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- 1 Tart cherry supplementation and recovery from strenuous exercise: a systematic review and
- 2 meta-analysis

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10 ABSTRACT

The aim of this study was to determine the efficacy of tart cherry supplementation on recovery 11 following strenuous exercise. A systematic review and meta-analysis was conducted using studies 12 investigating tart cherry supplementation on measures of muscle soreness, muscular strength, 13 14 muscular power, creatine kinase (CK), C reactive protein (CRP), Interleukin-6 (IL-6) and tumour necrosis factor alpha (TNF α). A literature search ending in July 2020 was conducted in 3 databases 15 (SPORTDiscus, Web of Science and Pubmed). Data from 14 studies was extracted and pooled for 16 analysis. Tart cherry supplementation had a small beneficial effect in reducing muscle soreness (ES 17 = -0.44, 95% CI [-0.87, -0.02]). A moderate beneficial effect was observed for recovery of muscular 18 strength (ES = -0.78, 95% CI [-1.11, -0.46]). A moderate effect was observed for muscular power 19 20 (ES = -0.53, 95% CI [-0.77, -0.29]), a further subgroup analysis on this variable indicated a large effect of tart cherry supplementation on recovery of jump height (ES = -0.82, 95% CI [-1.18, -0.45]) 21 and a small significant effect of supplementation on sprint time (ES = -0.32, 95% CI [-0.60, -0.04]). 22 A small effect was observed for both CRP (ES = -0.46, 95% CI [-0.93, -0.00]) and IL-6 (ES = -0.35, 23 24 95% CI [-0.68, -0.02]. No significant effects were observed for CK, and TNFa. These results indicate that the consumption of a tart cherry supplement can aid aspects of recovery from strenuous 25 exercise. 26

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28 Key Words: Muscle damage, prunus cerasus, Montmorency cherry, muscle function,

29 inflammation, functional foods

31 INTRODUCTION

The use of tart cherry (TC) products to aid recovery from strenuous exercise is becoming increasingly popular. Consumption of tart cherries is thought to enhance recovery and attenuate symptoms of exercise induced muscle damage (EIMD), this is likely due to the potent antioxidant and antiinflammatory properties of the cherry (Connolly et al., 2006; Bowtell et al., 2010; Bongiovanni et al, 2020).

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Strenuous exercise can cause structural damage to the muscle fibre, leading to an inflammatory 38 response that is characterised by the infiltration of neutrophils and macrophages to the affected area 39 (Clarkson and Sayers, 1999). The activity of these immune cells results in the production of reactive 40 oxygen and nitrogen species (RONS) which can lead to oxidative stress. Oxidative stress is 41 considered an imbalance between the natural antioxidant defence systems of the body and the 42 production of RONS (Betteridge, 2000), if the defence systems become overwhelmed there may be 43 an exacerbation in the damage to the muscle fibres (Halliwell & Chirico, 1993; Lowe et al., 1995; 44 45 Toumi & Best, 2003; Aoi et al., 2004). Montmorency tart cherries contain high levels of flavonoids and anthocyanins, the anti-inflammatory and antioxidant properties of these phytonutrients are 46 purported to reduce inflammation and RONS production via inhibition of the cyclooxygenase (COX-47 1 and COX-2) pathways (Marzocchella et al., 2011). Due to this the consumption of TC products is 48 49 thought to attenuate the inflammatory response and accelerate recovery from muscle damage, 50 however it is important to note that these observations have been in vitro or animal models, this has been reviewed in detail by Marzochella et al (2011). 51

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Research investigating the efficacy of TC products as a recovery strategy has been positive, with a number of studies supporting its use (Connolly et al., 2006; Howatson et al., 2010; Bowtell et al., 2011; Bell et al., 2014a), and a few studies finding no benefit (Beals et al., 2016; McCormick et al., 2016). However, there is wide variation in the responses of the dependent variables that have been measured throughout the research. For example, Connolly et al. (2006) observed reduced delayed onset muscle soreness (DOMS) with the consumption of TC juice following an eccentric exercise protocol involving maximal contractions of the elbow flexors, yet Beals et al. (2017) observed no difference between groups following maximal eccentric contractions of the quadriceps. Inconsistencies in findings could be related to differences in exercise modalities, exercise familiarity, duration and type of supplementation, with some studies supplementing with a juice (Howatson et al., 2008; Quinlan and Hill 2019) and others supplementing with a powder (Levers et al., 2015) or tablet (Kastello et al., 2014).

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Exercise modality is likely a factor influencing the effectiveness of TC supplementation, as the 67 underlying cause of symptoms associated with exercise induced muscle damage will vary depending 68 on exercise stimulus (Levers et al., 2015; Vitale et al., 2017). The majority of research on TC 69 supplementation following endurance activity supports the use of TC products to attenuate 70 inflammation (Howatson et al., 2010; Bell et al., 2014a; Levers et al., 2016) and oxidative stress 71 (Howatson et al., 2010; Bell et al., 2014a). However, there are inconsistencies in the response of 72 some markers across studies, for example, three studies observed a decrease in the inflammatory 73 marker CRP (Bell et al., 2014a; Bell et al 2014b; Howatson et al., 2008) and two observed no 74 differences (Bell et al., 2016; Quinlan and Hill., 2019). This makes it difficult to draw conclusions on 75 76 the effectiveness of TC as a strategy to reduce EIMD.

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The efficacy of TC supplementation in improving recovery following exercise inducing only 78 mechanical stress i.e. resistance exercise, is conflicting with studies supporting the use of TC 79 80 supplementation (Connolly et al., 2006; Kastello et al., 2014) and others showing no benefit (Beals 81 et al., 2016; Lamb et al., 2019). As such, a systematic review and meta-analysis of the research findings will clarify the efficacy of TC supplementation as a recovery strategy and help to identify the 82 variables most affected by supplementation. Therefore, the aim of this investigation was to conduct 83 a systematic review and meta-analysis on the efficacy of TC supplementation in recovery following 84 exercise. 85

87 MATERIALS AND METHODS

88 Literature Search

A systematic review and meta-analysis was conducted using guidelines outlined in the Preferred 89 Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 90 91 2009). An electronic search of the literature ending in July 2020 was conducted in PubMed, SPORTDiscuss and Web of Science using combinations of the following search terms; cherry OR 92 93 Montmorency cherry OR sour cherry OR Prunus cerasus OR Anthocyanin AND recovery OR athlete OR inflammation OR oxidative stress OR muscle damage OR muscle soreness OR muscle function 94 95 OR jump OR sprint OR strength OR exercise OR interleukin 6 OR C reactive protein OR tumor 96 necrosis factor alpha OR creatine kinase OR reactive oxygen species OR reactive nitrogen species. The reference lists of all included studies were also examined to identify any further articles. A three-97 98 stage search strategy was independently undertaken by two members of the review team (Title/Abstract Screen; Full Text Screen/Full Text Appraisal) and results were filtered using the 99 100 population, intervention, comparator, outcomes and study design (PICOS) criteria described in Table 101 1.

102 **Insert table 1 here**

103

104 Outcome Variables

The literature was examined for the effects of cherry supplementation on indices of recovery
following exercise that induced muscle damage. The following outcome variables were selected as
they reflect the most commonly assessed indices in the EIMD literature: muscular soreness,
muscular strength, muscular power, creatine kinase (CK), C reactive protein (CRP), interleukin-6 (ILand tumor necrosis factor alpha (TNFα).

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Measurements of muscle soreness were obtained from visual analogue or Likert scales.
Measurements of muscular strength were obtained from measurements of maximum isometric,

isokinetic or isotonic contraction of the muscle. Measurements of muscular power included any
activity that measured the power of the muscle; for example the counter movement jump (CMJ) or a
sprint. Measurements of CK, CRP, IL-6 and TNFα were obtained from capillary or venous sampling.

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118 Inclusion and Exclusion Criteria

119 Studies were included if they met the following criteria; (1) participants were randomised into a cherry 120 supplement or a placebo group; (2) if at least one outcome variable was measured at baseline and 121 again at 1 and/or 24 and/or 48 and/or 72 h after exercise; (3) the study population could be male or female, of any fitness level or training background; (4) the supplement could be administered before 122 123 or after the exercise session. Studies were excluded if: (1) the experimental group received multiple treatments; (2) the control group undertook any practice which could have affected recovery; (3) 124 125 there was insufficient data, or studies did not yield change score data; (4) a crossover design was used but not with a contralateral limb, this is due to the contralateral repeated bout effect (Howatson 126 and van Someren, 2007). 127

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129 Extraction of Data

130 Mean, SD and sample size data were extracted from all included studies and used to calculate 131 change from baseline scores. Where SD change scores were not reported, values were calculated 132 using a correlation coefficient. When it was not possible to calculate change scores for SD imputed SD was calculated in accordance with current guidelines (Higgins and Green, 2011). Where 133 necessary mean and SD data were extracted from figures using software ImageJ (NIH, USA). Risk 134 135 of bias (Figure 1a and 1b) was assessed following guidelines outlined by the Cochrane Collaboration (Higgins and Altman, 2008). The risk of bias assessment was carried out by two authors (JH and 136 GH) and any discrepancies were reviewed by a third author (KK). Data were extracted and compared 137 by two authors (JH and GH), where there were differences data was reviewed by a third author (KK). 138

140 ** Insert Figure 1a and Figure 1b here **

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142 Statistical Analysis

Analysis on the overall effect of tart cherry supplementation was carried out using Review Manager 143 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2011). Data were 144 analysed using a random-effect model. Standardised mean effect sizes (ES) and 95% confidence 145 146 intervals (CI's) were reported as (ES [LCL, UCL]), with LCL and UCL representing lower and upper 147 95% confidence limits respectively. Where sufficient datapoints allowed, a subgroup analysis was conducted. For measurement of muscular power, subgroup analysis was carried out on method of 148 149 assessing power. Studies were categorised based upon whether they assessed a measure of jump height or a sprint. For DOMS, strength, CK and CRP subgroup analysis was conducted on type of 150 151 damaging protocol used. Studies were categorised as either mechanical or metabolic. Where mechanical included studies utilising repetitive effort maximal contractions or maximal effort sprints 152 and metabolic included studies requiring prolonged engagement of the aerobic system such as a 153 marathon run or the Loughborough intermittent shuttle test (LIST). The classification for each study 154 155 (mechanical or metabolic) is indicated in table 2. The threshold values for effect sizes were set at: ≤0.2 (trivial), >0.2 (small), >0.5 (moderate) and >0.8 (large) (Batterham and Hopkins, 2006). 156 Heterogeneity was assessed using an I² statistic indicating the percentage of variability across the 157 studies that is due to heterogeneity (Higgins and Green et al., 2008). The significance level was set 158 as P≤0.05. 159

160

161 **RESULTS**

Database searches identified a total of 6608 records. The majority of these records were not relevant to this analysis, with many studies relating to other aspects of health, disease and nutrition and thus were excluded. Nineteen studies remained for assessment of eligibility. Five studies were further excluded due to: outcome variables not consistent with the inclusion criteria; variables measured at time points not consistent with the inclusion criteria; missing data; or if people were exposed to another treatment in addition to cherry supplementation which may have influenced the results (see Figure 2). Following this process 14 studies remained for inclusion in this meta-analysis (see Table 2).

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171 ** Insert Figure 2 here **

172 ** Insert Table 2 here **

173 A total number of 303 male and female participants were included in the dataset with a mean and 174 SD age of 26.8 (5.8) years. The training status of the participants was varied ranging from untrained 175 to well-trained athletes in a range of sports. The risk of bias assessment is demonstrated in Figure 1. Adequate sequence generation and allocation concealment was unclear for the majority of the 176 177 included studies, with five of the fourteen studies reporting how participants were allocated to groups and just one study reporting adequate allocation concealment. Adequate blinding occurred in all 178 included studies with the use of a placebo treatment, in addition outcome data appeared to be 179 addressed in all included studies. Selective outcome reporting was rated high for two studies as 180 181 outcome data was not fully reported or omitted completely. Six of the included studies were considered at risk of other bias and so were rated high. Of these studies four implemented either a 182 low phenolic diet or a dietary wash out period and three studies used a cross over study design. 183

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A total of 52 data points were extracted from original research papers and included in the analysis for DOMS (see Figure 3). A significant difference between groups in favour of cherry supplementation was evident (P<0.05, Z = 2.06). Supplementation with cherry products appears to have a small beneficial effect in attenuating soreness following strenuous exercise (ES = -0.44, 95% CI [-0.87, -0.02]). The I² statistic indicated high heterogeneity in the results (90%, Chi² = 530.19) (Higgins and Green, 2008). A subgroup analysis of exercise type revealed no meaningful reduction in heterogeneity, with I² values of 90% (Chi² = 255.90) and 89% (Chi² = 273.89) for the metabolic and mechanical groups, respectively. However, the subgroup analysis revealed that TC supplementation had a significant effect on attenuation of soreness in the mechanical group (P<0.05) but not the metabolic group (P>0.05).

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Analysis of 39 data points from 11 studies were included in the analysis for muscle strength (Figure 4). Analysis indicated a significant and moderate effect with the use of TC supplementation on the recovery of muscle strength (P<0.001, Z = 4.76, ES = -0.78, 95% CI [-1.11, -0.46]). A large amount of heterogeneity was observed across the studies (I² = 80%, Chi² = 186.10) (Higgins and Green, 2008). Further subgroup analysis indicated heterogeneity was reduced to 59% (Chi² = 26.65) in the metabolic exercise group indicating minor heterogeneity in this group, however remained high in the mechanical exercise group (84%, Chi² = 186.10).

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204 ** Insert Figure 3 here **

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206 ** Insert Figure 4 here **

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Twenty three data points were used in the analysis for power. When considering the overall results 208 for power recovery, TC supplementation had a significant and moderate benefit (P < 0.001, Z = 4.39, 209 210 ES = -0.53, 95% CI [-0.77, -0.29]) (Figure 5). A small amount of heterogeneity was observed across the studies ($I^2 = 29\%$ Chi² = 31.17) (Higgins and Green, 2008). A subgroup analysis carried out on 211 the type of measure for power revealed that supplementation with TC has a significant and large 212 effect on recovery of jump height (P < 0.001, Z = 4.41, ES = -0.82, 95% CI [-1.18, -0.45]), with small 213 heterogeneity ($I^2 = 28\%$, Chi² = 12.53). The analysis on sprint data revealed a small significant effect 214 of TC supplementation (P = 0.02, Z = 2.26, ES = -0.32, 95% CI [-0.60, 0.04]). Heterogeneity was 215 also low ($I^2 = 10\%$, Chi² = 13.33). 216

220 Consumption of TC had no significant effect on concentrations of CK between groups (P=0.26, Z 221 =0.26) (Figure 6). Analysis was conducted on a sample of 32 datapoints revealing small 222 heterogeneity ($I^2 = 17\%$, Chi² = 6.87) (Higgins and Green, 2008). Subgroup analysis showed no 223 significant benefit of TC supplementation on CK for metabolically induced (P=0.79) or mechanically 224 induced (P=0.10) muscle damage.

225 An overall small and significant effect in favour of TC supplementation was observed on concentrations of CRP, conducted on a sample of 20 data points (P=0.05, Z = 1.96, ES = -0.46, 95% 226 CI [-0.93, -0.00]) (Figure 7). Considerable heterogeneity was observed across the data points (I² = 227 78%, $Chi^2 = 87.59$) (Higgins and Green, 2008). Further subgroup analysis on exercise reduced the 228 heterogeneity to nothing in the metabolic group ($I^2 = 0\%$, Chi² = 9.98) and indicated a large positive 229 effect of consuming TC on concentrations of CRP following metabolically induced muscle damage 230 (P<0.001, Z = 5.62, ES = -0.84, 95% CI [-1.13, -0.54]). Contrasting this, the subgroup analysis 231 revealed no significant group differences for CRP following mechanically induced muscle damage 232 233 (P = 0.79).

234 Analysis for IL-6, carried out on 21 data points across 6 studies revealed a small significant benefit of TC supplementation on concentrations of IL-6 (P<0.05, Z = 2.08, ES = -0.35, 95% CI [-1.68, -235 0.02]) (Figure 8). Moderate heterogeneity was evident in the data set ($I^2 = 56\%$, Chi² = 40.95), 236 however no subgroup analysis was carried out as only one study induced muscle damage using a 237 protocol categorised as mechanical. No significant effects of TC supplementation were observed for 238 TNF α (P=0.27, Z = 1.09) (Figure 9). The heterogeneity across 19 datapoints was low (I² = 0%) 239 (Higgins and Green, 2008). Subgroup analysis was not conducted as only one study induced muscle 240 241 damage using a protocol categorised as mechanical.

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243 ** Insert Figure 6 here **

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251 DISCUSSION

There is an increasing body of literature investigating the effectiveness of TC supplementation as a 252 recovery strategy; however, the variation in methodological design, study population and exercise 253 254 stimulus have resulted in inconsistent findings throughout the literature, with the exception of CK for which no between group difference has consistently been observed. To the authors knowledge this 255 is the first study that has used a meta-analysis approach to evaluate the effectiveness of consuming 256 TC as a recovery strategy. This analysis suggests that supplementation with TC can attenuate losses 257 in strength and power, reduce the severity of DOMS and attenuate concentrations of CRP and IL-6. 258 No significant benefits were observed on concentrations of CK and TNFa following TC 259 260 supplementation.

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Both metabolic and mechanical factors contribute to the aetiology of EIMD, the contribution of which will vary depending on the type of exercise (Howatson and van Someren, 2008). Exercise modalities with a large endurance component are predominantly fuelled from aerobic pathways and are associated with high metabolic costs (Vitale et al., 2017; Bell et al., 2014a). Conversely, modalities with large eccentric components are typically fuelled via anaerobic pathways and are associated with higher mechanical stress (Levers et al., 2015; Bell et al., 2014a). Differences in relative contribution from the different energy systems is likely to impact the type and magnitude of stress caused by the exercise protocol (Bell et al., 2014a). Research has suggested that cherry
supplementation is suited to facilitating recovery from exercise with a large metabolic component
(Bell et al., 2014a). Due to this a subgroup analysis was carried out on exercise type, mechanical or
metabolic.

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A significant and large effect was observed for muscle strength indicating that TC supplementation 274 275 was able to accelerate the recovery of muscle strength. The subgroup analysis on exercise type 276 indicated this observation was consistent between the metabolic and mechanical exercise groups. Overall analysis for muscular power revealed a significant and moderate benefit. For this variable 277 278 sub-group analysis was carried out on method of assessment, jump height or sprint test. Subgroup 279 analysis revealed a significant and large beneficial effect of TC supplementation on jump height and 280 a significant but small beneficial effect on sprint speed. These differences in effect size between subgroups could be due to the mechanics of the different movements, with the CMJ utilizing the 281 stretch shortening cycle and containing both an eccentric and concentric phase within the movement. 282 In addition, previous research has indicated a large learning effect with sprint trials (Bell et al., 283 2014a). This study observed an improvement in sprint performance over time throughout the 72h 284 285 post trial period, this increase in performance was attributed to a learning effect and could explain a smaller effect size for this measure. 286

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Muscle damaging exercise leads to a decrease in the force generating capacity of the affected muscle, this is attributed to myofibrillar disruption and damage to the muscle fibre architecture (Clarkson and Hubal., 2002). Previous research has indicated that supplementation with TC can protect against the declines in muscle function that are observed following strenuous exercise (Bell et al., 2016). This has been proposed to occur as a result of a reduced acute inflammatory response (Bell et al., 2016). This is supported by attenuated inflammatory markers observed in this metaanalysis.

Supplementation with TC resulted in an overall significant but small effect on both CRP and IL-6 with 296 297 lower concentrations observed following TC consumption. Interestingly the subgroup analysis carried out for CRP revealed TC supplementation had no significant effect on exercise protocols 298 categorised as mechanical and a large and significant effect on exercise categorised as metabolic. 299 Reduced concentrations of CRP have previously been attributed to a reduction in cell damage that 300 301 occurs as a result of oxidative stress (Bell et al., 2014a). Thus, it might be that TC supplementation 302 is more beneficial to exercise that is more metabolically challenging. It is also possible that prolonged endurance exercise such as Marathon running could induce a systemic inflammatory response, 303 enhancing the ability of the TC supplement to have a greater blunting effect on the secondary muscle 304 damage response (Bell et al., 2014b). A possible explanation for the reduced inflammatory response 305 is that anthocyanins contained in the TC are able to inhibit the activity of prostaglandin enzymes, 306 which has been shown to mediate inflammation (Lanier, 2003). It should also be noted that the 307 exercise modalities classified as metabolic are not all free of mechanical damage. For example, 308 Marathon running has huge metabolic consequences but the repetitive eccentric contractions 309 occurring as part of the gait cycle will also induce mechanical damage. 310 No benefit of supplementation with TC was observed for TNFa. A subgroup analysis was not carried out for TNFa 311 and IL-6 due to the limited number of studies that measured these variables. 312

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Data from this study indicate that the consumption of TC can attenuate the severity of DOMS, with 314 the observation of a small beneficial effect in favour of TC. The subgroup analysis revealed there 315 was no significant effect of TC supplementation on soreness following exercise that is metabolic in 316 317 nature, however there was a significant and moderate reduction in soreness following exercise that is mechanical in nature. Soreness following damaging exercise has been attributed to increased 318 oxidative stress and inflammation (Beals et al., 2017), increased sensitivity of nociceptors and 319 mechanoreceptors to noxious chemicals, including prostaglandins, released during muscle damage 320 (Clarkson and Hubal., 2002) and microinjury to surrounding tissues that is exacerbated by immune 321 mediated inflammation (Sonkodi et al., 2020). It is possible that supplementation with TC can inhibit 322 323 the cyclooxygenase pathway, reducing the synthesis of prostaglandins (Marzocchella et al., 2011),

and dampening the secondary muscle damage response (Levers et al., 2015), this could result in reduced muscle soreness. Damage to the connective tissue and structures within the muscle fibres is likely to be greater following exercise that is mechanical in nature giving rise to a greater inflammatory response, this may explain why TC supplementation has a greater effect following exercise of a mechanical nature.

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330 No significant effect of TC supplementation was observed compared to placebo for creatine kinase. 331 This is not surprising given that none of the 11 studies included in the analysis observed a significant difference between groups for CK. High variability exists in the CK response between individuals 332 333 and in response to different types of exercise (Brancaccio et al., 2007). In addition to this training status of the participants greatly affects the CK response to exercise. The variability in population, 334 335 training status and exercise modalities used within the studies included in this meta-analysis may explain why no significant effects were observed. In addition to high inter-individual variability, there 336 is wide variability in the magnitude of change in CK across studies, for example Levers et al. (2016) 337 observed peak values of 870 IU/L in the TC group compared to Howatson et al. (2010) who observed 338 peak values of 2227 IU/L in the TC group. Due to this CK may not be a good marker for exercise 339 recovery but is a good indicator of the presence of EIMD. 340

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342 Supplementation with TC is thought to attenuate RONS induced membrane damage therefore limiting muscle damage and facilitating recovery. The results from this meta-analysis provide some 343 evidence to suggest that supplementation with TC can enhance certain aspects associated with 344 exercise recovery. A limitation of the present study is that oxidative stress was not included in the 345 analysis due to a lack of studies measuring the same markers of oxidative stress, therefore it is 346 347 difficult to get a mechanistic understanding of the effects of TC. In addition, whist we tried to classify 348 exercise modalities based upon exercise type, mechanical or metabolic, many exercise modalities 349 often incur both mechanical and metabolic stress. This is important to note. Further research should investigate exercise modalities that isolate metabolic or mechanical stress to better identify whether
 TC supplementation is more effective under specific conditions.

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Finally it is important to note that meta-analyses are limited by the data available and there are 353 several limitations in the literature; (1) the participants of several studies were of mixed gender, there 354 is no indication of how the menstrual cycle was controlled for in these studies; (2) the mode of 355 exercise and muscle groups involved varies greatly between studies, this is likely to induce different 356 357 levels of muscle damage via different mechanistic pathways, there was also variation in the training status of the participants, this will affect the severity of the muscle damage experienced; (3) the type 358 359 of TC supplement and supplementation protocol varies between studies, with studies administering various brands of juice (Howatson et al 2008; Bell et al., 2016; Quinlan and Hill 2019) and some 360 361 using a powder that is mixed with water (Levers 2015; Levers 2016; Beals et al., 2017). In addition to this several studies implemented dietary restrictions asking participants to follow a low phenolic 362 diet. This could lead to an over estimation of the intervention effect and has been acknowledged in 363 the risk of bias assessment. Limitations 1-3 could all have had an influence on the variability of the 364 data and may explain why there was large heterogeneity in some of the variables. 365 Finally(4) Independent variables were only included in the meta-analysis if three studies had measured and 366 reported them. Whilst some studies have assessed markers of oxidative stress, there is not one 367 marker that has been assessed by three separate studies. 368

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370 Conclusion

The results of this systematic review and meta-analysis indicate the supplementation with TC can aid the recovery of muscle function and attenuate soreness following strenuous exercise. It is possible that this occurs via a mediated inflammatory response as indicated by attenuations in the concentration of CRP and IL-6. Further research is needed that investigates the effects of TC supplementation on markers of oxidative stress, whilst taking into consideration the limitations of

376	these markers.	Although the physiologica	I mechanisms are yet	to be fully understood,	this meta-
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analysis provides support for the use of TC to facilitate recovery following strenuous exercise.

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379 ACKNOWLEDGMENT, AUTHORSHIPS, DECLARATIONS

- All authors had a role in study design, data analysis and manuscript preparation. All authors have
- 381 approved the final version of the paper.
- 382 Authors confirm there are no conflicts of interest.

383

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- **TABLES**
- **Table 1:** Review Inclusion Criteria

Population:	Healthy males and females with no restriction on age, activity level or
	training status.
Intervention:	Supplementation with a tart cherry product before, or before and after a
	single bout of exercise.
<u>Comparator:</u>	The effectiveness of supplementation with a tart cherry product on indices
	of recovery from exercise induced muscle damage in comparison to a
	control or placebo group.
Outcomes:	$\label{eq:measurements} Measurements \ of \ muscular \ soreness, \ muscular \ strength, \ muscular \ power$
	and blood biomarkers creatine kinase, C reactive protein, interleukin-6 and
	tumour necrosis factor alpha.
Study Design:	Randomised controlled trials, non-randomised controlled trials and cross
	over studies using a contralateral limb design.

Table 2. Summary of literature included in the meta-analysis

Author(s)	Participant cohort	Exercise intervention	Supplement type	Supplementation	Outcome variables and
	(training status, gender,			protocol	measurement times (h)
	number)				
Beals et	Recreationally active	Repetitive maximal effort	TC -30g TartVitaCherry freeze-dried powder with	Two servings per day for	↔ DOMS (24, 48, 96, 168)
al.	<i>n</i> =19 male, <i>n</i> =10 female	isokinetic eccentric	0.5% anthocyanins mixed with unsweetened	12 days. Four days prior,	\leftrightarrow Peak concentric torque (24, 48, 96,
(2017) †		contractions of the	Black-Cherry Kool-Aide.	the day of and 7 days	168)
		quadriceps to fatigue	PL -Sweetened black cherry mixed with 4 g of	following the exercise	
			nutribiotic plain rice protein powder.	protocol.	
Bell <i>et al.</i>	Male trained cyclists	High intensity stochastic	TC - 30ml Cherry Active mixed with 100ml water.	Two servings per day for	↔ CK (0, 24, 48)
(2014a) ‡	<i>n</i> =16	cycling trial lasting 109	PL mixed berry cordial with 100ml water and	7 consecutive days. Four	↓ IL-6 (0, 24, 48)
		minutes completed on 3	maltodextrin	days pre and on each trial	↓ C-RP (0, 24, 48)
		consecutive days		day.	↔ TNFα (0, 24, 48)
Bell <i>et al.</i>	Male trained cyclists	High intensity stochastic	TC - 30ml Cherry Active mixed with 100ml water.	Two servings per day for	↔ DOMS (24, 48, 72)
(2014b) ‡	<i>n</i> =16	cycling trial lasting 109	PL mixed berry cordial with 100ml water and	8 consecutive days. Four	\leftrightarrow 6s sprint cycle (24, 48, 72)
		minutes.	maltodextrin	days pre, the day of and 3	↑ MVIC (24, 48, 72)
				days post trial.	↔ CK (0, 1, 24, 48, 72)
					↓ IL-6 (0, 1, 24, 48, 72)
					↓ C-RP (0, 1, 24, 48, 72)
					↔ TNFα (0, 1, 24, 48, 72)
Bell <i>et al.</i>	Male semi-professional	Adapted Loughborough	TC - 30ml Cherry Active mixed with 100ml water.	Two servings per day for	↓ DOMS (24, 48, 72)
(2016) ‡	soccer players <i>n</i> =16	Intermittent Shuttle Test		7 consecutive days. Four	↑ MVIC (24, 48, 72)

			PL mixed berry cordial with 100ml water and	days pre, the day of and 2	↑ CMJ (24, 48, 72)
			maltodextrin	days post trial.	↓ 20m sprint (24, 48, 72)
					↔ CK (0, 1, 24, 48, 72)
					↓ IL-6 (0, 1, 24, 48, 72)
					↔ C-RP (0, 1, 24, 48, 72)
					$\leftrightarrow TNF\alpha\ (0,1,24,48,72)$
Bowtell et	Well trained male	Ten sets of 10 knee	TC - 30 ml Cherry Active concentrate.	Two servings per day for	↑ MVIC (1, 24, 48)
al.	participants from	extensions at 80% 1RM	PL - 30 ml Iso-energetic synthetically derived fruit	10 days. Seven days	↔ CK (1, 24, 48)
(2011) †	intermittent team sports	with an elongated	concentrate	before, the day of and 2	↔ C-RP (1, 24, 48)
	<i>n</i> =10	eccentric phase lasting 3		days after.	
		seconds.			
Brown et	Female dancers from a	Repeated sprint protocol	TC - 30ml Cherry Active mixed with 100ml water.	Two servings per day for	↔ DOMS (0, 24, 48, 72)
al.	University team <i>n</i> =20	consisting of 15x30 m	PL - 25ml of a synthetically derived fruit	8 days. Four days pre,	↔ MVC (0, 24, 48, 72)
(2019) †		maximal sprints with a	conentrate with negligible phytochemical content	the day of and 3 days	↑ CMJ (0, 24, 48, 72)
		rapid 10 m deceleration	diluted with 100ml of water and fortified with	post exercise.	↔ 30m sprint (0, 24, 48, 72)
		phase, each separated	maltodexterin and whey protein powder		↔ CK (0, 1, 24, 48, 72)
		by 60 s rest.			↔ C-RP (0, 1, 24, 48, 72)
Connolly	Male College students	40 (2 X 20) maximal	TC - 12oz bottle of Cherrypharm.	Two servings per day for	↓ DOMS (24, 48, 72, 96)
et al.	<i>n</i> =14	eccentric contractions of	PL - unsweetend black cherry Kool-aid mixed	8 days. Three days prior,	\leftrightarrow Proximal tenderness (24, 48, 72,
(2006) †		the elbow flexors	with water.	the day of and 4 days	96)
				post.	↑ MVIC (24, 48 72, 96)

Howatson	Marathon runners n=13	A marathon run	TC - 12oz bottle of Cherrypharm.	Two servings per day for	↔ DOMS (1, 24, 48)
et al.	male, n=7 female		PL - fruit flavoured concentrate mixed with 8 fl oz	8 days. Five days before,	↑ MVIC (1, 24, 48)
(2008) ‡			water.	the day of and 2 days	↔ CK (1, 24, 48)
				post.	↓ IL-6 (1, 24, 48)
					↓ C-RP (1, 24, 48)
Kastello	Untrained participants	Eccentric contractions of	TC - A tablet consisting of Cherry Flex paste.	One tablet twice a day for	↓ DOMS (12, 24, 48, 72)
et al.	<i>n</i> =10 male, <i>n</i> =4 female	the bicep. Ten	PL - tablet consisting of cooking oil and red food	16 days prior to and for 3	\leftrightarrow Peak torque (12, 24, 48, 72)
(2014) †		submaximal contractions	colouring	days following exercise	↔ CK (12, 24, 48, 72)
		followed by 5 sets of 10			↓ C-RP (12, 24, 48, 72)
		maximal contractions			
Kuehl et	Marathon runners n=36	Hood to Coast relay.	TC - 10.5oz bottle of Cherrish.	Two servings per day.	↓ DOMS (24)
al.	male, n=18 female	Average total running	PL - unsweetened fruit punch mixed with water	Seven days prior to and	
(2010) ‡		distance of 26.3±2.5km		the day of the race.	
Lamb et	Non-resistance trained	Five sets of 10 unilateral	TC – 30 ml of Cherry Active diluted with 220ml	Two servings per day	↔ DOMS (1, 24, 48, 72, 96)
al.	males n=24	eccentric elbow flexions	water	Four days prior to the day	↔ MVIC (1, 24, 48, 72, 96)
(2019) †			PL – 250ml of blackcurrant flavoured	of and 4 days post	↔ CK (1, 24, 48, 72, 96)
			maltodextrin sports drink	exercise.	
Levers et	Resistance trained males	Ten sets of 10 repetitions	TC - 480 mg Powdered tart cherry.	One serving per day for	↓ DOMS (1, 24, 48)
al.	<i>n</i> =23	of a bar bell back squat	PL - 480 mg rice flour mixed with water	10 days. Seven days	↔ MVIC (1, 24, 48)
(2015) †		at 70% 1RM with 3 min		before, the day of and 2	↔ CK (1, 24, 48)
		recovery between sets		days post exercise.	↔ IL-6 (1, 24, 48)

↔ TNFα (1, 24, 48)

Levers e	t Triathletes n=18 male	21.1km run under	TC - 480 mg Powdered tart cherry.	One serving per day for	↓ DOMS (1, 24, 48)
al.		simulated race	PL - 480 mg rice flour mixed with water	10 days. Seven days	↔ CK (1, 24, 48)
(2016) ‡		conditions		before, the day of and 2	↓ IL-6 (1, 24, 48)
				days post exercise.	↔ TNFα (1, 24, 48)
Quinlan	Team sport players n=8	Adapted LIST test	TC – 30ml of Montmorency tart cherry	Two servings per day.	↔ DOMS (1, 24, 48)
et al.	male, n=12 female		concentrate Holland and Barrett own brand	Five days before the day	↑ MVIC (1, 24, 48)
(2019) ‡			mixed with 70ml water	of and 2 days post	↑ CMJ (1, 24, 48)
			PL – 25ml of Robinsons summer fruit squash	exercise.	↓ 20m sprint (1, 24, 48)
			mixed with water		↔ CK (1, 24, 48)
					↔ C-RP (1, 24, 48)

539 CMJ, counter-movement jump; CK, creatine kinase; DOMS, delayed-onset muscle soreness; IL-6, interleukin-6; MVIC, maximum voluntary isometric contraction; PPT, pressure pain threshold; TNFa, tumor

necrosis factor alpha.

541 Increases or decreases represent improved performance or attenuations in a variable.

542 TC = tart cherry juice, PL = placebo

543 † denotes a study with an exercise protocol considered mechanical, ‡ denotes a study with an exercise protocol considered metabolic.

545 FIGURE CAPTIONS





- 548 Figure 1a. Risk of bias percentile chart, in accordance with the Cochrane Collaboration (Higgins
- 549 and Altman, 2008).



- **Figure 1b**. Risk of bias summary for each included study.



Figure 2. Study selection from initial identification to inclusion.



Figure 3. Forest plot demonstrating a comparison between the consumption of a tart cherry supplement or a placebo for measures of delayed-onset muscle soreness. The time point of measurement post exercise is displayed in brackets on the first column. a, b and c displayed in column 1 refer to soreness measured in different locations within the same study.

	Ex	perimenta	al		Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
.2.1 Metabolic									10
3ell 2014ii (24h)	-2.42	12.12	8	8.18	7.56	8	2.4%	-0.99 [-2.05, 0.06]	
lell 2014ii (48h)	0.61	10.61	8	12.43	7.88	8	2.4%	-1.20 (-2.29, -0.11)	
3ell 2014ii (72h)	-7.57	10.91	8	13.64	10.91	8	2.2%	-1.84 [-3.06, -0.61]	
lell 2016 (24h)	-1.6	12	8	15.86	10	8	2.3%	-1 49 [-2 64 -0 35]	
ell 2016 (48h)	-7.73	10	8	11.3	7	8	2.2%	-2 08 [-3 37 -0 80]	
ell 2016 (72h)	-4.02	13	8	5.81	7	8	2.5%	-0.89[-1.93_0.15]	
Iowatson 2010 (1h)	122	51 7919	10	108	58 2632	10	2.6%	0.24 [-0.64 1.12]	
lowatson 2010 (24h)	45	50 4301	10	71	55 692	10	2.6%	-0.47 [-1.36 0.42]	
lowateon 2010 (49h)	-3	50 1010	10	36	49 0551	10	2.070	-0.47 [1.50, 0.42]	
uinlan 2010 (40h)	-100	60.46	10	-54.7	71 02	10	2.0706	0.07 [0.00, 0.05]	
uinlan 2018 (0h) uinlan 2018 (24h)	20.2	50.45	10	-34.7	60 1 2	10	2.7 70	0.61 [0.20 1.52]	
uinian 2013 (241) Juiplop 2010 (49b)	-20.3	50.20	10	-30.7	70.05	10	2.0 %	0.01 [-0.25, 1.32]	
unnan 2019 (48n)	-4.7	52.63	109	54.5	70.65	109	2.0%	0.31[-1.64, 0.02]	
ubiotal (95% Cl)	27.042	20.05	100		C) 17 COO	100	23.070	-0.75 [-1.10, -0.20]	· · · · · · · · · · · · · · · · · · ·
ieterogeneity. Tau- = 0	.37, Chi-	= 26.65, u	11 = 11 (P = 0.00	o), in= 599	0			
est for overall effect. Z	= 3.17 (F	r = 0.002)							
2.2 Mechanical									
aple 2017 /160h	16.0	22 6016	15	20.2	10 0140	1.4	200	0.501047 1 22	
sais 2017 (1060) opio 2017 (24b)	-10.9	22.0010	15	-29.2	17 2022	14	2.0%	0.08 [-0.17, 1.32]	10 JUN 10
ears 2017 (24ff)	-1	21.5008	15	-4.7	17.2023	14	2.8%	0.18[-0.55, 0.91]	
eals 2017 (48h)	2.6	23.3795	15	-11.1	17.3076	14	2.8%	0.64 [-0.11, 1.39]	
eals 2017 (96h)	-6.6	22.521	15	-11.6	17.1306	14	2.8%	0.24 [-0.49, 0.97]	
owtell 2011 (1h)	34.7	2.8	10	34.7	3	10	2.7%	0.00 [-0.88, 0.88]	
owtell 2011 (24h)	9.8	3	10	15.3	2.8	10	2.4%	-1.82 [-2.89, -0.74]	
owtell 2011 (48h)	9.8	2.7	10	12.5	2.7	10	2.6%	-0.96 [-1.89, -0.02]	50
rown 2018 (0h)	7.7	38.9447	10	38.1	39.7337	10	2.6%	-0.74 [-1.65, 0.17]	
rown 2018 (24h)	31.6	42.4952	10	36.8	39.5336	10	2.7%	-0.12 [-1.00, 0.76]	
rown 2018 (48h)	13	42.5747	10	30.4	40.2966	10	2.6%	-0.40 [-1.29, 0.49]	
rown 2018 (72h)	17.8	32.8236	10	16.3	42.3413	10	2.7%	0.04 [-0.84, 0.91]	
onnolly 2006 (24h)	12.2	3.73	14	30.3	4.4	14	2.0%	-4.31 [-5.73, -2.88]	
onnolly 2006 (48h)	6.9	4.1	14	26.6	3.4	14	1.8%	-5.08 [-6.69, -3.46]	
onnolly 2006 (72h)	2.2	4.7	14	16.9	3.4	14	2.2%	-3.48 [-4.71, -2.25]	
onnolly 2006 (96h)	-6.25	4.4	14	12.2	3.4	14	1.9%	-4.56 [-6.04, -3.07]	ST
astello 2014 (12h)	17.9	4.2	14	23.5	4	14	2.7%	-1.33 [-2.16, -0.50]	10 00 00 00
astello 2014 (24h)	21	4	14	28.5	5	14	2.7%	-1.61 [-2.48, -0.74]	
(astello 2014 (48h)	22	4.8	14	24.5	4.5	14	2.8%	-0.52 [-1.28, 0.23]	
astello 2014 (72h)	11	5	14	13.3	6.7	14	2.8%	-0.38 [-1.13, 0.37]	
amb 2019 (0h)	19.36	16.13	12	28.088	20.33	12	2.7%	-0.46 [-1.27, 0.35]	
amb 2019 (24h)	24.16	17.15	12	25.343	15.45	12	2.7%	-0.07 [-0.87, 0.73]	
amb 2019 (48h)	21.18	21.74	12	22.696	20.55	12	2.7%	-0.07 [-0.87, 0.73]	
amb 2019 (72h)	12.99	22.42	12	15.245	22.42	12	2.7%	-0.10 [-0.90, 0.70]	
amb 2019 (96h)	9.804	20.72	12	13.627	21,91	12	2.7%	-0.17 [-0.98, 0.63]	
evers 2015 (1h)	310	299.847	11	453	169,193	12	2.7%	-0.57 [-1.41, 0.26]	
evers 2015 (24h)	197	320.671	11	311	177.833	12	2.7%	-0.43 [-1.26, 0.40]	
evers 2015 (48h)	311	300 557	11	348	163.614	12	2.7%	-0.15[-0.97, 0.67]	
ubtotal (95% CI)	9.11		335			334	70.2%	-0.81 [-1.23, -0.40]	•
leterogeneity: Tau ² = 1	00: Chiž	= 158.86	df = 26	(P < 0 0	0001): I ² =	84%			1
est for overall effect: Z	= 3.82 (F	P = 0.0001)	, 0.0		70			
otal (95% CI)			443			442	100.0%	-0.78 [-1.11, -0.46]	•
leterogeneity: Tau ^z = 0	.82; Chi ²	= 186.10,	df = 38	(P < 0.0	0001); I ^z =	80%		5	 \ \
est for overall effect: Z	= 4.76 (F	, o < 0.0000	1)	8	1953				-4 -2 U Z 4
AL 2523 14 1980		hiz - 0.07	df = 1	/D = 0.70	N 17 - 0.04				r avours [experimental] Favours [control]

Figure 4. Forest plot demonstrating a comparison between the consumption of a tart cherry

supplement or a placebo for measures of strength. The time point of assessment post exercise is

566 displayed in brackets on the first column.

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		Experimental			Control		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.3.1 Jump									6
Bell 2016 (24h)	7	5	8	12	3	8	3.6%	-1.15 [-2.23, -0.06]	· · · · · · · · · · · · · · · · · · ·
Bell 2016 (48h)	5	4	8	11	5	8	3.6%	-1.25 [-2.35, -0.15]	
Bell 2016 (72h)	6	4	8	9	4	8	4.0%	-0.71 [-1.73, 0.31]	
Brown 2018 (0h)	11.5	7.5	10	16	5	10	4.7%	-0.68 [-1.58, 0.23]	
Brown 2018 (24h)	8	6	10	15	15	10	4.8%	-0.59 [-1.49, 0.31]	
Brown 2018 (48h)	4	4.5	10	14	4.5	10	3.3%	-2.13 [-3.27, -0.98]	
Brown 2018 (72h)	1.5	7.5	10	13	7	10	4.0%	-1.52 [-2.54, -0.50]	· · · · · · · · · · · · · · · · · · ·
Quinlan 2019 (0h)	2.31	7.2	10	3.05	5.22	10	4.9%	-0.11 [-0.99, 0.76]	
Quinlan 2019 (24h)	1.17	6.83	10	3.32	5.16	10	4.9%	-0.34 [-1.22, 0.54]	
Quinlan 2019 (48h)	0.05	6.87	10	2.75	5.32	10	4.8%	-0.42 [-1.31, 0.47]	
Subtotal (95% CI)			94			94	42.6%	-0.82 [-1.18, -0.45]	•
Test for overall effect:	Z= 4.41	(P < 0.0001)							
2.3.2 Sprint									12210
Bell 2014ii (24h)	-80	157.0003822	8	8	129.0004	8	4.1%	-0.58 [-1.59, 0.43]	
Bell 2014ii (48h)	-123	181.4369312	8	-24	131.034	8	4.0%	-0.59 [-1.60, 0.42]	
Bell 2014ii (72h)	-126	167.0013174	8	-24	127.6064	8	4.0%	-0.65 [-1.66, 0.36]	2
Bell 2016 (24h)	0.06	0.09444575	8	0.13	0.11257	8	4.0%	-0.64 [-1.65, 0.38]	National Contraction of the
Bell 2016 (48h)	0.03	0.08634813	8	0.18	0.162776	8	3.7%	-1.09 [-2.16, -0.02]	
Bell 2016 (72h)	-0.01	0.09444575	8	-0.12	0.120316	8	3.8%	0.96 [-0.09, 2.01]	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Brown 2018 (0h)	0.1	0.23026072	10	0.18	0.185365	10	4.9%	-0.37 [-1.25, 0.52]	
Brown 2018 (24h)	0.07	0.21718656	10	0.09	0.172	10	4.9%	-0.10 [-0.97, 0.78]	1
Brown 2018 (48h)	0.13	0.21501163	10	0.3	0.259368	10	4.7%	-0.68 [-1.59, 0.22]	10 Barrier (10)
Brown 2018 (72h)	0.05	0.24758837	10	0.15	0.180466	10	4.8%	-0.44 [-1.33, 0.45]	
Quinlan 2019 (Oh)	0.158	0.35	10	0.242	0.32	10	4.9%	-0.24 [-1.12, 0.64]	10
Quinlan 2019 (24h)	0.66	0.33	10	0.215	1.122	10	4.8%	0.52 [-0.38, 1.41]	
Quinlan 2019 (48h)	0.01	0.34	10	0.144	0.33	10	4.8%	-0.38 [-1.27, 0.50]	
Subtotal (95% CI)			118			118	57.4%	-0.32 [-0.60, -0.04]	•
Heterogeneity: Tau² = Test for overall effect:	0.03; Cł Z = 2.26	ni² = 13.33, df = (P = 0.02)	12 (P =	: 0.35); I	²=10%				
Total (95% CI)			212			212	100.0%	-0.53 [-0.77, -0.29]	•
Heterogeneity: Tau ² =	0.10; Cł	ni ^z = 31.17, df =	22 (P =	0.09);1	* = 29%			2	
Test for overall effect:	Z=4.39	(P < 0.0001)							-2 -1 U 1 2 Eavours (experimental) Eavours (control)
Test for subaroup diff	erences	Chi ² = 4.59, df	= 1 (P =	= 0.03).	I ² = 78.2%				r avours [experimental] Pavours [control]

Figure 5. Forest plot demonstrating a comparison between the consumption of a tart cherry

571 supplement or a placebo for measures of power. The time point of assessment post exercise is

572 displayed in brackets on the first column.



Figure 6. Forest plot demonstrating a comparison between the consumption of a tart cherry

supplement or a placebo for creatine kinase. The time point of assessment post exercise is

displayed in brackets on the first column.



Figure 7. Forest plot demonstrating a comparison between the consumption of a tart cherry

supplement or a placebo for C reactive protein. The time point of assessment post exercise is

584 displayed in brackets on the first column.

	E	perimental	1		Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Bell 2014i (0h)	1.75	0.994706	8	3.65	1.809005	8	4.7%	-1.23 [-2.33, -0.13]	
Bell 2014i (24h)	1.11	0.917388	8	3.05	2.437324	8	4.8%	-1.00 [-2.05, 0.06]	
Bell 2014i (48h)	0.95	0.360333	8	2.48	1.390971	8	4.5%	-1.42 [-2.56, -0.29]	
Bell 2014ii (0h)	2.6	0.770101	8	3.73	1.887786	8	5.0%	-0.74 [-1.76, 0.28]	
Bell 2014ii (1h)	0.75	0.478539	8	1.34	0.696276	8	4.9%	-0.93 [-1.98, 0.11]	
Bell 2014ii (24h)	0.27	0.353667	8	-0.39	0.381293	8	4.3%	1.70 [0.51, 2.89]	(1) (1) (1) (1) (1) (1) (1) (1) (1) (1)
Bell 2014ii (48h)	-0.35	0.311987	8	-0.62	0.39982	8	5.0%	0.71 [-0.31, 1.73]	
Bell 2016 (0h)	3.8	1.19499	8	6.2	2.761902	8	4.8%	-1.07 [-2.13, 0.00]	
Bell 2016 (1h)	2	0.368782	8	3.8	1.931321	8	4.7%	-1.22 [-2.32, -0.13]	
Bell 2016 (24h)	0.25	0.324037	8	0.3	0.50448	8	5.2%	-0.11 [-1.09, 0.87]	10 10 10 10 10 10 10 10 10 10 10 10 10 1
Bell 2016 (48h)	-0.2	0.363318	8	-0.35	0.497293	8	5.2%	0.33 [-0.66, 1.31]	
Bell 2016 (72h)	-0.2	0.5	8	-0.35	0.497293	8	5.2%	0.28 [-0.70, 1.27]	10 10 10 10 10 10 10 10 10 10 10 10 10 1
Howatson 2010 (1h)	41.8	0.2	10	80.3	36.02515	10	5.1%	-1.45 [-2.46, -0.44]	10 10 10 10 10 10 10 10 10 10 10 10 10 1
Howatson 2010 (24h)	0	0	10	-0.6	2.717057	10		Not estimable	
Howatson 2010 (48h)	0	0	10	-0.9	2.807063	10		Not estimable	
Levers 2015 (1h)	0.45	0.874172	11	0.27	0.985657	12	6.0%	0.19 [-0.63, 1.01]	10 10 10 10 10 10 10 10 10 10 10 10 10 1
Levers 2015 (24h)	0.11	0.923146	11	-0.01	0.888063	12	6.0%	0.13 [-0.69, 0.95]	
Levers 2015 (48h)	-0.02	0.89509	11	-0.08	0.844779	12	6.0%	0.07 [-0.75, 0.88]	
Levers 2016 (1h)	1.18	1.038194	11	1.58	1.014735	16	6.3%	-0.38 [-1.15, 0.40]	
Levers 2016 (24h)	-0.25	0.779357	11	-0.06	0.325644	16	6.3%	-0.33 [-1.11, 0.44]	
Levers 2016 (48h)	-0.35	0.815772	11	-0.07	0.325143	16	6.2%	-0.47 [-1.25, 0.31]	
Total (95% CI)			192			210	100.0%	-0.35 [-0.68, -0.02]	•
Heterogeneity: Tau ² = 0.	.30; Chi ²	= 40.95, df	= 18 (P	= 0.003	2); I ^z = 56%			5	
Test for overall effect: Z	= 2.08 (F	^o = 0.04)	10						-2 -1 U 1 2 Favoure [experimental] Favoure [control]
	20								Tavouis [experimental] Favouis [control]

Figure 8. Forest plot demonstrating a comparison between the consumption of a tart cherry
supplement or a placebo for IL-6. The time point of assessment post exercise is displayed in
brackets on the first column.

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	Ex	perimenta	al l		Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Bell 2014i (0h)	0.25	0.36093	8	0.07	0.523393	8	4.5%	0.38 [-0.61, 1.37]	
Bell 2014i (24h)	0.25	0.352	8	-0.25	0.550863	8	3.9%	1.02 [-0.04, 2.08]	
Bell 2014i (48h)	0.04	0.319	8	-0.11	0.539231	8	4.5%	0.32 [-0.67, 1.31]	
3ell 2014ii (0h)	0.12	0.31882	8	0.02	0.52192	8	4.6%	0.22 [-0.77, 1.20]	
Bell 2014ii (1h)	0.03	0.319	8	-0.14	0.525623	8	4.5%	0.37 [-0.62, 1.36]	
3ell 2014ii (24h)	-0.12	0.31882	8	-0.37	0.521268	8	4.4%	0.55 [-0.46, 1.55]	
3ell 2014ii (48h)	-0.27	0.32259	8	-0.44	0.521584	8	4.5%	0.37 [-0.62, 1.36]	
3ell 2014ii (72h)	-0.27	0.34037	8	-0.21	0.525623	8	4.6%	-0.13 [-1.11, 0.85]	
Bell 2016 (0h)	-0.43	0.25764	8	0.19	0.558627	8	3.6%	-1.35 [-2.47, -0.23]	
3ell 2016 (1h)	0.02	0.20955	8	-0.01	0.539559	8	4.6%	0.07 [-0.91, 1.05]	
3ell 2016 (24h)	0.2	0.24123	8	0.06	0.577096	8	4.6%	0.30 [-0.69, 1.29]	
3ell 2016 (48h)	0.06	0.23636	8	0.01	0.549618	8	4.6%	0.11 [-0.87, 1.09]	
Bell 2016 (72h)	0.2	0.32658	8	0.11	0.605485	8	4.6%	0.17 [-0.81, 1.16]	
_evers 2015 (1h)	0.06	0.71099	11	0.03	1.157395	12	6.6%	0.03 [-0.79, 0.85]	
_evers 2015 (24h)	-0.11	0.71061	11	-0.32	0.993937	12	6.6%	0.23 [-0.59, 1.05]	
evers 2015 (48h)	-0.32	0.70578	11	-0.45	0.986913	12	6.6%	0.14 [-0.67, 0.96]	
evers 2016 (1h)	0.11	0.85187	11	0.28	0.950326	16	7.5%	-0.18 [-0.95, 0.59]	
_evers 2016 (24h)	-0.22	0.58658	11	-0.26	0.751862	16	7.5%	0.06 [-0.71, 0.82]	
_evers 2016 (48h)	-0.4	0.56246	11	-0.25	0.750706	16	7.5%	-0.21 [-0.98, 0.56]	
fotal (95% CI)			170			188	100.0%	0.12 [-0.09, 0.33]	+
Heterogeneity: Tau ² =	= 0.00; C	hi ^z = 12.89), df = 1	8 (P = 0	.80); I ^z = 0%	6		2	
est for overall effect	Z=1.09	9 (P = 0.27)	1	8				-2 -1 U 1 2 Favours [experimental] Favours [control]

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Figure 9. Forest plot demonstrating a comparison between the consumption of a tart cherry supplement or a placebo for TNF α . The time point of assessment post exercise is displayed in brackets on the first column.