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Tart cherry juice has no acute effects on uric acid, vascular function and inflammation: a randomised crossover trial.

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Tart cherry juice has no acute effects on uric acid, vascular function and inflammation: a randomised crossover trial.

Abstract

Background

Hyperuricaemia increases the risk of gout, and cardiovascular disease, thus dietary modifications that reduce urate are of interest. Cherries have been reported to lower urate, but studies examining acute effects have mostly failed to include a control group, despite urate being known to exhibit diurnal fluctuations, typically falling throughout the day.

Aim

This study aimed to determine the acute effects of a single serving of tart cherry juice on uric acid metabolism and risk factors for cardiovascular disease relative to a control drink.

Methods

In an open-label, randomised, controlled, crossover design, 12 healthy adults (mean age 41.1 (± 11.1) y; mean body mass index 26.4 (± 4.3) kg/m^2; 7 men and 5 women) consumed 250 mL tart cherry juice (containing 30 mL of concentrate) and 250 mL water (control) on separate occasions ≥ 7 days apart. Serum uric acid, central and brachial blood pressure, augmentation index, and pulse wave velocity were measured at baseline, 1, 2, 3, 5, and 24 hours, post-drink, serum c-reactive protein at baseline, 2 and 5 hours, and creatinine-adjusted urinary uric acid at 0-2, 2-4, and 4-5 hours.

Results

There were no statistically significant main effects of drink type or drink by time interactions (all outcomes $p > 0.05$). However, independent of drink type, serum uric acid ($p = 0.008$), urinary uric acid ($p < 0.001$), c-reactive protein ($p = 0.023$), and measures of blood pressure (all $p < 0.05$) changed with different temporal patterns throughout the day (main effects of time, $p < 0.05$).

Conclusion

These results indicate that diurnal fluctuations may partly explain the beneficial acute effects of cherry consumption on uric acid metabolism and inflammation previously reported in studies without a comparator control group.

Trial registry name and URL: ClinicalTrials.gov https://clinicaltrials.gov/study/NCT04960527

Trial Registration number: (NCT04960527)

Keywords: cherry juice; uric acid; inflammation; blood pressure; vascular function.

Introduction

Hyperuricaemia has been associated with elevated risk of gout, renal disease, cardiovascular disease (CVD) and metabolic dysfunction (Kuo et al., 2016; Terkeltaub et al., 2006). Several

dietary modifications have been proposed for the prevention of hyperuricaemia, including restricting intakes of purine-rich and fructose-rich foods, limiting alcohol consumption, remaining hydrated, and increasing cherry consumption (Collins et al., 2019; Schlesinger, 2005). The potential of cherries to prevent hyperuricaemia has been ascribed to their high content of polyphenols, especially anthocyanins (Chaovanalikit and Wrolstad, 2004; Kelley et al., 2018; Kirakosyan et al., 2009). Cherry consumption has been suggested to reduce serum uric acid (sUA) by: (i) inhibiting hepatic xanthine oxidoreductase and/or (ii) increasing the glomerular filtration of UA and inhibiting its tubular reabsorption, thereby increasing urinary uric acid (UUA) excretion (Haidari et al., 2009; Jacob et al., 2003; Kirakosyan et al., 2018; Zhang et al., 2012).

To our knowledge, three studies have reported that cherries decrease sUA in the hours after consumption (Bell et al., 2014a; Hillman and Uhranowsky, 2021; Jacob et al., 2003), two of which (Bell et al., 2014a; Jacob et al., 2003) also measured an increase in UUA excretion. However, these studies had methodological limitations. Two studies (Bell et al., 2014a; Jacob et al., 2003) had no control group. Whereas the third, which investigated the effect of one and two daily servings of tart cherry (TC) in capsules and as juice, only contained placebo groups for the once daily servings (Hillman and Uranowsky, 2021). Since sUA is known to exhibit a diurnal rhythm, falling as the day progresses (Sennels et al., 2012), the failure to include control groups complicates the interpretation of these studies. Thus, the primary aim of the present study was to determine the acute effects of TC juice consumption on sUA and UUA excretion relative to a control drink.

Hyperuricemia is a risk factor for CVD possibly because it promotes hypertension and increases arterial stiffness (Borghi et al., 2022; An et al., 2024). Within vascular endothelial cells, elevated UA promotes oxidative stress, inflammation, and depletes nitric oxide causing endothelial dysfunction and vasoconstriction (Ndrepepa 2025). The consumption of TC might

71 be expected to reduce blood pressure (BP) and arterial stiffness by lowering urate or via the
72 anti-inflammatory and antioxidant actions of its content of polyphenols. However, the results
73 of human intervention studies investigating the effect of TC on BP and arterial stiffness have
74 been mixed (Desai et al., 2021; Keane et al., 2016a; Kimble et al., 2021; Lynn et al., 2014).
75 Thus, the secondary aim of this study was to determine the acute effects of TC juice on
76 inflammation, blood pressure (BP), and arterial stiffness.
77

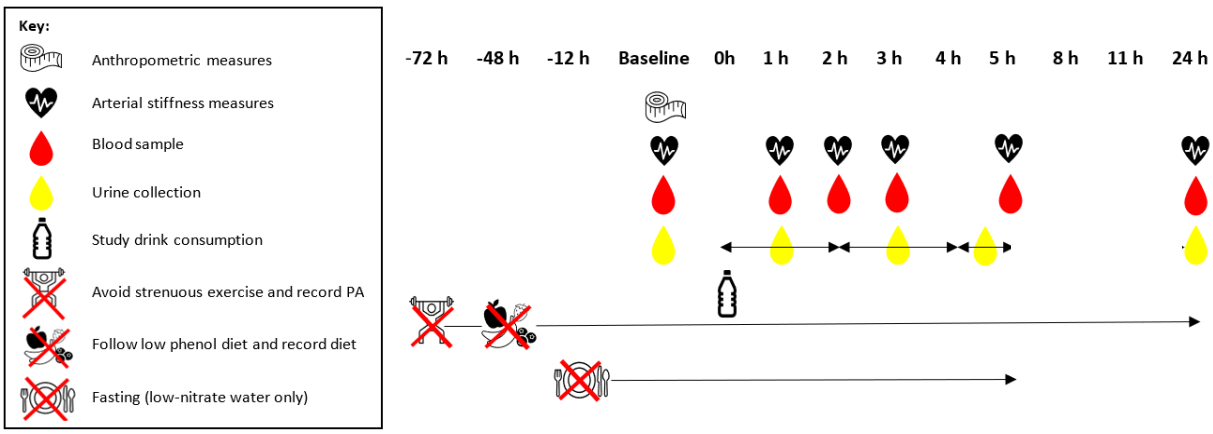
78 **Methods**

79 This study was reported in line with the CONSORT 2010 statement (Dwan et al., 2019).

80 ***Trial Design***

81 The study was an open-label, 2-arm, randomised, placebo-controlled, crossover trial of thirteen
82 healthy adults. Participants consumed 250 mL of TC juice (30 mL TC concentrate with 220
83 mL water) or 250 mL of water on two separate occasions, separated by a wash-out period of ≥
84 7 days. Blood, urine, and vascular measurements were collected at baseline and multiple time-
85 points over 24 hours following each drink (**Fig 1).** Each participant attended each of their test
86 sessions at the same time (between 9 and 10am).
87

Fig. 1 Study protocol. PA; physical activity



The study opened recruitment in July 2021 and closed at the end of February 2022. It was approved by Sheffield Hallam University (SHU) ethics committee (ER9199256) and registered at ClinicalTrials.gov (NCT04960527) before recruitment commenced. The study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments.

Participants and settings

A total of 13 healthy, non-smoking, adult volunteers were recruited through word-of-mouth. Inclusion criteria were, aged between 18 and 85 years, and no history of, gout, type 1 or type 2 diabetes, gastrointestinal disorders, CVD, or kidney disease. Interested individuals were provided with a participant information sheet containing further details of the study. Potential participants also received a verbal explanation of the study and were screened for inclusion criteria. Written informed consent was gained from all participants. Measurements were made at the Nutrition Research Laboratory of SHU, Sheffield, United Kingdom, United Kingdom.

Dietary Interventions

During the active intervention arm of the study, participants consumed 250 mL of TC juice, consisting of 30 mL Montmorency TC concentrate (CherryActive®, ActiveEdge™, Hanworth, UK) and 220 mL low-nitrate water (Buxton®, UK). Analysis of the TC concentrate in our

106 nutrition research laboratory revealed that each serving contained a mean phenol content of
107 408 (SD 5.4) mg gallic acid equivalents (Folin-Ciocalteu method; Singleton and Rossi, 1965)
108 and an anthocyanin content of 3.8 (SD 0.3) mg cyanidin-3-glucoside equivalents (pH
109 differential method; Lee et al., 2005). During the control arm, participants consumed 250 mL
110 of low-nitrate water (Buxton®, UK). A low-nitrate water was selected for the control drink to
111 minimise vascular effects (Hobbs et al., 2013) and avoid bioactive compounds such as
112 polyphenols. The two study arms were separated by a wash-out period of ≥ 7 days. The wash-
113 out duration was based on the known pharmacokinetics of cherry polyphenols (Keane et al.,
114 2016b) and likely transient nature of any effects on the outcome measures. An investigator not
115 involved in data collection generated a block randomised allocation sequence using
116 www.random.org (block size 4) and assigned participants to their sequence of interventions.
117 The use of a water control meant it was impossible to conceal this sequence from participants
118 or the researcher collecting data.

119 Participants were provided with a dietary advice sheet containing meal
120 recommendations to help them follow a low-polyphenolic diet, including avoiding fruits,
121 vegetables, wholegrains, and nuts, for 48 hours prior to each test day. The evening prior to each
122 test day participants were provided with a low-phenol spaghetti carbonara ready-meal
123 (Sainsbury's PLC, UK), low-phenol dessert (Bonne Maman®, Somerset, UK), and low-nitrate
124 water (Buxton®, UK) to consume. Participants attended the laboratory following an overnight
125 fast of ≥ 10 hours, although low-nitrate water was permitted.

126 Participants remained fasted during the first 5 hours post drink consumption; however,
127 500 mL low-nitrate water was provided during this time. Participants were advised to drink
128 when thirsty but avoid consuming large volumes at a single time-point to minimise possible
129 effects on vascular function (Callegaro et al., 2007). A low-phenol lunch of sandwiches made
130 from white bread and ham, ready salted crisps, and a plain Greek yoghurt were provided

immediately following the 5-hour measurements. Participants were also provided with low-phenol snacks, a low-phenol macaroni cheese ready-meal, and low-nitrate water to consume over the rest of the day. Participants returned to the laboratory following another overnight fast of ≥ 10 hours for their 24-hour measurements.

Participants were asked to record their dietary intake throughout the first arm of the study and instructed to replicate this during the second arm. Participants were also asked to avoid strenuous exercise from 72 hours before each test day until after their 24-hour measurements.

Outcomes

The primary outcome measure was between-treatment difference in the change in sUA from baseline to 24 hours post-drink. Secondary outcome measures were between-treatment differences in the change in the inflammatory marker, serum CRP from baseline to 5 hours post-consumption, and changes in UUA excretion and vascular function (resting brachial and central BP and arterial stiffness) from baseline to 24 hours post-consumption. Non-efficacy outcomes included physical activity (PA) and dietary intake measures, for example consumption of high-phenolic foods.

Anthropometry

Height (to 0.1 cm) and mass (to 0.1 kg) of participants were measured during their first visit to the laboratory and used to calculate body mass index (BMI) (mass (kg)/height $(m)^2$).

Arterial Stiffness and Blood Pressure (BP)

A Vicorder® device (SMT Medical, Germany) was used to measure brachial and central BP, carotid-femoral PWV, and augmentation index (AIx). Participants were familiarised with the Vicorder® prior to their first experimental session to reduce the effects of anxiety on BP and

other vascular measures (Franklin et al., 2013). Familiarisation consisted of practice measurements with carotid, arm, and femoral cuffs, so participants could become accustomed to the sensation of each cuff inflating. BP, PWV, and AIx were measured at baseline and 1, 2-, 3-, 5-, and 24-hours post-drink consumption. Following the Vicorder® instructions, brachial DBP values were also used as central DBP values. Three replicate measures with 1-minute intervals were taken at each time-point. Participants rested in a supine position for 15 minutes before the measurements and remained still throughout.

Collection and Processing of Blood Samples

Blood was collected at baseline, 1, 2, 3, 5, and 24 hours, post-consumption. Samples were centrifuged at 2500 x g for 15 minutes at 18 °C to separate serum (Hermle Z 36 HK, HERMLE Labortechnik GmbH, Germany), which was stored at -80ºC until analysis.

Serum C-reactive Protein (CRP) and Uric Acid (sUA)

CRP was measured in serum collected at baseline, 2, and 5 hours using a CRP Quantikine enzyme-linked immunosorbent assay kit (R&D systems, Abingdon, UK). The intra-assay CV was 5.5%. sUA was determined in serum collected at baseline, 1, 2, 3, 5, and 24 hours using a UA (Amplex® Red, Invitrogen™, UK) assay kit. The intra-assay CV was 3.9%. Both analytes were measured on a microplate reader (BioTek synergy HT, Winooski, USA).

Urine collection and analysis

Spot urine samples were collected at baseline and 24 hours post-drink consumption. Urine was also collected between 0-2, 2-4, and 4-5 hours. Samples were centrifuged twice at 2800 x g for 15 minutes to remove unwanted cells and material (Hermle Z 36 HK, HERMLE Labortechnik GmbH, Germany) and stored at -80 °C until analysis. Urine samples were analysed for UUA (Amplex® Red, Invitrogen™, UK) and creatinine (ELISA; R&D systems, Abingdon, UK)

concentrations, using a microplate reader (BioTek synergy HT, Winooski, USA). The intra-assay CV was 2.0% for UUA and 2.1% for urinary creatinine. UUA (µmol) was corrected for creatinine concentration (µMol) to provide a UUA to urinary creatinine excretion ratio.

Assessment of Diet and Physical Activity (PA)

From 48 hours prior to baseline until 24-hour post-consumption, participants completed a food diary. Participants recorded PA in a diary from 72 hours prior to their two main laboratory sessions until their 24-hour post-consumption measurements.

Statistical Methods

The primary outcome was change in sUA concentration. Change in UUA, CRP, BP, and arterial stiffness were secondary outcomes. The effect of treatment (TC versus water) on all outcomes was analysed as the percentage change from baseline using two-way repeated measures analyses of variance (ANOVA) with Bonferroni post-hoc tests. Partial Eta-Squared (ηp^2) effect sizes for ANOVA were classified as small (0.01 – 0.059), moderate (0.06-0.137), and large (≥ 0.138) (Pallant, 2010). Further exploratory analyses investigating between-sex differences on the effect of cherry consumption on sUA and UUA were undertaken by adding sex as a between-subjects factor in two-way repeated measures ANOVAs. Baseline data is presented as mean (SD) or median and interquartile range (IQR), as appropriate. Results are reported as mean % and SD for continuous data. All analyses were conducted using IBM SPSS Statistics v24. The critical value for statistical significance was set at $p < 0.05$.

A sample size of thirteen was determined sufficient to detect a decrease in sUA of 15 µmol/L with 80% power at a significance level of 0.05, using data from White et al. (2018).

Results

Participant Characteristics

Thirteen participants started the study however one dropped out following completion of the control treatment. Of the 12 participants (7 male/5 female) who completed the study, mean age was 41.1 (± 11.1; range 27 to 60) years, and average BMI 26.4 (± 4.3; range 20.1 to 35.1) kg/m^2. Baseline clinical data did not differ between TC juice and control drink visits ($p > 0.05$ for all), **Table 1**.

Table 1 Baseline clinical data of participants prior to the provision of 250 mL tart cherry juice and 250 mL water. Data are presented as mean ± SD or median (IQR)

	Tart cherry juice	**Water (control)**
Brachial systolic blood pressure, mmHg	126.2 ± 11.0	123.6 ± 8.4
Brachial diastolic blood pressure, mmHg	65.8 ± 6.1	64.9 ± 6.4
Central systolic blood pressure, mmHg	120.3 ± 11.8	118.7 ± 8.6
Pulse wave velocity, m/s	8.2 (2.6)	7.3 (2.0)
Augmentation index, %[a]	14.8 ± 7.3	18.2 ± 9.8
Serum uric acid, µmol/L	155.4 ± 59.2	168.3 ± 57.1
Urinary urate:urinary creatinine, mmol/mmol	0.4 ± 0.1	0.5 ± 0.2
C-reactive protein, mg/L	0.4 (0.7)	0.6 (1.8)

$n = 12$ for both treatment arms except for [a] where $n = 10$.

Dietary Adherence and Avoidance of High-Intensity Physical Activity

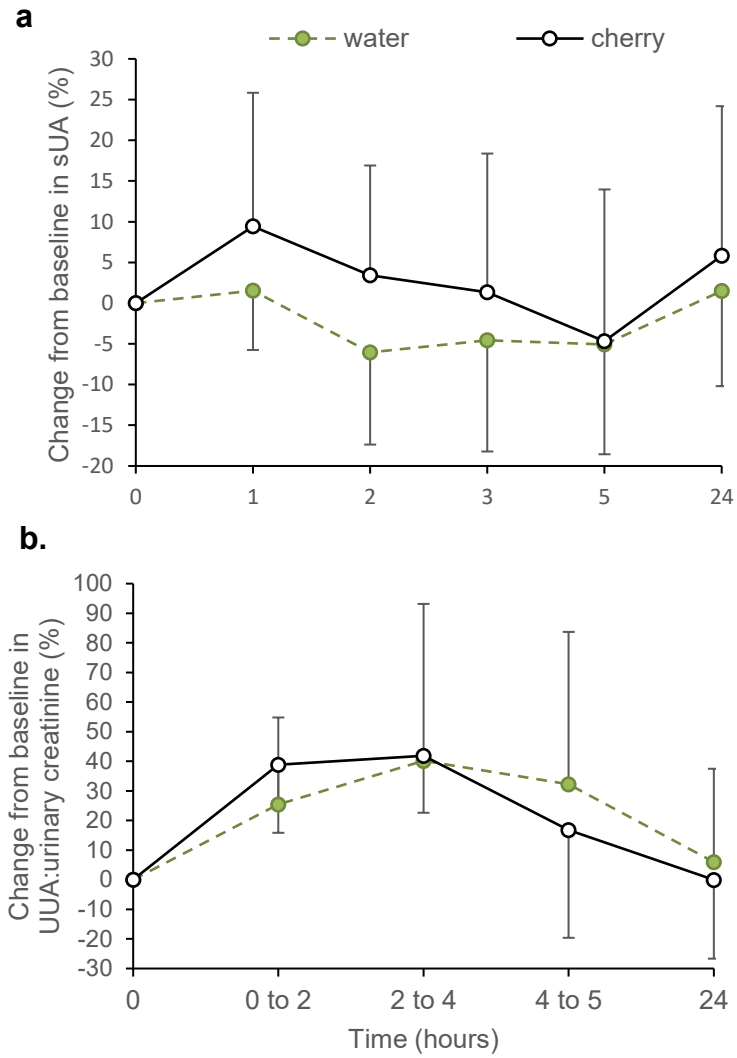
Evaluation of participants' diet and PA diaries indicated that participants complied with the low-phenol diet and physical activity guidance.

Serum Uric Acid (sUA)

There was a large-sized main effect of time on sUA following consumption of the drinks ($F_{5,55}$ = 3.529, p = 0.008, ηp^2 = 0.243) with a mean 10.4% reduction in sUA between 1 hour and 5 hours post-consumption (p = 0.034) and a mean 8.5% increase from 5 hours to 24 hours post-consumption (p = 0.022) (**Fig 2a,** Table 2**).** However, no drink type ($F_{1,11}$ = 2.061, p = 0.179, ηp^2 = 0.158) or drink by time interaction ($F_{5,55}$ = 1.222, p = 0.311, ηp^2 = 0.100) effects were found. Furthermore, there were no between-sex differences in response ($F_{5,55}$ = 1.151, p = 0.347, ηp^2 = 0.103).

Urinary Uric Acid (UUA)

As shown in **Fig 2b (**and Table 2), creatinine-adjusted UUA fluctuated significantly over time and this main effect was large ($F_{4,44}$ = 11.656, $p < 0.001$, ηp^2 = 0.514). The greatest increase in UUA above baseline (0 hours) was observed at 2-4 hours (41.0 %; p = 0.001), followed by 0-2 hours (32.2 %; $p < 0.001$). UUA was significantly lower at 24 hours than at 0-2 hours ($p <$ 0.001) and 2-4 hours (p = 0.005). There were no statistically significant main effects of drink type ($F_{1,11}$ = 0.015, p = 0.906, ηp^2 = 0.001) or drink by time interaction ($F_{4,44}$ = 1.084, p = 0.358, ηp^2 = 0.090). There were also no between-sex differences in response ($F_{4,44}$ = 1.397, p = 0.263, ηp^2 = 0.123).



230 **Fig. 2** Effect of tart cherry juice and water on percentage change from baseline values in **a)**
231 serum uric acid (sUA) concentration and **b)** urinary uric acid (UUA) to urinary creatinine ratio.
232 Data are presented as mean ± SD, n = 12 for both outcomes.

233 ***C-reactive Protein***

234 There was a large-sized main effect of time for change in CRP from baseline ($F_{2,22}$ = 4.488, p
235 = 0.023, ηp^2 = 0.290), with a statistically significant 7.4 % reduction between 2 hours and 5
236 hours (p = 0.020) **(Fig 3** and Table 2**)**. Despite this, CRP at 5 hours was not significantly
237 different from baseline (p = 0.202) and no main effect of drink type ($F_{1,11}$ = 0.434, p = 0.524,
238 ηp^2 = 0.038) or drink by time interaction ($F_{2,22}$ = 0.644, p = 0.525, ηp^2 = 0.055) were detected.

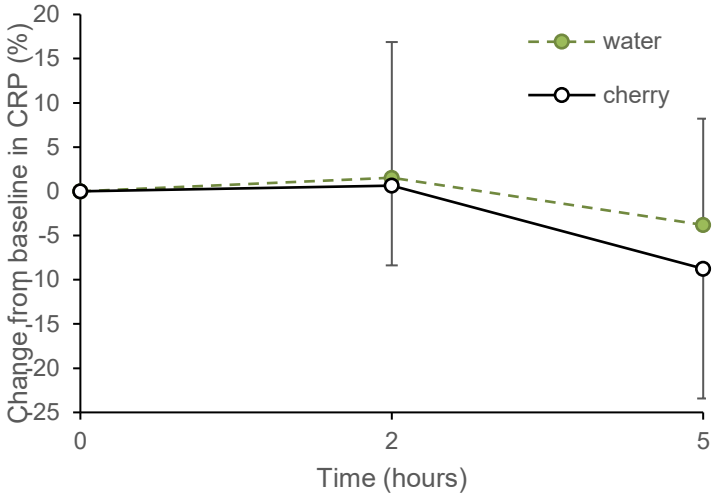


Fig. 3 Effect of tart cherry juice and water on percentage change in c-reactive protein (CRP) concentration from baseline values. Data are presented as mean ± SD, $n = 12$.

Blood Pressure

Brachial Systolic BP (SBP)

A large main effect of time ($F_{5,55} = 5.360$, $p < 0.001$, $\eta p^2 = 0.328$) was detected for brachial SBP (**Fig 4a,** and Table 2**)**, with a mean reduction of 4.6 % between 5 hours and 24 hours ($p < 0.001$). There was a non-significant large main effect of drink ($F_{1,11} = 3.654$, $p = 0.082$, $\eta p^2 = 0.249$); estimated marginal mean for brachial SBP was 3.0 % (95% CI -6.5, 0.5) lower in the water arm than in the TC juice arm. No drink by time interaction effect ($F_{5,55} = 1.459$, $p = 0.218$, $\eta p^2 = 0.117$) was observed.

Central Systolic BP (SBP)

A large main effect of time ($F_{5,55} = 3.403$, $p = 0.009$, $\eta p^2 = 0.236$) was detected for central SBP, with a 4.0 % reduction observed between 5 hours and 24 hours ($p = 0.014$) (**Fig 4b,** Table 2**)**. There was no drink by time interaction effect ($F_{5,55} = 1.866$, $p = 0.154$, $\eta p^2 = 0.145$) or main effect of drink type ($F_{1,11} = 3.234$, $p = 0.100$, $\eta p^2 = 0.227$).

Brachial and Central Diastolic BP (DBP)

Brachial DBP values were used as central DBP values, in accordance with the Vicorder® instructions. There was a large significant main effect of time ($F_{5,55} = 5.908$, $p < 0.001$, $\eta p^2 = 0.349$) for DBP (**Fig 4c,** Table 2**)**. On average, DBP fell by 5.4 % between 2 hours and 24 hours ($p = 0.027$) and by 5.9 % between 3 hours and 24 hours ($p = 0.001$). There was no drink by time interaction effect ($F_{5,55} = 0.718$, $p = 0.612$, $\eta p^2 = 0.061$) or main effect of drink type ($F_{1,11} = 1.782$, $p = 0.209$, $\eta p^2 = 0.139$).

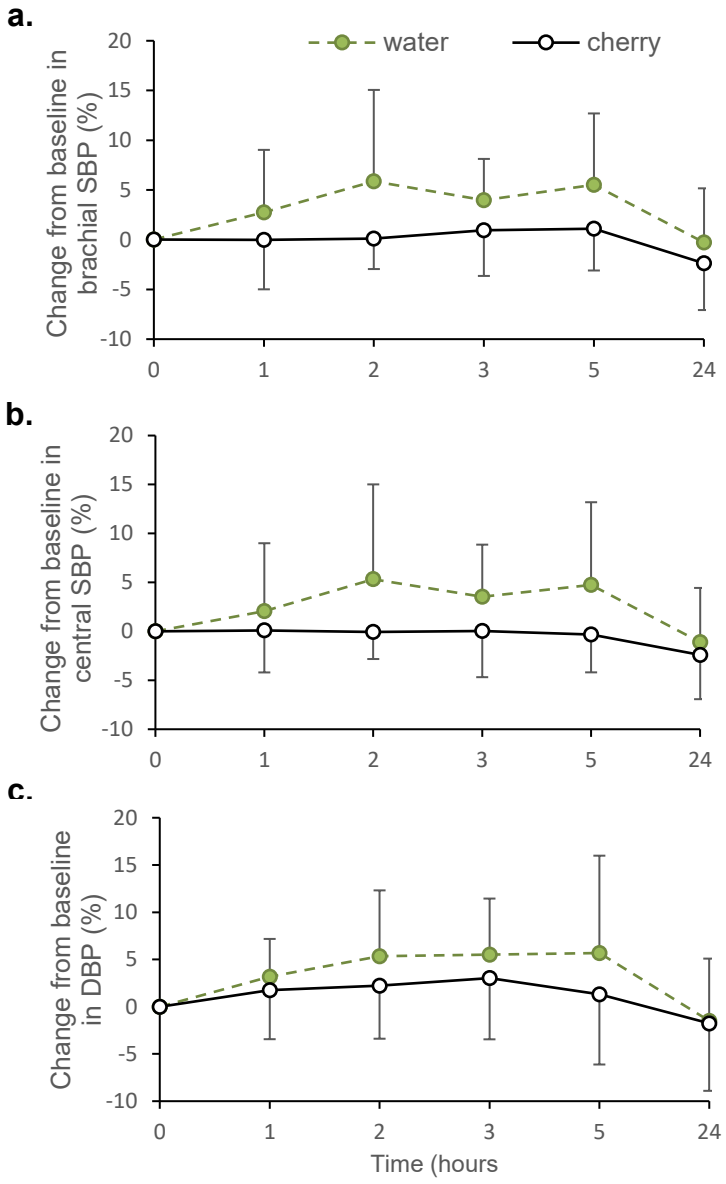


Fig. 4 Effect of tart cherry juice and water on percentage change from baseline values in **a)** brachial systolic blood pressure (SBP), **b)** central systolic blood pressure (SBP), and **c)** brachial

and central diastolic blood pressure (DBP). Data are presented as mean (± SD); $n = 12$ for all outcomes.

Arterial Stiffness

Pulse Wave Velocity (PWV)

Carotid-femoral PWV fluctuated over the measurement period (Table 2), however, these fluctuations were not statistically significant (time: $F_{5,50} = 0.493$, $p = 0.667$, $\eta p^2 = 0.047$). There were no main effects of drink type ($F_{1,10} = 1.948$, $p = 0.193$, $\eta p^2 = 0.163$) or drink by time interaction ($F_{5,50} = 1.257$, $p = 0.297$, $\eta p^2 = 0.112$), ($n = 12$).

Augmentation Index (AIx)

AIx was measured in ten of the twelve participants. For two participants, AIx could not be consistently measured due to low pulse amplitude so these participants were excluded from analysis. There were no main effects of time ($F_{5,45} = 1.819$, $p = 0.204$, $\eta p^2 = 0.168$) or drink type ($F_{1,9} = 2.688$, $p = 0.136$, $\eta p^2 = 0.230$), and no drink by time interaction ($F_{5,45} = 1.085$, $p = 0.344$, $\eta p^2 = 0.108$) for AIx (Table 2).

Harms

No adverse effects were reported.

280 **Table 2** Acute effects of 250 ml tart cherry juice versus water (control) on vascular function, inflammation and urate[1].

		Time (hours)					
Outcome	**Study drink**	**Baseline**	**1**	**2**	**3**	**5**	**24**
Brachial systolic blood pressure, mmHg*	Cherry	126.2 ± 11.0	126.1 ± 12.4	126.2 ± 9.8	127.2 ± 10.8	127.4 ±10.0	122.9 ± 9.0
	Water (control)	123.6 ± 8.4	126.9 ± 11.3	130.6 ± 12.2	128.3 ± 8.2	130.2 ± 9.7	123.0 ± 7.9
Brachial and central diastolic blood pressure, mmHg*	Cherry	65.8 ± 6.1	66.9 ± 5.8	67.1 ± 5.1	67.6 ± 5.4	66.6 ± 6.8	64.4 ± 4.5
	Water (control)	64.9 ± 6.4	67.0 ± 6.9	68.3 ± 6.9	68.3 ± 6.9	68.3 ± 6.0	63.7 ± 4.2
Central systolic blood pressure, mmHg*	Cherry	120.3 ± 11.8	120.4 ± 12.7	120.1 ± 10.8	120.2 ± 12.1	119.7 ± 10.0	117.1 ± 8.9
	Water (control)	118.7 ± 8.6	121.2 ± 12.8	124.9 ± 13.7	122.8 ± 10.1	124.1 ± 10.9	117.2 ± 7.9
Pulse wave velocity, m/s,	Cherry	7.9 ± 1.4	7.2 ± 1.2	7.3 ± 1.7	7.8 ± 1.4	7.4 ± 1.4	7.2 ± 1.4
	Water (control)	8.1 ± 2.8	7.6 ± 1.2	7.4 ± 1.4	7.2 ± 1.1	7.4 ± 0.8	7.3 ± 1.4
Augmentation index, %	Cherry	14.8 ± 7.3	14.9 ± 7.4	14.7 ± 7.5	14.5 ± 8.9	14.3 ± 8.0	16.1 ± 6.7
	Water (control)	18.2 ± 9.8	15.5 ± 7.7	15.2 ± 8.2	15.2 ± 9.0	15.2 ± 8.7	16.8 ± 7.7

Serum uric acid, µmol/L*	Cherry	155.4 ± 59.2	170.2 ± 70.3	163.3 + 77.6	160.2 ± 76.4	149.9 ± 74.0	165.8 ± 78.9
	Water (control)	168.3 ± 57.1	171.0 ± 60.3	159.3 ± 59.6	164.0 ± 69.3	163.8 ± 71.8	169.7 ± 61.4
C-reactive protein, mg/L,*	Cherry	0.69 ± 0.61		0.68 ± 0.60		0.61 ± 0.54	
	Water (control)	1.16 ± 1.45		1.13 ± 1.43		1.04 ± 1.21	
				0-2	**2-4**	**4-5**	**24**
Urinary urate:urinary creatinine, mmol/mmol *	Cherry	0.42 ± 0.13		0.57 ± 0.15	0.58 ± 0.14	0.47 ± 0.15	0.41 ± 0.12
	Water (control)	0.46 ± 0.16		0.55 ± 0.17	0.61 ± 0.23	0.58 ± 0.19	0.46 ± 0.14

[1]All values are means ± SD; n = 12 for all outcomes except augmentation index were n = 10. There were no significant main effects of drink type or drink x time interactions. * indicates a significant main effect of time ($p < 0.05$)

Discussion

The primary aim of the present study was to investigate the effect of TC juice on sUA. In contrast to other studies, we did not find evidence that TC juice reduces sUA for up to 24 hours post-consumption. We also found no evidence that TC juice acutely increases UUA excretion or lowers inflammation, BP, or arterial stiffness.

The failure of TC juice to reduce sUA and increase UUA excretion contrasts with previous studies of sweet and tart cherries. Jacob et al. (2003) reported that 280 g of sweet cherries and Bell et al. (2014a) reported that 30 mL and 60 mL of TC concentrate (diluted with 100 mL of H_2O) lowered sUA and increased UUA excretion post-consumption in healthy adults. This contrast may be partly explained by the failure of Jacob et al. (2003) and Bell et al. (2014a) to include a control group, because sUA has previously been reported to fall from morning onwards (Sennels et al., 2012), a phenomenon observed in our participants after consumption of both placebo and TC drinks. The maximal decrease observed in sUA of 10% and increase in UUA excretion of 41% was comparable to that reported by Jacob et al. (2003) (sUA -14% & UUA +69%) in women with similar baseline sUA to our participants, but much lower than reported by Bell et al. (20.14a) (sUA -36% and UUA +250%), but their participants had much greater baseline sUA (approximately 480 μmol/L) than our participants (162 μmol/L), despite being described as healthy young adults. Notwithstanding the difficulty of interpreting the results of Bell et al. (2014a) because of the lack of a control arm, it is possible that the UA lowering effect of TC juice may partly depend on baseline sUA. Hillman & Uhranowsky (2021) reported that one and two daily servings of TC in powdered form (480 mg per capsule) and two daily servings of TC juice reduced sUA over a 48-hour period, whereas one daily serving of TC juice (30 mL of concentrate diluted to 240 mL with H_2O) seemed ineffective leading to a small increase in sUA at 8 hours post-consumption. The lack of benefit of a single daily serving of TC juice containing 30 mL of concentrate is broadly consistent with

our findings. Interpretation of the results of Hillman & Uhranowsky (2021) is complicated by the inclusion of apple juice in their TC drinks, because it is known to increase sUA (White et al., 2018), and lack of clarity whether reported treatment effects are in comparison to a placebo (and if so, which of the two placebos in their study) or within arm baseline values. Our findings challenge the results of previous acute studies reporting beneficial effects of cherries on urate metabolism and highlight the need for future studies to include a control group. However, our participants were healthy and there is a need to confirm whether TC acutely alters urate metabolism in individuals with elevated sUA such as those suffering from gout.

Processed TC products (Ou et al., 2012), whole TC extracts (Seeram et al., 2001), or anthocyanins found in TC, namely cyanidin-3-glucosylrutinoside and cyanidin-3-rutinoside (Wang et al., 1999) have been shown to exert anti-inflammatory effects *in vitro* (Virgen Gen et al., 2020), reduce exercise-induced inflammation (Bell et al., 2014b, 2015, 2016, Dimitriou et al., 2015; Howatson et al., 2009; Levers et al., 2016), and lower serum CRP for up to 5 hours after consumption in an uncontrolled study of purportedly healthy young adults with raised baseline CRP (Bell et al., 2014a). In contrast, we failed to observe a significant difference between TC and water with CRP falling between 2 and 5 hours after the consumption of both drinks. This finding demonstrates the difficulty of interpreting results from uncontrolled studies. This is further illustrated by studies with longer intervention periods. For example, in healthy adults with normal CRP at baseline (Lynn et al., 2014) and obese adults with raised CRP at baseline (Martin et al., 2018) TC failed to lower CRP, relative to control groups, whereas an uncontrolled study reported that sweet cherry consumption lowered serum CRP after 14 and 28 days (Kelley et al., 2006).

The consumption of cherries has been proposed to reduce BP by altering the synthesis and activity of vasodilators and vasoconstrictors (Kelley et al., 2018). However, we observed no effect of TC juice on brachial or central BP or measures of arterial stiffness. The lack of

348 modulation of BP contrasts with two studies that reported that TC reduced SBP for up to 3
349 hours post consumption in men with early hypertension (Keane et al., 2016a) and middle-aged
350 adults with moderately raised SBP (Keane et al., 2016c). The disagreement with our study may
351 be explained by the lower baseline BP of our participants. In a review of factors influencing
352 the effects of dietary anthocyanins on the regulation of BP, elevated baseline BP was
353 highlighted as a major determinant of whether anthocyanins exerted hypotensive effects
354 (Vendrame and Klimis-Zacas, 2019). The quantity of TC juice would also be expected to be
355 important. Keane et al. (2016a) and Keane et al. (2016c) adminstered 60 mL of TC concentrate
356 whereas we used 30 mL of concentrate. However, 30 mL is the typical suggested serving size
357 for TC concentrate and therefore may be the amount commonly drunk by consumers. In
358 agreement with our study, Desai et al. (2021) observed no acute effect of a single 30 mL serving
359 of TC concentrate on SBP in individuals with metabolic syndrome, but they did report that 24
360 h ambulatory BP was reduced at the end of a 7-day intervention period. Thus, it is possible that
361 a longer duration of intake is needed for 30 mL servings of TC concentrate to lower BP,
362 although Lynn et al. (2014) failed to find an effect of 30 mL/d of TC concentrate consumed for
363 4 weeks by normotensive adults when BP was measured at laboratory visits.
364 TC might be expected to reduce arterial stiffness via urate lowering or through putative
365 anti-oxidant and anti-inflammatory effects. However, we found no significant differences in
366 PWV or AIx between TC and water over the 24-hour measurement period. This is in line with
367 Keane et al. (2016a) who reported no effect of 60 mL of TC concentrate on PWV or AIx over
368 an 8-hour measurement period. The lack of an acute effect of TC juice on PWV and AIx is
369 consistent with studies of other polyphenol rich fruits (Del Bo et al., 2014; Richter et al., 2017;
370 Rodriguez-Mateos et al., 2013, 2016), indicating that neither measure of arterial stiffness is
371 particularly amenable to rapid modulation by polyphenol rich fruits.

This study has several limitations. First, our participants were apparently healthy, and TC might only benefit individuals with elevated sUA and markers of cardiovascular risk. Second, it is possible that TC juice may have changed some outcome markers outside the time-period we took measurements. Third, the TC concentrate we used may not have supplied sufficient bioactive compounds to exert an effect. Whilst our analyses of the TC concentrate revealed that a serving supplied a dose of total phenols within the range shown in other TC interventions to exert physiological effects (Keane et al. 2016a; Connolly et al. 2006), its content of intact anthocyanins was relatively low (Martin & Coles 2010; Bell et al. 2014a). This could partly explain our null findings if intact anthocyanins are the primary compounds driving the biological actions of TC. Fourth, the study was not blinded, but this might have been expected to increase the likelihood of finding a treatment effect for an outcome such as BP which is particularly susceptible to the placebo effect (Howard et al., 2016). Fifth, although each participant arrived at the same time for both of their study visits we could not control their wake time, which could have introduced variability into our measurements given that many have been reported to exhibit diurnal patterns (Shimizu et al. 2023; Hernandez et al. 2024;). Sixth, the final sample size was one less than the pre-determined sample size, because one participant dropped out. It is unlikely however that one more participant completing the study would have meaningfully changed the outcome for sUA, because the difference between TC and control was not close to statistically significant. The sample size was determined to detect a change in sUA so the study may have been underpowered to detect changes in other outcomes. Also, we did not power the study to investigate between sex differences in the response of urate metabolism to TC so the results of these analyses should be interpreted cautiously.

This study has several strengths. First, unlike some studies reporting a UA lowering effect of cherries (Bell et al., 2014a; Jacob et al., 2003), there was a control group. Second, diet

was controlled during the study by giving participants standardised meals low in polyphenols the evening before and during the 24-hour measurement periods and by providing clear guidance on consuming a diet low in polyphenols for the duration of the study. Third, the low-nitrate water control drink was devoid of factors that could influence uric acid metabolism and vascular function such as fructose and nitrate (Hobbs et al., 2013).

In conclusion, the present study found no evidence that a single serving of TC benefits urate metabolism, inflammation, or markers of vascular function in healthy adults compared with a control drink of water. However, following consumption of both TC and water, changes in urate metabolism, inflammation and BP occurred over the 24-hour measurement period likely reflecting diurnal fluctuations. Our findings need to be considered when interpreting the results of previous uncontrolled studies that have reported beneficial acute effects of TC juice or sweet cherries in healthy adults. Future controlled studies are needed to determine whether TC consumption exerts beneficial acute effects in individuals with hyperuricaemia or gout.

Ethical Statements

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Availability of data: The data that support the findings of this study are available from the corresponding author, AL, upon reasonable request.

Conflict of interest: AL has previously been a recipient of a research grant from the Cherry Marketing Institute, Michigan, USA. The authors report no further conflicts of interest.

Consent: Written informed consent was obtained from all study participants.

Ethical approval: The study was approved by the ethics committee of Sheffield Hallam University, UK.

References

An, L., Wang, Y., Liu, L. et al. (2024) High serum uric acid is a risk factor for arterial stiffness in a Chinese hypertensive population: a cohort study. *Hypertension Research* 47: 1512–1522 https://doi.org/10.1038/s41440-024-01591-

Bell PG, Gaze DC, Davison GW et al. (2014a) Montmorency tart cherry (Prunus cerasus L.) concentrate lowers uric acid, independent of plasma cyanidin-3-O-glucosiderutinoside. *Journal of Functional Foods* 11: 82–90. https://doi.org/10.1016/j.jff.2014.09.004

Bell PG, Walshe IH, Davison GW et al. (2014b) Montmorency cherries reduce the oxidative stress and inflammatory responses to repeated days high-intensity stochastic cycling. *Nutrients* 6(2): 829–843. https://doi.org/10.3390/nu6020829

Bell PG, Walshe IH, Davison GW et al. (2015) Recovery facilitation with Montmorency cherries following high-intensity, metabolically challenging exercise. *Applied Physiology, Nutrition, and Metabolism* 40(4): 414–423. https://doi.org/http://dx.doi.org/10.1139/apnm-2014-0244

Bell PG, Stevenson E et al. (2016) The effects of montmorency tart cherry concentrate supplementation on recovery following prolonged, intermittent exercise. *Nutrients* 8(441): 1–11. https://doi.org/10.3390/nu8070441

Borghi C, Agnoletti D, Cicero AFG et al. (2022) Uric Acid and Hypertension: a Review of Evidence and Future Perspectives for the Management of Cardiovascular Risk. *Hypertension*. 79(9):1927-1936.

https://doi: 10.1161/HYPERTENSIONAHA.122.17956.

444 Callegaro CC, Moraes RS, Negrão CE et al. (2007) Acute water ingestion increases
445 arterial blood pressure in hypertensive and normotensive subjects. *Journal of Human*
446 *Hypertension* 21(7): 564–570. https://doi.org/10.1038/sj.jhh.1002188
447 Chaovanalikit A and Wrolstad RE (2004) Total anthocyanins and total phenolics of
448 fresh and processed cherries and their antioxidant properties. *Journal of Food Science*
449 69(1): 67–72. https://doi.org/https://doi.org/10.1111/j.1365-2621.2004.tb17858.x
450 Collins MW, Saag KG and Singh JA (2019) Is there a role for cherries in the
451 management of gout? *Therapeutic Advances in Musculoskeletal Disease* 11: 1–16.
452 https://doi.org/10.1177/1759720X19847018
453 Connolly, DAJ, McHugh MP and Padilla-Zakour OI (2006). Efficacy of a tart cherry
454 juice blend in preventing the symptoms of muscle damage. *British journal of sports*
455 *medicine*, *40*(8), 679-683.
456 Del Bo C, Porrini M, Fracassetti D et al. (2014) A single serving of blueberry (V.
457 corymbosum) modulates peripheral arterial dysfunction induced by acute cigarette
458 smoking in young volunteers: A randomized-controlled trial. *Food and Function* 5(12):
459 3107-3116. https://doi.org/10.1039/C4FO00570H
460 Desai T, Roberts M and Bottoms L (2021) Effects of short-term continuous
461 Montmorency tart cherry juice supplementation in participants with metabolic
462 syndrome. *European Journal of Nutrition* 60(3): 1587–1603.
463 https://doi.org/10.1007/s00394-020-02355-5
464 Dimitriou L, Hill JA, Jehnali A et al. (2015) Influence of a Montmorency cherry juice
465 blend on indices of exercise-induced stress and upper respiratory tract symptoms
466 following marathon running - A pilot investigation. *Journal of the International Society*
467 *of Sports Nutrition* 12(1): 1–7. https://doi.org/10.1186/s12970-015-0085-8

468 Dwan K, Li T, Altman DG and Elbourne D (2019) CONSORT 2010 statement:
469 Extension to randomised crossover trials. *British Medical Journal* 366(14378): 1-16.
470 https://doi.org/10.1136/bmj.l4378
471 Franklin SS, Thijs L, Hansen TW et al. (2013) White-coat hypertension: new insights
472 from recent studies. *Hypertension* 62(6): 982-987.
473 https://doi.org/10.1161/HYPERTENSIONAHA.113.01275
474 Haidari F, Mohammad Shahi M et al. (2009) Inhibitory effects of tart cherry (Prunus
475 cerasus) juice on xanthine oxidoreductase activity and its hypouricemic and antioxidant
476 effects on rats. *Malaysian Journal of Nutrition* 15(1): 53–64.
477 Hernández LM, Byrne ML, Taylor MK. (2024) Salivary C-reactive protein exhibits a
478 diurnal pattern and relates to biobehavioral health in military men. Brain Behaviour and
479 Immunity. 2024 Nov;122:465-470. https://doi.org 10.1016/j.bbi.2024.08.040.
480 Hillman AR and Uhranowsky K (2021) Acute ingestion of Montmorency tart cherry
481 reduces serum uric acid but has no impact on high sensitivity c-reactive protein or
482 oxidative capacity. *Plant Foods for Human Nutrition* 76*:* 83–89.
483 https://doi.org/10.1007/s11130-021-00879-7
484 Hobbs DA, George TW and Lovegrove JA (2013) The effects of dietary nitrate on
485 blood pressure and endothelial function: A review of human intervention studies.
486 *Nutrition Research Reviews* 26(2): 210–222.
487 https://doi.org/10.1017/S0954422413000188
488 Howard JP, Shun-Shin MJ, Hartley A et al. (2016) Quantifying the 3 biases that lead to
489 unintentional overestimation of the blood pressure–lowering effect of renal
490 denervation. *Circulation: Cardiovascular Quality and Outcomes* 9(1): 14-22.
491 https://doi.org/10.1161/CIRCOUTCOMES.115.002533

492 Howatson G, McHugh MP, Hill JA et al. (2009) Influence of tart cherry juice on indices
493 of recovery following marathon running. *Scandinavian Journal of Medicine and*
494 *Science in Sports* 20(6): 843–852. https://doi.org/10.1111/j.1600-0838.2009.01005.x
495 Jacob R, Spinozzi G, Simon V et al. (2003) Consumption of cherries lowers plasma
496 urate in healthy women. *Journal of Nutrition* 133: 1826–1829.
497 https://doi.org/10.1093/jn/133.6.1826
498 Keane KM, George TW, Constantinou CL et al. (2016a) Effects of Montmorency tart
499 cherry (*Prunus Cerasus L.*) consumption on vascular function in males with early
500 hypertension. *American Journal of Clinical Nutrition* 103(6): 1531–1539.
501 https://doi.org/10.3945/ajcn.115.123869.
502 Keane KM, Bell PG, Lodge JK et al. (2016b) Phytochemical uptake following human
503 consumption of Montmorency tart cherry (L. *Prunus cerasus*) and influence of phenolic
504 acids on vascular smooth muscle cells in vitro. *European Journal of Nutrition* 55(4):
505 1695–1705. https://doi.org/10.1007/s00394-015-0988-9
506 Keane KM, Haskell-Ramsay CF et al. (2016c) Montmorency tart cherries (*Prunus*
507 *cerasus L.*) modulate vascular function acutely, in the absence of improvement in
508 cognitive performance. *British Journal of Nutrition* 116(11): 1935–1944.
509 https://doi.org/10.1017/S0007114516004177
510 Kelley DS, Rasooly R, Jacob RA et al. (2006) Consumption of Bing sweet cherries
511 lowers circulating concentrations of inflammation markers in healthy men and women.
512 *Journal of Nutrition* 136(4): 981–986. https://doi.org/10.1093/jn/136.4.981
513 Kelley D, Adkins Y and Laugero K (2018) A review of the health benefits of cherries.
514 *Nutrients* 10(3): 368-390. https://doi.org/10.3390/nu10030368
515 Kimble R, Keane KM, Lodge JK, et al. (2021) The Influence of Tart Cherry (*Prunus*
516 *cerasus, cv* Montmorency) Concentrate Supplementation for 3 Months on

517 Cardiometabolic Risk Factors in Middle-Aged Adults: A Randomised, Placebo-
518 Controlled Trial. *Nutrients* 13(5):1417. doi: 10.3390/nu13051417.
519 Kirakosyan A, Seymour EM, Llanes DEU et al. (2009) Chemical profile and
520 antioxidant capacities of tart cherry products. *Food Chemistry* 115(1): 20–25.
521 https://doi.org/10.1016/j.foodchem.2008.11.042
522 Kirakosyan A, Gutierrez E, Ramos Solano B et al. (2018) The inhibitory potential of
523 Montmorency tart cherry on key enzymes relevant to type 2 diabetes and cardiovascular
524 disease. *Food Chemistry* 252: 142–146.
525 https://doi.org/10.1016/j.foodchem.2018.01.084
526 Kuo CF, Grainge MJ, Mallen C et al. (2016) Comorbidities in patients with gout prior
527 to and following diagnosis: case-control study. *Annals of the Rheumatic Diseases* 75(1):
528 210–217. https://doi.org/10.1136/annrheumdis-2014-206410
529 Lee J, Durst RW and Wrolstad RE (2005) Determination of total monomeric
530 anthocyanin pigment content of fruit juices, beverages, natural colorants, and wines by
531 the pH differential method: Collaborative study. *The Journal of AOAC International*
532 88(5): 1269–1278. https://doi.org/10.1093/jaoac/88.5.1269
533 Lee SG, Vance TM, Nam TG et al. (2016) Evaluation of pH differential and HPLC
534 methods expressed as cyanidin-3-glucoside equivalent for measuring the total
535 anthocyanin contents of berries. *Journal of Food Measurement and Characterization*
536 10: 562-568. https://10.1007/s11694-016-9337-9.
537 Levers K, Dalton R, Galvan E et al. (2016) Effects of powdered Montmorency tart
538 cherry supplementation on acute endurance exercise performance in aerobically trained
539 individuals. *Journal of the International Society of Sports Nutrition* 13(22): 1–23.
540 https://doi.org/10.1186/s12970-016-0133-z

Lynn A, Mathew S, Moore CT et al. (2014) Effect of a tart cherry juice supplement on arterial stiffness and inflammation in healthy adults: A randomised controlled trial. *Plant Foods for Human Nutrition* 69(2): 122–127. https://doi.org/10.1007/s11130-014-0409-x

Martin KR & Coles 2010

Martin KR, Burrell L and Bopp J (2018) Authentic tart cherry juice reduces markers of inflammation in overweight and obese subjects: a randomized, crossover pilot study. *Food and Function* 9(10): 5290–5300. https://doi.org/10.1039/c8fo01492b

Ndrepepa G. (2025) Uric acid and cardiovascular disease—recent evidence on the association and underlying mechanisms. *Journal of Laboratory and Precision Medicine* 10 (8): DOI: 10.21037/jlpm-25-8.

Ou B, Bosak KN, Brickner PR et al. (2012) Processed tart cherry products - Comparative phytochemical content, in vitro antioxidant capacity and in vitro anti-inflammatory activity. *Journal of Food Science* 77(5): 105–112. https://doi.org/10.1111/j.1750-3841.2012.02681.x

Pallant J (2010) Statistical techniques to compare groups. In: Pallant J (ed) *SPSS Survival Manual*, 4th edn, McGraw-Hill, pp. 210.

Richter CK, Skulas-Ray AC, Gaugler TL et al. (2017) Incorporating freeze-dried strawberry powder into a high-fat meal does not alter postprandial vascular function or blood markers of cardiovascular disease risk: A randomized controlled trial. *American Journal of Clinical Nutrition* 105(2): 313-322. https://doi.org/10.3945/ajcn.116.141804

Rodriguez-Mateos A, Feliciano RP, Boeres A et al. (2016) Cranberry (poly) phenol metabolites correlate with improvements in vascular function: A double-blind,

randomized, controlled, dose-response, crossover study. *Molecular Nutrition and Food Research* 60(10): 2130-2140. https://doi.org/10.1002/mnfr.201600250

Rodriguez-Mateos A, Rendeiro C, Bergillos-Meca T et al. (2013) Intake and time dependence of blueberry flavonoid–induced improvements in vascular function: a randomized, controlled, double-blind, crossover intervention study with mechanistic insights into biological activity. *American Journal of Clinical Nutrition* 98(5): 1179-1191. https://doi.org/10.3945/ajcn.113.066639

Schlesinger N (2005) Dietary factors and hyperuricaemia. *Current Pharmaceutical Design* 11(32):4 133–4138. https://doi.org/10.2174/138161205774913273

Schumacher HR, Pullman-Mooar S, Gupta SR et al. (2013) Randomized double-blind crossover study of the efficacy of a tart cherry juice blend in treatment of osteoarthritis (OA) of the knee. *Osteoarthritis and Cartilage* 21(8): 1035-1041. https://doi.org/10.1016/j.joca.2013.05.009

Seeram NP, Momin RA et al. (2001) Cyclooxygenase inhibitory and antioxidant cyanidin glycosides in cherries and berries. *Phytomedicine* 8(5): 362–369. https://doi.org/10.1078/0944-7113-00053

Sennels HP, Jørgensen HL et al. (2012) Rhythmic 24-hour variations of frequently used clinical biochemical parameters in healthy young males - The Bispebjerg study of diurnal variations. *Scandinavian Journal of Clinical and Laboratory Investigation* 72(4): 287–295. https://doi.org/10.3109/00365513.2012.662281

Shimizu M, Naito R, Sato A, et al. (2023). Diurnal Variations in Serum Uric Acid, Xanthine, and Xanthine Oxidoreductase Activity in Male Patients with Coronary Artery Disease. *Nutrients*, *15*(20), 4480. https://doi.org/10.3390/nu15204480

588 Singleton VL and Rossi JA (1965) Colorimetry of Total Phenolics with
589 Phosphomolybdic-Phosphotungstic Acid Reagents. *American Journal of Enology and*
590 *Viticulture* 16(3): 144–158. http://www.ajevonline.org/content/16/3/144.abstract
591 Terkeltaub R, Bushinsky DA and Becker MA (2006) Recent developments in our
592 understanding of the renal basis of hyperuricemia and the development of novel
593 antihyperuricemic therapeutics. *Arthritis Research and Therapy* 8(1): 1–9.
594 https://doi.org/10.1186/ar1909
595 Vendrame S and Klimis-Zacas D (2019) Potential factors influencing the effects of
596 anthocyanins on blood pressure regulation in humans: a review. *Nutrients* 11(6): 1431-
597 1450. doi:10.3390/nu11061431
598 Vírgen Gen JJ, Guzmán-Gerónimo RI, Martínez-Flores K et al. (2020) Cherry extracts
599 attenuate inflammation and oxidative stress triggered by monosodium urate crystals in
600 THP-1 cells. *Journal of Food Biochemistry* 44(10): 1–9.
601 https://doi.org/10.1111/jfbc.13403
602 Wang H, Nair MG, Strasburg GM et al. (1999) Antioxidant and antiinflammatory
603 activities of anthocyanins and their aglycon, cyanidin, from tart cherries. *Journal of*
604 *Natural Products* 62(2): 294–296. https://doi.org/10.1021/np980501m
605 White SJ, Carran EL, Reynolds AN et al. (2018) The effects of apples and apple juice
606 on acute plasma uric acid concentration: a randomized controlled trial. *American*
607 *Journal of Clinical Nutrition* 107(2): 165–172. https://doi.org/10.1093/ajcn/nqx059
608 Zhang Y, Neogi T, Chen C et al. (2012) Cherry consumption and decreased risk of
609 recurrent gout attacks. *Arthritis and Rheumatology* 64(12): 4004–4011.
610 https://doi.org/10.1002/art.34677
611