Eur J Nutr
DOI 10.1007/s00394-011-0263-7

ORIGINAL CONTRIBUTION

Effect of tart cherry juice (*Prunus cerasus*) on melatonin levels and enhanced sleep quality

Glyn Howatson · Phillip G. Bell · Jamie Tallent · Benita Middleton · Malachy P. McHugh · Jason Ellis

Received: 7 July 2011 / Accepted: 10 October 2011

Abstract
Background Tart Montmorency cherries have been reported to contain high levels of phytochemicals including melatonin, a molecule critical in regulating the sleep-wake cycle in humans.
Purpose The aim of our investigation was to ascertain whether ingestion of a tart cherry juice concentrate would increase the urinary melatonin levels in healthy adults and improve sleep quality.
Methods In a randomised, double-blind, placebo-controlled, crossover design, 20 volunteers consumed either a placebo or tart cherry juice concentrate for 7 days. Measures of sleep quality recorded by actigraphy and subjective sleep questionnaires were completed. Sequential urine samples over 48 h were collected and urinary 6-sulfatoxymelatonin (major metabolite of melatonin) determined; cosinor analysis was used to determine melatonin circadian rhythm (mesor, acrophase and amplitude). In addition, total urinary melatonin content was determined over the sampled period. Trial differences were determined using a repeated measures ANOVA.
Results Total melatonin content was significantly elevated ($P < 0.05$) in the cherry juice group, whilst no differences were shown between baseline and placebo trials. There were significant increases in time in bed, total sleep time and sleep efficiency total ($P < 0.05$) with cherry juice supplementation. Although there was no difference in timing of the melatonin circadian rhythm, there was a trend to a higher mesor and amplitude.
Conclusions These data suggest that consumption of a tart cherry juice concentrate provides an increase in exogenous melatonin that is beneficial in improving sleep duration and quality in healthy men and women and might be of benefit in managing disturbed sleep.

Keywords Tart cherries · Melatonin · Sleep · Recovery

Introduction

Tart Montmorency cherries (*Prunus cerasus*), rich in numerous phytochemicals, provide a range of health benefits that include reduction in symptoms associated with gout [1], down-regulation of circulating inflammatory markers [2], analgesic effects following long-distance running [3], reduced oxidative stress [4], improved recovery following damaging exercise [5–7] and recently, improved sleep quality in late-life insomnia [8]. Mechanistically, it is thought the phenolic compounds within tart cherries act as 'free radical' scavengers that reduce oxidative stress [2]. In addition, the anti-inflammatory properties [9] of tart cherries have been reported to be at a level comparable to a number of non-steroidal anti-inflammatory drugs [10]. In particular, the anthocyanin content of tart cherries, which compares

G. Howatson (✉) · P. G. Bell · J. Tallent · J. Ellis
School of Life Sciences, Northumbria University, Northumberland Building, Newcastle upon Tyne NE1 8ST, UK
e-mail: glyn.howatson@northumbria.ac.uk

G. Howatson
Centre for Aquatic Research, Department of Zoology, University of Johannesburg, Johannesburg, South Africa

B. Middleton
Centre for Chronobiology, Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK

M. P. McHugh
Nicholas Institute of Sports Medicine and Athletic Trauma, Lenox Hill Hospital, New York, NY, USA

Published online: 30 October 2011

favourably with other fruits such as sweet cherries [11], seems to be of most interest, and these are likely to be responsible for the anti-oxidative and anti-inflammatory effects.

A number of recent studies have shown that consumption of tart cherry juice can accelerate recovery following strenuous exercise [5–7], where temporary perturbations in inflammation and oxidative stress can occur. These recovery effects have been attributed to the actions of the antioxidant and anti-inflammatory phytochemicals contained in tart cherries. Pigeon et al. [8] anecdotally reported claims of improved sleep with cherry juice supplementation in participants from a previous trial [6]. Interestingly, in addition to the aforementioned phenolic compounds, tart cherries contain high concentrations of melatonin [12]. Melatonin has a strong influence on the sleep-wake cycle in humans and is associated with sleep-promoting properties [13]. Physiologically, endogenous melatonin secretion adjusts according to the light/dark cycle and can directly influence nocturnal core temperature and hence facilitate the propensity for sleep [14]. Additionally, a strong positive relationship between increased melatonin and total sleep time in healthy, young individuals has been previously demonstrated [15]. Interestingly, the balance of evidence would suggest that exogenous melatonin in the treatment of insomnia is equivocal at best; however, there is a good body of support for melatonin use in managing circadian rhythm disturbance, such as those seen from travelling time zones [16].

In a recent study, the efficacy of tart cherry juice consumption on sleep indices in a population with late-life insomnia was examined [8]. They reported modest improvements in subjective quality of sleep; however, no objective measures of sleep, such as actigraphy, were taken, and the potential mechanisms responsible for the reported sleep improvements (e.g. melatonin) were impossible to discern. The authors [8] speculated that increased dietary melatonin associated with consumption of tart cherry juice might be responsible for the changes. However, there is an alternative hypothesis; the anti-inflammatory properties of tart cherries may have some influence on the pro-inflammatory cytokines involved in sleep regulation [17]. Given the potential benefits of tart cherry juice in delivering exogenous melatonin and improving sleep quality, we hypothesised that the consumption of a tart cherry juice concentrate in young, healthy adults would increase urinary 6-sulfatoxymelatonin and improve indices of sleep quality. Therefore, the aim of this investigation was to examine the effects of tart Montmorency cherry juice concentrate on urinary 6-sulfatoxymelatonin and sleep quality using a double-blind, placebo-controlled, crossover design.

Methods

Participants

Following institutional ethical approval from the School of Life Sciences Ethics Committee at Northumbria University, UK in accordance with the Helsinki Declaration, 20 healthy men ($n = 10$) and women ($n = 10$) volunteered to participate. The mean (±SD) age, height, body mass and BMI were 26.6 (±4.6) years, 1.71 (±0.10) m, 72.5 (±15.0) kg and 24.7 (±3.5) kg m^{-2}, respectively. The age range was restricted to 18–40 years to reduce the potential for age-related sleep disturbances that have been reported in older adults [13]. In addition, all volunteers were physically active and participated in moderate physical exercise for at least 150 min/week. After being informed of the experimental procedures, participants were asked to complete a health screening questionnaire to ascertain contra-indications to participation (prescription medicines, sleep disturbance, special dietary habits, shift work or underlying medical pathology), and volunteers then provided written informed consent.

Experimental overview and study design

Participants were supplemented with a tart cherry juice concentrate or placebo in a randomised, double-blind, placebo-controlled, crossover study design, during normal daily routine. Dependent variables were urinary 6-sulphatoxymelatonin (aMT6s), diet recall, objective activity recorded through actigraphy (variables) and subjective sleep quality. A schematic of the study design is presented in Fig. 1. Initially, participants provided sequential urinary voids across a 48 h period (days 1 and 2) in order to analyse baseline measures of aMT6s. Over the same 2-day period, participants were issued with an activity monitor and completed online daily diet recalls and a sleep diary immediately following morning awakening. Participants then continued to complete the questionnaires and diaries and wear the activity monitors for the remainder of the trial period.

Following the 48-h baseline period, participants were randomly assigned to either the tart cherry juice concentrate or placebo (starting on day 3) for a period of 7 days; this was based on loading phases from previous studies showing efficacy using cherry juice [5–8]. Participants were instructed to consume two servings of either tart cherry juice concentrate or fruit-flavoured cordial each day, for 7 days. In the last 48 h of this supplementation period, urine was again collected in an identical manner as previously described for the baseline period. Following a 14-day washout period, participants repeated the baseline

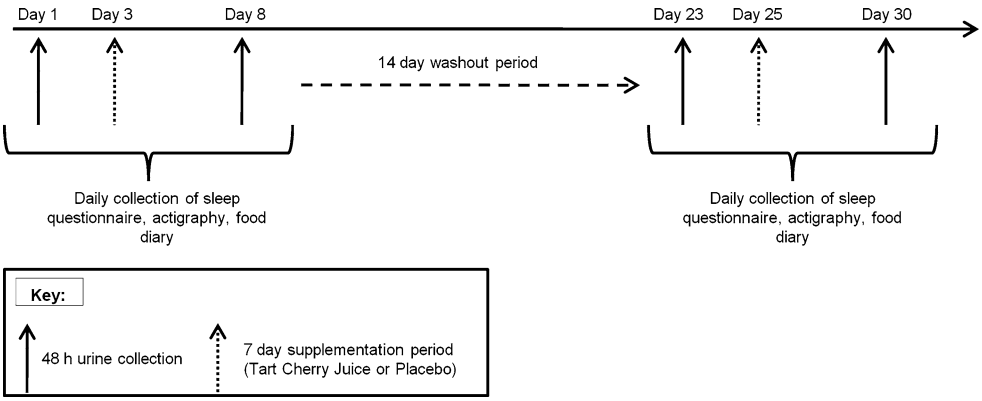

Fig. 1 A schematic outlining the implemented protocol. Supplementation periods consisted of two 30-mL servings per day of either a tart cherry juice concentrate of placebo

and experimental period whilst consuming the other supplement.

Dietary control

All volunteers completed a dietary recall throughout the baseline and supplementation periods. Participants were asked to replicate their diet during the first supplementation period as closely as possible during the second period in order to standardise the dietary intake between trials. Additionally, in order to isolate dietary melatonin as closely as possible, participants were issued with a list of foods that are known to contain or influence melatonin and were subsequently asked to abstain from consuming these for the duration of the trial. Portions of foods thought to contain antioxidants were totalled for each day then averaged across the experimental period.

Supplementation

Prior to starting the experiment, participants were informed that the trial was to ascertain the influence of two fruit concentrates on melatonin levels and sleep quality; however, the nature of the trial regarding tart cherry juice concentrate was only revealed when the study had been completed. A serving of 30 mL of tart Montmorency cherry juice (*Prunus cerasus*) concentrate (Cherry Active, Sunbury, UK) was consumed within 30 min of wakening and 30 min before the evening meal on each of the 7-day supplementation periods. Each 30 mL serving was estimated to contain the equivalent of approximately 90–100 tart cherries and was diluted with approximately 200 mL of water. An independent laboratory (Atlas Bioscience Inc., Tuscan, AZ) conducted melatonin analysis of the cherry juice concentrate adapting an established HPLC method [18]. The concentration of melatonin was 1.42 μg mL^{-1}, which equates to a dose of ~42.6 μg/30 mL serving or ~85.2 μg day^{-1}. Literature suggests that daily melatonin doses of ~0.5–5 mg confer a positive effect in managing disturbed sleep rhythm [19]. In addition, other active compounds contained within the tart cherry juice were verified by the aforementioned laboratory and included anthocyanins such as malvidin, cyanidin, pelargonidin, peonidin, delphinidin, petunidin (total anthocyanin content = 9.117 mg mL^{-1}), vitamin A—as beta-carotene (22.64 IU mL^{-1}) and vitamin C—ascorbic acid (0.324 mg mL^{-1}).

The placebo was a commercially available, economy, mixed fruit cordial (containing less than 5% fruit) that was reported to contain no melatonin or anthocyanins and a trace of vitamin C. Participants were instructed to take the same dose (30 mL) diluted with ~200 mL of water.

Dependent variables

Urine collection and analysis

Sequential urinary voids were collected 48-h periods to ensure the entire circadian cycle was captured during each part of the trial to allow for cosinor analysis that provided measures of acrophase, mesor and amplitude. Urine was collected in a sterilised measuring cylinder. Void volume, time and date were recorded, before a 10 mL aliquot of urine was retained, refrigerated and returned to the laboratory the following morning for labelling and immediate storage at −80 °C for later analysis for urinary aMT6s.

Urinary 6-sulphatoxymelatonin, aMT6s

Urinary 6-sulphatoxymelatonin, aMT6s (the major metabolite of melatonin) was analysed in duplicate using a radioimmunoassay [20]. Samples belonging to the same participant were measured in the same assay run; the intra-assay coefficient of variation was <8%; the limit of detection was 0.25 ng mL^{-1}. Evaluation of aMT6s profiles was performed using cosinor analysis, based upon the least square approximation of the time series using a cosine function with a period of 24 h [21]. Parameters obtained

from this analysis included the following: *acrophase time:* the time of peak aMT6s concentration or the maximum of the fitted cosinor function; *mesor:* the mean aMT6s values for all samples included in the cosinor anlaysis; and *amplitude:* the difference between mesor and peak aMT6 concentrations. Acrophase time was classed as normal if it occurred between midnight and 06:00 h [22]. 'Goodness of fit' measures were used to determine the validity of the cosinor-derived indices: (1) the % rhythm or variability accounted for by the cosine curve: 100% rhythm = all data points fall on the cosine curve and 0% rhythm = none of the data points fall on the cosine curve and (2) the likelihood of data points fitting a straight line as opposed to a cosine curve, expressed as a P value. Data were considered acceptable if the cosinor fit was significant ($P \leq 0.05$) and the % rhythm ≥50% [21]. Finally, the total aMT6s excreted per 24 h was calculated and a mean for each 48-h collection period determined.

Actigraphy

Polysomnography (PSG) offers the most accurate assessment of sleep and sleep quality; however, given the nature of the study, we utilised actigraphy that has been shown to be reliable and has good agreement with PSG [23]. Participants were issued with actigraphy that was worn on the wrist of the non-dominant arm (Actiwatch 7, CamnTech, Cambridge, UK). These were worn for the duration of the study and removed only for bathing, showering or other aquatic activities. Participants were asked to activate the marker function on the watch when getting into bed and when rising the following morning. Analysis was made on sleep efficiency (SE), sleep onset latency (SOL), time in bed (TIB), fragmentation index (FRAGI), total sleep time (TST) and sleep efficiency total (SET); these variables were calculated using Actiwatch software (Actiwatch, CamnTech, Cambridge, UK). The mean values for each sample period were used for data analysis.

Subjective measures

Online subjective sleep diaries were reported immediately following awakening each day during both baseline and trial periods. This commonly used self-reporting method tool has been to be a reliable (90%) measure [24] and allowed calculation of the following: SE, SOL, wake after sleep onset (WASO), napping (NAP), TST and SET [25].

Statistical analyses

Values are reported as mean (±SD), unless otherwise stated. The cosinor data, total aMT6s and all quantitative (actigraphy)- and qualitative (questionnaire)-dependent sleep variables were analysed with a repeated measures ANOVA (condition, placebo vs. cherry juice 2; time, pre vs. post). In addition, 95% confidence intervals were also determined to illustrate the magnitude of change. Finally, baseline measures were examined for differences using a paired samples t test. Significance was set at an alpha level of 0.05.

Results

Baseline measures taken before the placebo and cherry juice trials were not different for any of the dependent variables ($P > 0.05$). All variables returned an observed power value ranging from 0.156 to 0.999. Although we did not quantify all the food consumption using dietary analysis, participants reported a similar diet across the trials. In an attempt to quantify this more fully, we recorded the number of food portions thought to contain antioxidants (including melatonin) across the supplementation periods, 22.8 versus 22.4 for the cherry juice and placebo groups, respectively. A paired samples t test showed no significant differences between groups ($t = 1.162$, $P = 0.259$).

Urinary 6-sulphatoxymelatonin (aMT6s)

The baseline measures preceding the placebo and cherry juice supplements were not different ($t = 0.921$, $P = 0.369$). The repeated measures ANOVA showed a significant trial effect ($F = 23.0$, $P < 0.001$). A significant interaction ($F = 23.0$, $P < 0.001$) was also found and *post hoc* analysis revealed that the cherry juice trial was significantly greater than baseline and placebo trials ($P < 0.001$; 95% CI = 2,828–5,393 ng and 2,519–5,450 ng, respectively); there was no difference between baseline or placebo groups (Fig. 2).

Despite the significant increase in total urinary aMT6 s, the cosinor analysis examining circadian rhythm of aMT6s showed no differences between trials for any variable (Table 1). Cosinor analysis relies on a significant 'fit' of the melatonin response; of the 80 sets of data collected, 22.5% ($n = 18$) were excluded because they did not significantly fit according to the cosinor algorithm. Of the remaining data, there were small non-significant rises in the amplitude and mesor in the cherry juice trial, whilst the acrophase remained largely unchanged throughout. A representative example where urinary voids were collected for a single participant at similar times of the day between the placebo and cherry juice trials is presented in Fig. 3; these data span the circadian changes in aMT6s over sequential 48-h periods.

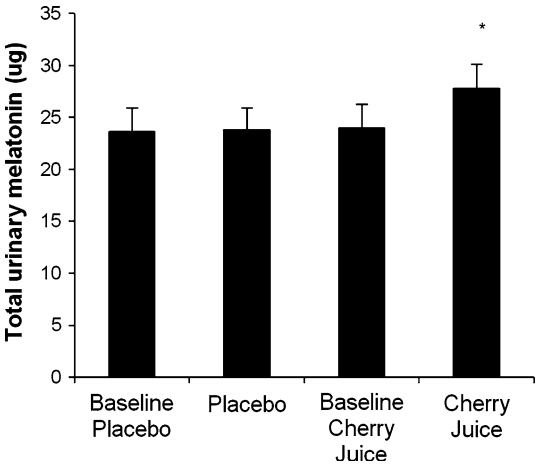

Fig. 2 Mean (±SEE) urinary melatonin (aMT6) secretion for the group following baseline placebo (control), placebo, baseline cherry juice (control) and cherry juice trials.*Asterisk* denotes that cherry juice supplementation resulted in significantly greater aMT6s than baseline and placebo trials ($P \leq 0.05$)

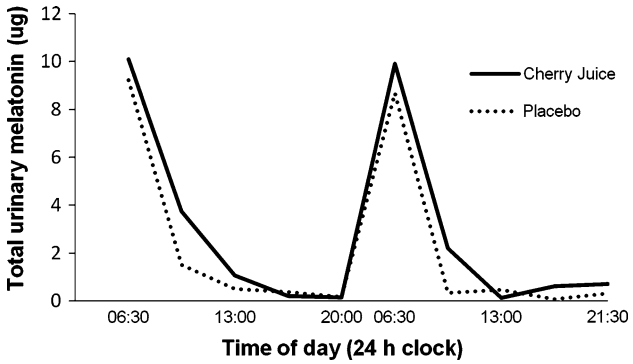

Fig. 3 A representative example of a single subject's circadian rhythm for urinary melatonin (aMT6s) during the placebo and cherry juice trials over sequential 48-h periods

Sleep indices: subjective questionnaire and actigraphy

There was a 100% completion rate for the sleep questionnaires. There was no differences across the different trials for SET, SOL, TST and WASO; however, napping time did show a significant trial and interaction effect ($F = 5.591$, $P = 0.029$), with significantly less napping time in the cherry juice trial compared to baseline and the placebo trials ($P \leq 0.031$; 95% CI = 0.7–13.6 and 0.7–11.1 min, respectively), and there were no differences between baseline measures and the placebo trial (Table 2).

Whilst all participants wore the activity monitor for the duration of the trials, 17 out of 80 trials (21.3%) were excluded from analysis due to missing data. There were no differences in SOL and FRAGI; however, there was a significant trial and interaction effect for TIB ($F = 7.056$, $P = 0.016$) where cherry juice significantly increased time in bed compared to both baseline and placebo trails ($P \leq 0.017$; 95% CI = 4.5–45.2 and 4.7–40.2 min, respectively). Furthermore, TST showed a trial and interaction effect ($F = 11.189$, $P = 0.003$), where the cherry juice trial was significantly greater TST than baseline and placebo trials ($P \leq 0.003$; 95% CI = 15.2–39.7, 14.7–63.6, respectively). In addition, SET showed significant trial and interaction effects ($F = 5.410$, $P = 0.031$), where the cherry juice trial was greater than the baseline and placebo trials ($P \leq 0.017$; 95% CI = 2.1–7.5 and 0.5–9.4, respectively). A summary of these data is presented in Table 3.

Discussion

The aim of this investigation was to ascertain whether the supplementation of tart Montmorency cherry juice concentrate would (1) increase the urinary aMT6s content and (2) improve the objective and subjective sleep indices of young, healthy individuals. We hypothesised that urinary aMT6s would rise and that sleep parameters would improve as a consequence. This is the first investigation to demonstrate that dietary tart cherry juice concentrate increases urinary melatonin levels and provides improved sleep time and quality in a healthy adult population.

The sleep diary information showed that napping time decreased with the administration of cherry juice, whereas the actigraphy showed an increase in TIB, TST and SET, a global measure of sleep quality. Notwithstanding the relatively low baseline SET observed from the actigraphy in these apparently good sleepers, the cherry juice nonetheless showed a 5–6% increase in SET, which likely to be influenced by the significant increase in TST. In addition, given that napping decreased and total time in bed also increased during the cherry juice trial, this is perhaps unsurprising. What is also interesting to note is that there

Table 1 Mean (±SD) cosinor analysis based on melatonin circadian rhythm for all experimental conditions

	Baseline placebo	Placebo	Baseline cherry juice	Cherry juice
Mesor (ng × h^{-1})	17.98 (6.04)	19.17 (7.37)	18.64 (9.76)	21.59 (6.85)
Amplitude (μg × h^{-1})	27.39 (15.78)	27.54 (8.37)	27.05 (10.72)	28.57 (15.01)
Acrophase (time)	4.03 (1.03)	3.55 (1.22)	4.05 (1.40)	4.01 (1.01)

Of the possible 80 data sets, 18 did not significantly fit the cosinor curve and were excluded from the analysis

Table 2 Subjective sleep questionnaire variables for all conditions; values are mean (±SD)

	Baseline placebo	Placebo	Baseline cherry juice	Cherry juice
SE (%)	89.3 (7.3)	91.7 (4.0)	90.0 (6.2)	91.1 (4.9)
SOL (mins)	40.3 (31.6)	39.5 (23.2)	39.8 (25.6)	34.2 (20.5)
WASO (mins)	36.0 (33.0)	19.2 (31.2)	28.8 (30.6)	27.6 (28.2)
Naps (mins)	9.0 (15.1)	7.8 (10.7)	8.6 (13.2)	1.9 (3.5)*
TST (mins)	447 (60)	476 (31)	452 (49)	475 (30)
SET (%)	88.1 (6.8)	90.4 (4.4)	89.4 (5.8)	90.7 (4.9)

SE sleep efficiency, *SOL* sleep onset latency, *WASO* wake after sleep onset, *total SET* sleep efficiency total, *TST* total sleep time

* Denotes significantly different from all other conditions ($P \leq 0.05$)

Table 3 Actigraphy variables for all conditions; values are mean (± SD)

	Baseline placebo	Placebo	Baseline cherry juice	Cherry juice
SE (%)	82.8 (15.7)	84.1 (5.8)	83.9 (7.8)	86.8 (3.6)
SOL (mins)	28.9 (21.3)	30.5 (34.8)	29.1 (26.8)	21.4 (11.1)
Time in bed (mins)	491.8 (36.7)	492.2 (40.6)	490.0 (32.9)	514.7 (17.0)*
FRAGI (AU)	36.8 (8.2)	35.2 (9.3)	35.8 (8.9)	34.2 (7.6)
TST (mins)	392 (28)	380 (49)	385 (30)	419 (22)*
SET (%)	77.5 (5.9)	77.4 (8.5)	76.8 (6.9)	82.3 (3.6)*

Of the possible 80 data sets, 17 were excluded due to technical issues

SE sleep efficiency, *SOL* sleep onset latency, *FRAGI* fragmentation index, *total SET* sleep efficiency total, *TST* total sleep time

* Denotes significantly different from all other conditions ($P \leq 0.05$)

were non-significant trends towards decreased SOL, which is also likely to have influenced the SET.

Only one study has investigated tart Montmorency cherry juice and sleep parameters (a fresh pressed cherry juice blended with apple juice, as opposed to a pure cherry juice concentrate) [8]. They found that elderly individuals, with moderate/severe insomnia, reported improved sleep quality, and it was hypothesised that this was due to the increased exogenous melatonin content afforded by the cherry juice. Unfortunately, they did not measure melatonin; however, data from our investigation lend additional evidence that improved sleep quality is mediated by the increase in dietary melatonin contained within the cherries. Interestingly, a recent addition to the literature [26] examined the increase in melatonin content from dietary intake of Jert Valley cherries (seven varieties, none of which were Montmorency tart cherries). They showed that in a very small population of middle-aged and elderly volunteers, there was an increase in urinary melatonin and some modest improvements in sleep parameters. This investigation [26] based its observations on the first morning void only, whereas all urinary voids were captured for a 48-h period during each part of the current trial. This approach, whilst still having limitations, allows for cosinor analysis and tracking of the circadian rhythm and provides a more comprehensive picture of the dietary effects of cherries on melatonin metabolism across the course of the day. This is especially important when one considers that the half-life of melatonin is relatively short and it is possible to miss fluctuations in melatonin throughout the day.

Further, there is no indication in the aforementioned studies [8, 25] of an experimental control or record of dietary intake, which makes interpretation of the data problematic. Although we were not able to quantify the exact nutritional content for each subject, food intake was estimated. Participants replicated diet as closely as possible from trial to trial. This was based on number of portions thought to contain antioxidants—there were no differences between trials. Support for the efficacy of this approach can be seen by the fact that aMT6s and sleep parameters were unchanged in baseline and placebo trials, whereas aMT6s was significantly elevated in the cherry juice trial. Given the dietary control used in the current investigation, coupled with the significant changes melatonin, we can add support to research showing cherries [26], and specifically in this case, Montmorency cherries improve sleep parameters in healthy individuals, which is likely due to the increase in dietary melatonin. These data support previous work showing improved sleep in healthy younger adults with exogenous melatonin supplementation [14]; but additionally, it provides a potential alternative to traditional melatonin supplementation in the form of a functional food.

The secretion of melatonin is influenced by light/dark cycles and ultimately is instrumental in the sleep/wake cycle [13]. From a physiological perspective, given that endogenous melatonin influences core temperature and facilitates sleep [14], it makes the expectation tenable that increased exogenous melatonin will further facilitate changes in core temperature and hence be responsible for the improvements in sleep quality. Further work examining the potential physiological outcomes (such as core temperature and EEG in polysomnographic paradigms) from exogenous melatonin, specifically from functional foods, would be useful additions to the literature. In an attempt to elucidate the relationship between the change in SET and the change in melatonin, we conducted a Pearson's correlation coefficient analysis and found that there was a modest relationship ($r = 0.416$, $P > 0.05$), indicating that other factors may influence the variables associated with sleep quality. Importantly, a limitation with our data is that ~21% of the actigraphy data were missing, which may have influenced this correlation and also the non-significant trends in other actigraphy-dependent variables. Furthermore, 50% of our sample was women, and it is conceivable that they were in different stages of the menstrual cycle, which may also influence core temperature and hence the propensity for sleep disturbance [27]. Future research might wish to consider this issue in future experiments.

Melatonin is not the only candidate mechanism, given that sleep regulation is also influenced by pro-inflammatory cytokines [17]. Tart cherries have been shown to contain numerous phenolic compounds that have anti-inflammatory and antioxidant properties that can increase antioxidant capacity [5, 26]. Furthermore, cherry juice has been shown to decrease oxidative stress and inflammation following strenuous exercise [5] making it possible that these antioxidant and/or anti-inflammatory properties modulated indices of sleep in this study, although this remains to be demonstrated in an experimental model.

It has been previously speculated that the positive effects on sleep seen from tart cherries might be due to improvements in circadian regulation [8]. We observed no changes in mesor, amplitude or acrophase, although there was a trend towards a higher mesor (essentially equating to the mean value across the circadian cycle). This is perhaps not surprising given that the total urinary melatonin did increase with cherry juice supplementation. An obvious difference with the previous work lies within the subject populations; Pigeon et al. [8] used older adults suffering from moderate/severe insomnia and did not measure circadian rhythm or melatonin, whereas the current investigation used asymptomatic younger adults (≤37 years) and did measure circadian rhythm and melatonin. Conceivably, cherries might help regulate circadian rhythm in those with disturbed sleep [8]; however, our evidence shows (from cosinor analysis) that despite increased total sleep time and improved sleep quality, this is not the case in asymptomatic, healthy younger adults. Notwithstanding this, aMT6s levels are increased with tart cherry juice consumption, but an investigation that examines elderly individuals, perhaps with disturbed sleep, that incorporates measures of circadian rhythms and sleep quality would be a valuable addition to the literature.

In conclusion, this is the first study to show direct evidence that dietary supplementation with a tart Montmorency cherry juice concentrate increases circulating melatonin and can provide modest improvements in sleep time and quality in healthy adults with no reported disturbed sleep. Although the interaction of other phytochemicals cannot be completely ruled out, these data provide a mechanism of action for the previously conjectural reports of improved sleep quality with cherry juice supplementation. Subsequently, Montmorency tart cherry juice concentrate might therefore present a suitable adjunct intervention for disturbed sleep across a number of scenarios in healthy and symptomatic individuals.

Acknowledgments Gratitude is extended to Kelly Mitcheson for her help in data collection and to CherryActive (Sunbury, UK) for donating the cherry juice concentrate.

References

1. Jacob RA, Spinozzi GM, Simon VA, Kelley DS, Prior RL, Hess-Pierce B, Kader AA (2003) Consumption of cherries lowers plasma urate in healthy women. J Nutr 133(6):1826–1829
2. Kelley DS, Rasooly R, Jacob RA, Kader AA, Mackey BE (2006) Consumption of Bing sweet cherries lowers circulating concentrations of inflammation markers in healthy men and women. J Nutr 136(4):981–986
3. Kuehl K, Perrier E, Elliot D, Chesnutt J (2010) Efficacy of tart cherry juice in reducing muscle pain during running: a randomized controlled trial. J Int Soc Sports Nut 7(1):17
4. Traustadottir T, Davies SS, Stock AA, Su Y, Heward CB, Roberts LJ II, Harman SM (2009) Tart cherry juice decreases oxidative stress in healthy older men and women. J Nutr 139(10): 1896–1900. doi:10.3945/jn.109.111716
5. Howatson G, McHugh MP, Hill JA, Brouner J, Jewell AP, Van Someren KA, Shave RE, Howatson SA (2010) Influence of tart cherry juice on indices of recovery following marathon running. Scand J Med Sci Sports 20(6):843–852. doi:10.1111/j.1600-0838.2009.01005.x
6. Connolly DAJ, McHugh MP, Padilla-Zakour OI (2006) Efficacy of a tart cherry juice blend in preventing the symptoms of muscle damage. Br J Sports Med 40(8):679–683. doi:10.1136/bjsm.2005.025429
7. Bowtell JL, Sumners DP, Dyer A, Fox P, Mileva K (2011) Montmorency cherry juice reduces muscle damage caused by intensive strength exercise. Med Sci Sports Exerc 43(8):1544–1551
8. Pigeon WR, Carr M, Gorman C, Perlis ML (2010) Effects of a tart cherry juice beverage on the sleep of older adults with insomnia: a pilot study. J Med Food 13(3):579–583. doi: 10.1089/jmf.2009.0096

9. Wang H, Nair MG, Strasburg GM, Chang Y-C, Booren AM, Gray JI, DeWitt DL (1999) Antioxidant and antiinflammatory activities of anthocyanins and their aglycon, cyanidin, from tart cherries. J Nat Prod 62(2):294–296. doi:10.1021/np980501m
10. Kim D-O, Heo HJ, Kim YJ, Yang HS, Lee CY (2005) Sweet and sour cherry phenolics and their protective effects on neuronal cells. J Agric Food Chem 53(26):9921–9927. doi:10.1021/jf0518599
11. Wang H, Nair MG, Iezzoni AF, Strasburg GM, Booren AM, Gray JI (1997) Quantification and characterization of anthocyanins in Balaton tart cherries. J Agric Food Chem 45(7):2556–2560. doi:10.1021/jf960896k
12. Burkhardt S, Tan DX, Manchester LC, Hardeland Rd, Reiter RJ (2001) Detection and quantification of the antioxidant melatonin in Montmorency and Balaton tart cherries (*Prunus cerasus*). J Agric Food Chem 49(10):4898–4902. doi:10.1021/jf010321+
13. Hughes RJ, Sack RL, Lewy AJ (1998) The role of melatonin and circadian phase in age-related sleep-maintenance insomnia: assessment in a clinical trial of melatonin replacement. Sleep 21(1):52–66
14. Claustrat B, Brun J, Chazot G (2005) The basic physiology and pathophysiology of melatonin. Sleep Med Rev 9(1):11–24
15. Morris M, Lack L, Barrett J (1990) The effect of sleep/wake state on nocturnal melatonin excretion. J Pineal Res 9(2):133–138. doi:10.1111/j.1600-079X.1990.tb00701.x
16. Ferguson SA, Rajaratnam SMW, Dawson D (2010) Melatonin agonists and insomnia. Expert Rev Neurother 10(2):305–318
17. Opp MR (2004) Cytokines and sleep: the first hundred years. Brain Behav Immun 18(4):295–297
18. Iinuma F, Hamase K, Matsubayashi S, Takahashi M, Watanabe M, Zaitsu K (1999) Sensitive determination of melatonin by precolumn derivatization and reversed-phase high-performance liquid chromatography. J Chromatogr A 835(1–2):67–72
19. Herxheimer A, Pertrie KJ (2002) Melatonin for the prevention of jet lag. Cochrane Database Syst Rev 9:11–24
20. Aldhous ME, Arendt J (1988) Radioimmunoassay for 6-sulphatoxymelatonin in urine using an iodinated tracer. Ann Clin Biochem 25(3):298–303
21. Minors DS, Waterhouse JM (1988) Mathematical and statistical analysis of circadian rhythms. Psychoneuroendocrinology 13(6):443–464
22. Lockley SW, Skene DJ, Tabandeh H, Bird AC, Defrance R, Arendt J (1997) Relationship between napping and melatonin in the blind. J Biol Rhythm 12(1):16–25. doi:10.1177/074873049701200104
23. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP (2003) The role of actigraphy in the study of sleep and circadian rythyms. Sleep 26(3):342–392
24. Rogers AE, Caruso CC, Aldrich MS (1993) Reliability of sleep diaries for assessment of sleep/wake patterns. Nurs Res 42(6):368–372
25. Lockley SW, Skene DJ, Arendt J (1999) Comparison between subjective and actigraphic measurement of sleep and sleep rhythms. J Sleep Res 8(3):175–183. doi:10.1046/j.1365-2869.1999.00155.x
26. Garrido M, Paredes SD, Cubero J, Lozano M, Toribio-Delgado AF, Muñoz JL, Reiter RJ, Barriga C, Rodríguez AB (2010) Jerte valley cherry-enriched diets improve nocturnal rest and increase 6-sulfatoxymelatonin and total antioxidant capacity in the urine of middle-aged and elderly humans. J Gerontol Ser A Biol Sci Med Sci. doi:10.1093/gerona/glq099
27. Coyne MD, Kesick CM, Doherty TJ, Kolka MA, Stephenson LA (2000) Circadian rhythm changes in core temperature over the menstrual cycle: method for noninvasive monitoring. Am J Physiol Regul Integr Comp Physiol 279:R1316–R1320