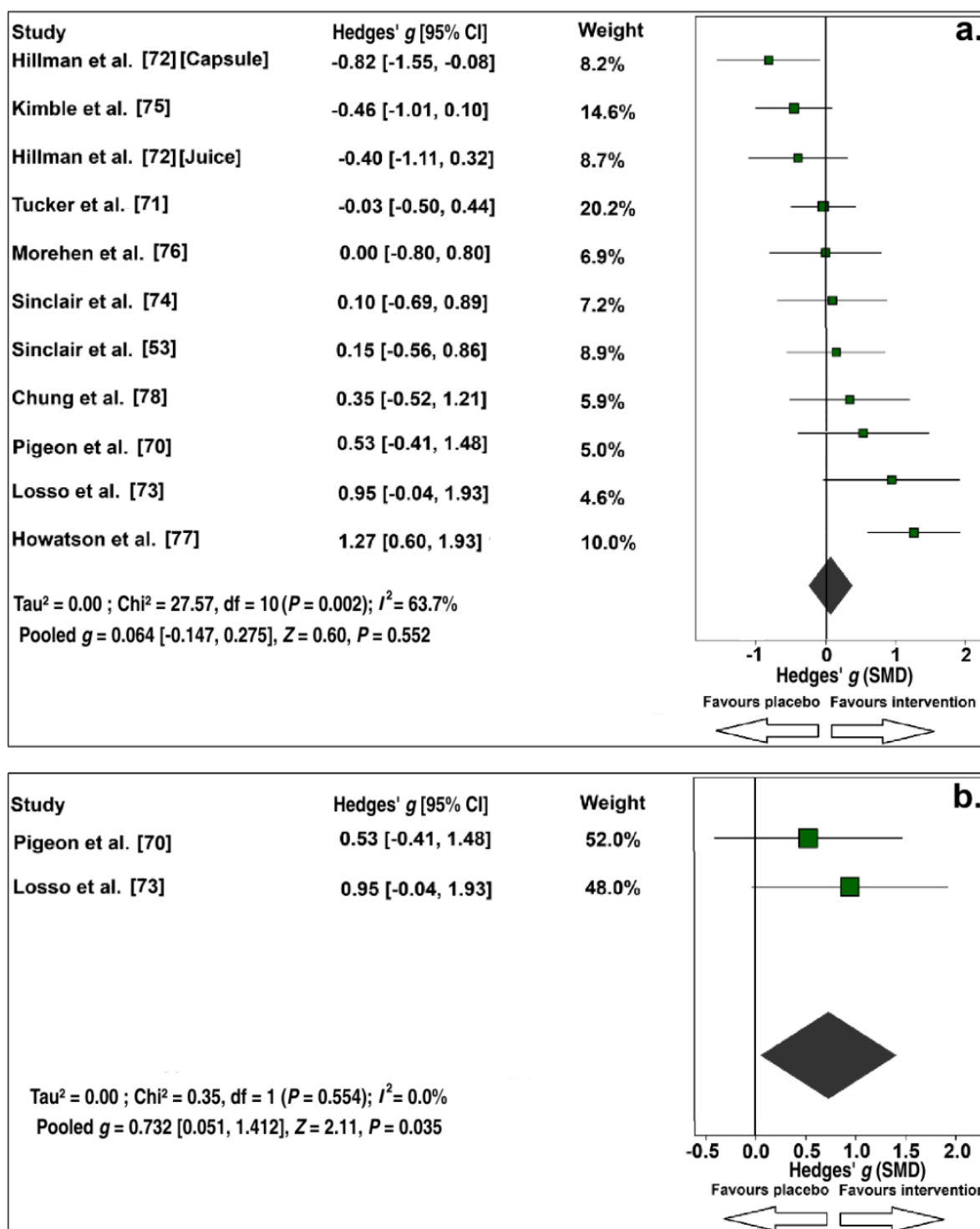


Figure 2 Forest plots for change-from-baseline outcomes comparing tart cherry with placebo. (a) Overall sleep quality and (b) Individuals with insomnia. Note. Squares represent individual comparison estimates, with square size proportional to inverse-variance weight; horizontal lines represent 95% confidence intervals and diamonds represent pooled random-effects estimates. Positive Hedges' *g* values favour tart cherry. CI, confidence interval; df, degrees of freedom; *I*², percentage of variability attributable to heterogeneity; *P*, probability value; SMD, standardised mean difference; Tau², estimated between-study variance; Chi², Cochran's heterogeneity statistic; *Z*, test statistic for the pooled effect.

Two trials examined the effects of tart cherry in individuals with insomnia [70, 73], and assessed overall sleep quality using the PSQI [73] and Insomnia Severity Index [70]. Data from both studies included in the meta-analysis produced an effect estimate favouring tart cherry. The pooled meta-analysis demonstrated a significant improvement in sleep quality following tart cherry supplementation compared with placebo (Hedges' $g = 0.732$; 95% CI 0.051 to 1.412; $P = 0.035$), with low heterogeneity ($I^2 = 0\%$) (Figure 2b).

3.5.2 Melatonin

Three studies [72, 77, 78] assessed melatonin levels following tart cherry supplementation. Data from all three trials produced an effect estimate favouring tart cherry. The pooled meta-analysis demonstrated non-significant increases in melatonin following tart cherry supplementation compared with placebo (Hedges' $g = 0.273$; 95% CI -0.082 to 0.627; $P = 0.132$), with low heterogeneity ($I^2 = 0\%$) (Figure 3a). Egger's test was non-significant ($P = 0.601$).

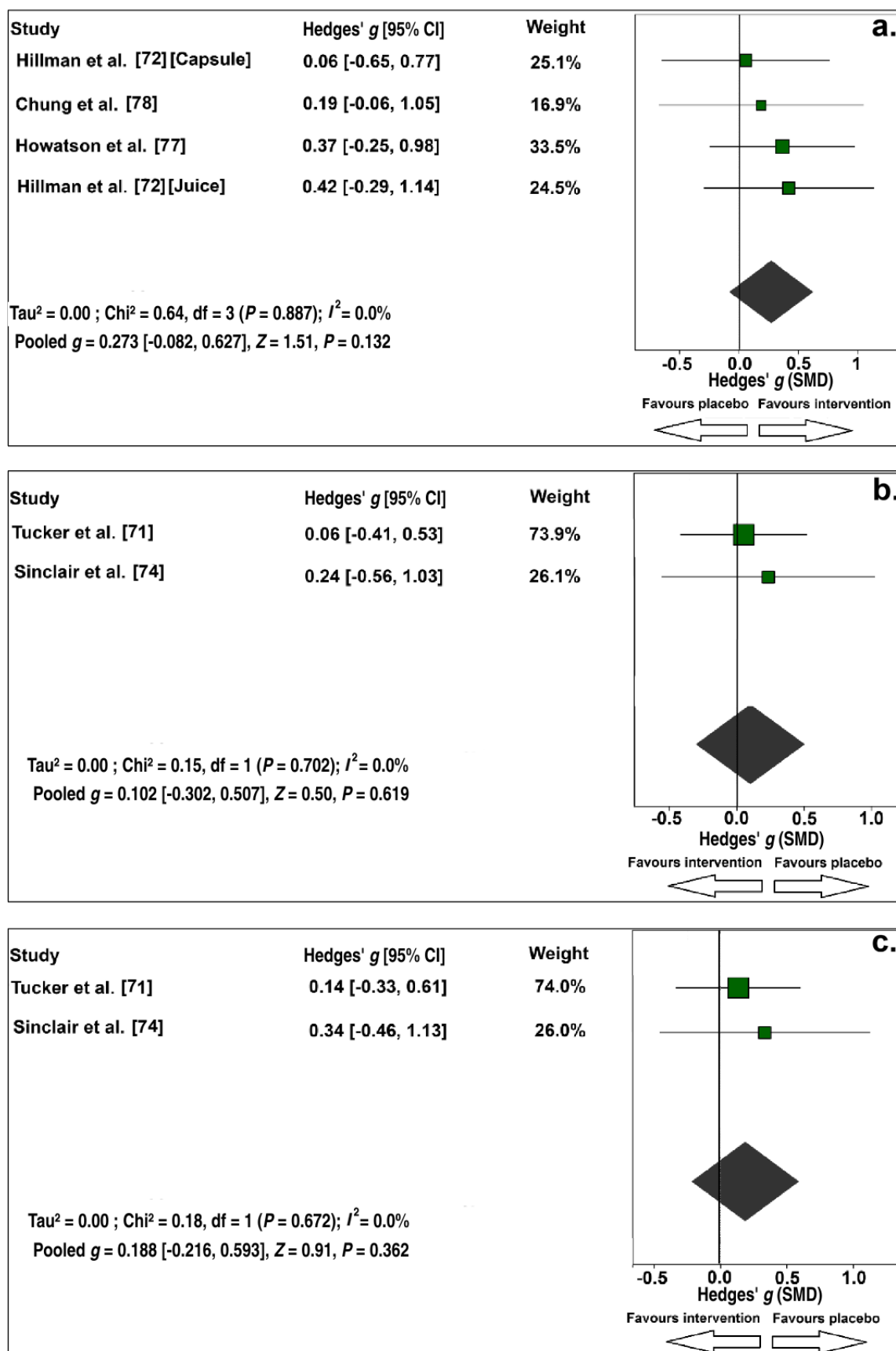


Figure 3 Forest plots for change-from-baseline melatonin and inflammatory biomarkers comparing tart cherry with placebo. (a) Melatonin, (b) TNF- α and (c) C-reactive protein (CRP). Note. Squares represent individual comparison estimates, with square size

proportional to inverse-variance weight; horizontal lines represent 95% confidence intervals and diamonds represent pooled random-effects estimates. For melatonin, positive Hedges' g values indicate a greater increase with tart cherry supplementation. For TNF- α and CRP, negative values indicate greater reductions with tart cherry supplementation. CI, confidence interval; df, degrees of freedom; I^2 , percentage of variability attributable to heterogeneity; P , probability value; SMD, standardised mean difference; Tau^2 , estimated between-study variance; Chi^2 , Cochran's heterogeneity statistic; Z , test statistic for the pooled effect.

3.5.3 TNF- α

Two studies [71, 74] assessed TNF- α as a biomarker of inflammation. Data from both trials favoured placebo over tart cherry. The pooled meta-analysis demonstrated a non-statistically significant increase in TNF- α following tart cherry supplementation compared with placebo (Hedges' $g = 0.102$; 95% CI -0.302 to 0.507; $P = 0.619$), with low heterogeneity ($I^2 = 0\%$) (Figure 3b).

3.5.4 CRP

Two studies [71, 74], assessed CRP as a biomarker of inflammation. Data from both trials favoured placebo over tart cherry. The pooled meta-analysis demonstrated a non-statistically significant increase in CRP following tart cherry supplementation compared with placebo (Hedges' $g = 0.188$; 95% CI -0.216 to 0.593; $P = 0.362$), with low heterogeneity ($I^2 = 0\%$) (Figure 3c).

3.5.5 Interleukins

Two studies [71, 76], assessed IL-6 as a biomarker of inflammation. Data from both trials favoured tart cherry over placebo. The pooled meta-analysis demonstrated a non-statistically significant decrease in IL-6 following tart cherry supplementation compared with placebo (Hedges' $g = -0.128$; 95% CI -0.534 to 0.278; $P = 0.538$), with low heterogeneity ($I^2 = 0\%$) (Figure 4a).

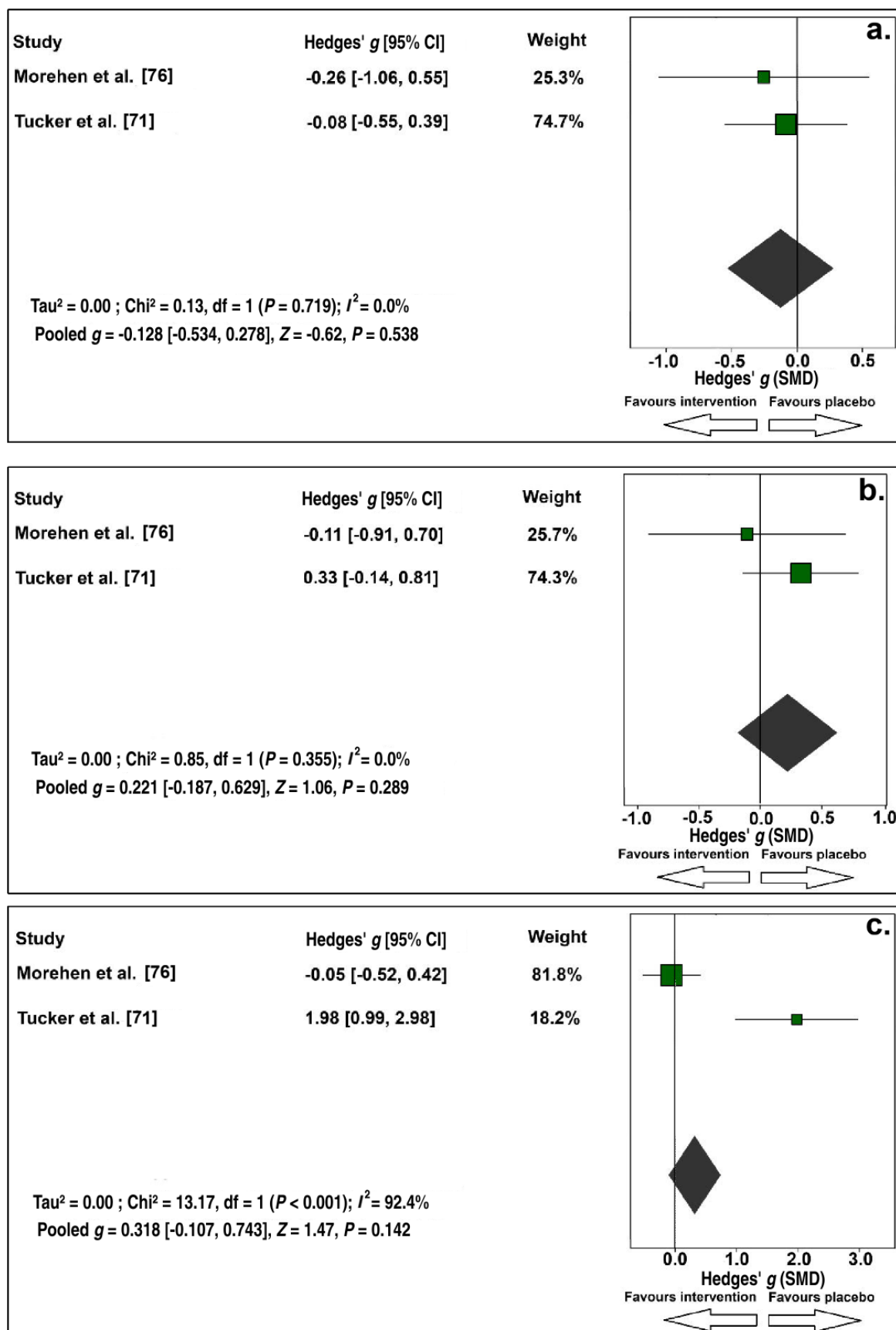


Figure 4 Forest plots for change-from-baseline inflammatory biomarkers comparing tart cherry with placebo. (a) IL-6, (b) IL-8 and (c) IL-10. Note. Squares represent individual comparison estimates, with square size proportional to inverse-variance weight;

horizontal lines represent 95% confidence intervals and diamonds represent pooled random-effects estimates. Effect sizes were retained in their natural direction: negative Hedges' g values indicate lower post-intervention biomarker values with tart cherry supplementation, whereas positive values indicate higher values. CI, confidence interval; df, degrees of freedom; I^2 , percentage of variability attributable to heterogeneity; P , probability value; SMD, standardised mean difference; Tau^2 , estimated between-study variance; Chi^2 , Cochran's heterogeneity statistic; Z , test statistic for the pooled effect.

Two studies [71, 76], assessed IL-8 as a biomarker of inflammation. Data from one trial favoured tart cherry over placebo [76] and the other had the opposite effect [71]. The pooled meta-analysis demonstrated a non-statistically significant increase in IL-8 following tart cherry supplementation compared with placebo (Hedges' $g = 0.221$; 95% CI -0.187 to 0.629; $P = 0.289$), with low heterogeneity ($I^2 = 0\%$) (Figure 4b).

Two studies [71, 76], assessed IL-10 as a biomarker of inflammation. Data from one trial favoured tart cherry over placebo [71] and the other had the opposite effect [76]. The pooled meta-analysis demonstrated a non-statistically significant increase in IL-10 following tart cherry supplementation compared with placebo (Hedges' $g = 0.318$; 95% CI -0.107 to 0.743; $P = 0.142$), with considerable heterogeneity ($I^2 = 92.4\%$) (Figure 4c).

3.6 Ongoing Trials

The trial-registry searches identified one relevant registered study for which no published results were available at the time of the January 2026 search. CherryZZZ (NCT06786494) was a randomised, triple-masked crossover pilot comparing tart cherry juice with placebo juice in 20 older adults with insomnia or sleep problems. Registered outcomes included feasibility, sleep quantity and quality, urinary 6-sulphatoxymelatonin, the kynurenine:tryptophan ratio, urinary cortisol, IL-6 and CRP. Because no published outcome data were available, the study was not eligible for inclusion in the review or meta-analysis.

3.7 Risk of Bias

Risk of bias was assessed across the ten included studies using the Cochrane RoB 2.0 tool and the RoB 2.0 extension for randomised crossover trials, following recommended guidance. None of the ten sleep-outcome assessments was judged to have a low overall risk of bias. Seven had some concerns and three, Hillman *et al.* [72], Losso *et al.* [73] and Howatson *et al.* [77], were judged to have a high overall risk. For the randomisation domain, one study was at low risk and nine had some concerns. For deviations from intended interventions, seven were at low risk and three had some concerns. For missing outcome data, two were at low risk, six had some concerns and two were at high risk. For outcome measurement, six were at low risk and four had some concerns. For selection of the reported result, four were at low risk and six had some concerns. Summary risk of bias is presented in Figure 5.

	Risk domain							
	1	2	3	4	5	6		
Sinclair et al. [74]	-	+	-	+	+	-	+	Low risk of bias
Sinclair et al. [53]	-	-	+	+	+	-	-	Some concerns
Tucker et al. [71]	-	-	-	-	+	-	X	High risk of bias
Hillman et al. [72]	-	+	X	-	-	X		
Kimble et al. [75]	+	+	-	+	-	-		
Morehen et al. [76]	-	-	+	-	-	-		
Losso et al. [73]	-	+	X	+	+	X		
Howatson et al. [77]	-	+	-	+	-	X		
Chung et al. [78]	-	+	-	+	-	-		
Pigeon et al. [70]	-	+	-	-	-	-		

Rob 2 domains:

1. Randomization process
2. Deviation from intended interventions
3. Missing outcome data
4. Measurement of the outcome
5. Selection of the reported result
6. Overall risk of bias

Figure 5 Risk-of-bias judgements for the included trials using the revised Cochrane risk-of-bias tool for randomised trials (RoB 2).

3.8 Certainty of Evidence

Certainty was very low for overall sleep quality in mixed populations, TNF- α , CRP, IL-6, IL-8 and IL-10. Certainty was low for overall sleep quality in the insomnia subgroup and for melatonin. The primary reasons for downgrading were risk of bias and imprecision across most outcomes, with imprecision largely driven by 95% confidence intervals crossing the line of no effect and, in smaller evidence bases, the optimal information size not being reached. Indirectness further reduced certainty for inflammatory biomarkers because participant characteristics and clinical contexts differed across the contributing trials. Inconsistency was also a concern for IL-10 because heterogeneity was considerable. No evidence of publication bias was detected where assessment was possible, and formal evaluation was limited for outcomes informed by only two studies (Figure 6). The insomnia subgroup was informed by Pigeon *et al.* [70] and Losso *et al.* [73]. TNF- α and CRP were informed by Tucker *et al.* [71] and Sinclair *et al.* [74], while the interleukin analyses were informed by Tucker *et al.* [71] and Morehen *et al.* [76].

Outcome	No. of Studies/ No of participants	Study Design Grade	Risk of bias/certainty (Downgrade 1 if ≥50% of domains rated as 'some concerns' or 'high' on risk of bias on Cochrane risk-of-bias tool version 2)	Indirectness of evidence (Downgrade 1 if significant differences in PICO factors that may result in change of outcome)	Heterogeneity or inconsistency of effect (Potential downgrade if wide variance of point estimates across studies; minimal/no overlap of CIs; wide (<2) PI or significant heterogeneity tests)	Imprecision (Does the 95% CI cross the line of no effect? If yes, Downgrade 1. If no, Is the OIS† reached? If no, Downgrade 1)	Publication bias*	Certainty of Evidence
Overall sleep quality	10 RCT's (N=294)	High	-1	0	-1	-1	0	•○○○ Very low
Overall sleep quality (insomnia only)	2 RCTs (N=27)	High	-1	0	0	-1	0	••○○ Low
Melatonin	3 RCTs (n=112)	High	-1	0	0	-1	0	••○○ Low
TNF-α	2 RCTs (n=58)	High	-1	-1	0	-1	0	•○○○ Very low
CRP	2 RCTs (n=58)	High	-1	-1	0	-1	0	•○○○ Very low
IL-6	2 RCTs (n=45)	High	-1	-1	0	-1	0	•○○○ Very low
IL-8	2 RCTs (n=45)	High	-1	-1	0	-1	0	•○○○ Very low
IL-10	2 RCTs (n=45)	High	-1	-1	-1	-1	0	•○○○ Very low

Figure 6 GRADE assessment for the examined measures. Note. Randomised controlled evidence began at high certainty and was downgraded according to the domains shown. Filled circles indicate retained certainty and empty circles indicate downgrading. CI, confidence interval; CRP, C-reactive protein; GRADE, Grading of Recommendations Assessment, Development and Evaluation; IL, interleukin; OIS, optimal information size; PICO, population, intervention, comparator and outcome; RCT, randomised controlled trial; TNF-α, tumour necrosis factor alpha.

4. Discussion

This systematic review and meta-analysis evaluated the effects of tart cherry supplementation on overall sleep quality and melatonin. It also examined the inflammatory biomarkers IL-6, IL-8, IL-10, CRP and TNF-α. To our knowledge, this is the first systematic review and meta-analysis to quantify the effects of tart cherry supplementation on sleep quality and related biomarkers. The review aimed to integrate the available RCT evidence and inform future research and clinical practice. Ten RCTs met the eligibility criteria of this review. Interventions varied in duration, formulation and population. They ranged from short protocols to 12-week regimens, used capsules or juice-based products and included clinically heterogeneous participant groups.

With respect to the main clinical outcome of overall sleep quality, which was assessed across all ten RCTs, tart cherry supplementation was associated with a small, non-significant improvement in overall sleep quality compared with placebo (Hedges' $g = 0.064$). Although six studies favoured tart cherry over placebo [53, 70, 73, 74, 77, 78], the pooled estimate and confidence interval indicate that, across mixed populations and outcome instruments, tart cherry supplementation did not significantly improve overall sleep quality. However, when trials recruiting participants with insomnia were examined separately [70, 73], a small to moderate and statistically significant improvement in sleep quality was observed (Hedges' $g = 0.732$), with low heterogeneity. This finding may be clinically relevant because insomnia is common, often persistent, and associated with substantial societal costs [7], while insufficient or poor-quality sleep has been linked directly or indirectly with all ten leading causes of death in the United States [8-15]. However, the insomnia

subgroup comprised only these two trials. Although no statistical heterogeneity was detected, the certainty of evidence was low, the risk of bias was judged to be some concerns to high, and publication bias and small-study effects could not be assessed [59]. These findings therefore suggest a possible benefit but do not establish therapeutic efficacy of tart cherry supplementation, and should be interpreted cautiously. Replication is required in larger, rigorously designed RCTs using standardised and validated sleep outcomes. One possible explanation for the subgroup finding is that participants with clinically meaningful insomnia had greater scope for improvement than healthy adults or athletes whose sleep was less impaired at baseline. Differences in outcome measurement may also have contributed: the insomnia trials used disorder-specific or clinically oriented measures, whereas the remaining studies assessed sleep using a heterogeneous range of questionnaires, sleep records, actigraphy and EEG, which may have differed in their sensitivity to intervention-related changes.

In relation to biochemical outcomes, three trials assessed melatonin [72, 77, 78], two assessed TNF- α and CRP [71, 74], and two assessed IL-6, IL-8 and IL-10 [71, 76]. No significant pooled effects were found for melatonin, TNF- α , CRP, IL-6, IL-8 or IL-10. Poor sleep has been associated with dysregulation of inflammatory cytokines and acute phase proteins, including interleukins, TNF- α and CRP [29, 30], while melatonin is a central circadian signal implicated in sleep propensity and sleep duration [31-33]. The absence of detectable changes in these biomarkers does not support a consistent mechanistic effect of tart cherry supplementation on inflammatory or melatonin-mediated pathways in the populations studied. Importantly, although tart cherry products contain measurable quantities of melatonin, the absolute dose delivered in most trials appears modest. For example, Howatson *et al.* [77] reported a melatonin concentration of 1.42 $\mu\text{g/mL}$ in tart cherry concentrate, equating to approximately 85 $\mu\text{g/day}$ under the dosing regimen used. This quantity is substantially lower than doses used in clinical trials of exogenous melatonin, which commonly range from 0.5 to 5 mg/day [31, 79]. It therefore remains uncertain whether the melatonin content of tart cherry products alone is sufficient to exert clinically meaningful circadian or hypnotic effects. Any observed benefit may reflect synergistic actions of polyphenols, indirect modulation of inflammatory signalling, or effects on substrates involved in melatonin synthesis rather than a direct pharmacological melatonin effect [46-50, 73]. Interpretation from the current meta-analysis is constrained by imprecision and low certainty, with very low to low GRADE ratings for all biochemical outcomes and risk-of-bias concerns across the contributing trials. The considerable IL-10 heterogeneity may reflect differences in study design, sampling time, assay procedures, participant characteristics and intervention composition between the two contributing studies [71, 76].

Taken together, the findings from this review provide preliminary support for tart cherry supplementation as a potentially useful adjunctive strategy for insomnia management, while offering little evidence for improvements in sleep quality when examined across broader, mixed cohorts. Across the included studies, compliance, where reported, was high, and tart cherry supplementation was generally well tolerated during the relatively short interventions that reported adverse-event data. However, adverse-event reporting was incomplete in several trials, and the small total sample and short follow-up prevent firm conclusions about safety. The evidence therefore indicates short-term tolerability rather than establishing safety. This distinction is important given the limitations and potential harms associated with pharmacological insomnia treatments, including residual next-day impairment and safety concerns [19-28]. While the current

data do not demonstrate consistent improvements in sleep quality across all populations, the observations across insomnia trials suggest that baseline symptom severity or clinical phenotype may moderate responsiveness. This raises the hypothesis that nutritional interventions may be most effective when targeted to individuals with established disturbances in sleep physiology, rather than applied indiscriminately across otherwise healthy groups. The two insomnia trials [70, 73] did not measure melatonin or the biomarkers pooled in this review, namely IL-6, IL-8, IL-10, CRP and TNF- α . However, Losso *et al.* [73] measured the kynurenine:tryptophan ratio and PGE₂ and assessed IDO inhibition in vitro. These findings provide preliminary mechanistic evidence related to tryptophan availability and inflammation, but the biological basis of the subgroup effect remains uncertain.

4.1 Limitations

Several limitations should be acknowledged. Methodological strengths include adherence to PRISMA and Cochrane guidance [58, 59], exclusive inclusion of randomised controlled designs, and the combined evaluation of sleep outcomes alongside biomarkers relevant to inflammation and melatonin biology. Restricting inclusion to English-language publications may have introduced language or publication bias. The modest number of studies also precluded reliable subgroup and dose-response analyses. We could not therefore examine differences by formulation, polyphenol or anthocyanin dose, melatonin content, intervention timing or participant phenotype beyond insomnia. The variation in baseline sleep status, age, physical activity, clinical conditions, intervention formulation, dose and outcome measurement also restricts the generalisability of the overall pooled estimate. The result should not be interpreted as applying uniformly to healthy adults, athletes and people with clinically defined insomnia. With the exception of overall sleep quality, most meta-analyses were informed by only two studies, limiting power and increasing susceptibility to imprecision. Risk-of-bias judgements ranged from some concerns to high across the included trials, and the certainty of evidence was predominantly very low to low. Intervention durations were relatively short (≤ 3 months), leaving longer-term efficacy and safety unclear. Finally, sleep quality was assessed using heterogeneous instruments, ranging from questionnaire-derived indices to actigraphy and EEG-derived measures, which likely contributed to between-study inconsistency and complicates interpretation of pooled effects.

Future research should prioritise adequately powered, well-controlled RCTs with extended intervention and follow-up periods to confirm both efficacy and durability of tart cherry supplementation effects on sleep quality, particularly in individuals with clinically defined insomnia or chronic sleep disturbance. Trials should implement robust randomisation, allocation concealment, and blinding procedures, and should routinely report blinding efficacy and adherence. Standardisation is also needed in intervention characterisation, including quantification of polyphenol, anthocyanin and melatonin content, dose, timing relative to bedtime, and formulation, to improve comparability and enable dose-response analyses. Consistent selection of validated sleep outcomes, ideally combining patient-reported measures with objective sleep parameters, would strengthen clinical interpretability. Mechanistic work is also required. The present synthesis did not identify consistent changes in inflammatory interleukins, CRP, TNF- α , or melatonin, yet the two insomnia trials showing improvements in sleep quality did not measure these biomarkers, leaving the biological basis for benefit unresolved. Future studies should therefore embed mechanistic endpoints within insomnia-focused trials, using standardised sampling protocols and

clinically meaningful biomarker panels aligned to established sleep-immune and circadian pathways [29-31]. Finally, tart cherry supplementation and supplementation approaches more broadly are not currently incorporated into clinical management guidelines for insomnia [80, 81]. Incorporating patient-centred outcomes such as acceptability, taste burden for juice regimens, long-term adherence, and cost-effectiveness will be essential if future evidence is to support guideline integration.

5. Conclusions

In conclusion, this systematic review and meta-analysis found that tart cherry supplementation was not associated with a significant improvement in overall sleep quality across mixed populations. A statistically significant improvement was observed among participants with insomnia; however, this subgroup finding was derived from only two small trials and should therefore be considered preliminary. The low certainty of evidence, risk-of-bias judgements ranging from some concerns to high, small number of studies and heterogeneity in outcome measurement prevent firm conclusions regarding efficacy. Tart cherry supplementation appeared to be generally well tolerated during the relatively short interventions, with high compliance and few adverse events where reported. However, incomplete adverse-event reporting, the small total sample and limited follow-up mean that the available evidence supports short-term tolerability rather than establishing safety. Larger, rigorously designed RCTs with standardised and validated sleep outcomes, longer intervention and follow-up periods, detailed supplement-composition reporting and relevant mechanistic biomarkers are required to confirm clinically meaningful benefit and determine safety. Such evidence is needed before tart cherry supplementation can be integrated into evidence-based, multimodal approaches to insomnia management.

Abbreviations

BMI	body mass index
CI	confidence interval
CRP	C-reactive protein
EEG	electroencephalography
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IDO	indoleamine 2,3-dioxygenase
IL	interleukin; PGE ₂ , prostaglandin E ₂
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSQI	Pittsburgh Sleep Quality Index
RCT	randomised controlled trial
RoB 2.0	revised Cochrane risk-of-bias tool for randomised trials
SD	standard deviation
SMD	standardised mean difference
TNF- α	tumour necrosis factor alpha
TPC	total phenolic content
WHO	World Health Organization
REM	rapid eye movement

Author Contributions

Jonathan Sinclair: Conceptualization; Methodology; Data curation; Formal analysis; Investigation; Software; Validation; Visualization; Writing-original draft; Writing-review & editing. Lauren Baker: Conceptualization; Methodology; Supervision; Validation; Writing-review & editing; Project administration. Lindsay Bottoms: Conceptualization; Methodology; Supervision; Validation; Writing-review & editing; Project administration.

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Competing Interests

The authors declare that they have no conflicts of interest.

Data Availability Statement

This systematic review was prospectively registered in an international database of systematic reviews in health-related research (<https://www.crd.york.ac.uk/PROSPERO/view/CRD420251229156>).

AI-Assisted Technologies Statement

Artificial intelligence (AI) tools were used solely for basic grammar correction and language refinement in the preparation of this manuscript. Specifically, OpenAI's ChatGPT was employed to improve the readability and linguistic clarity of the English text. All scientific content, data interpretation, and conclusions were developed independently by the author. The authors have thoroughly reviewed and edited the AI-assisted text to ensure its accuracy and accept full responsibility for the content of the manuscript.

Additional Materials

The following additional materials are uploaded at the page of this paper.

1. Supplementary Material 1: Search Strategy.
2. Supplementary Material 2: Sensitivity Analyses.

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