Tart Cherry (*Prunus cerasus)*

Cherries have a long history of being used for many medicinal purposes. Often times, tart and sweet cherries are grouped together. For our purposes, we have determined that tart cherries provide more beneficial compounds. We closely monitor the science behind all of our products and update information and products based on what the science says.

Tart cherries offer more anthocyanins, which have a host of benefits (reduced proliferation of mice and human colon cancer cells) and tart cherries are also much lower in sugar than traditional cherries. Tart cherries have been shown to decrease inflammation from a variety of reasons including exercise and gout and may have analgesic properties as well. Tart cherries also contain high levels of naturally-occurring melatonin. In a sleep study, participants who consumed tart cherries demonstrated improved sleep quality, duration and amount of time in bed.

1. **Influence of a Montmorency cherry juice blend on indices of exercise-induced stress and upper respiratory tract symptoms following marathon running—a pilot investigation.**

   BACKGROUND: Prolonged exercise, such as marathon running, has been associated with an increase in respiratory mucosal inflammation. The aim of this pilot study was to examine the effects of Montmorency cherry juice on markers of stress, immunity and inflammation following a Marathon. **METHODS:** Twenty recreational Marathon runners consumed either cherry juice (CJ) or placebo (PL) before and after a Marathon race. Markers of mucosal immunity secretory immunoglobulin A (sIgA), immunoglobulin G (IgG), salivary cortisol, inflammation (CRP) and self-reported incidence and severity of upper respiratory tract symptoms (URTS) were measured before and following the race. **RESULTS:** All variables except secretory IgA and IgG concentrations in saliva showed a significant time effect ($P < 0.01$). Serum CRP showed a significant interaction and treatment effect ($P < 0.01$). The CRP increase at 24 and 48 h post-Marathon was lower ($P < 0.01$) in the CJ group compared to PL group. Mucosal immunity and salivary cortisol showed no interaction effect or treatment effect. The incidence and severity of URTS was significantly greater than baseline at 24 h and 48 h following the race in the PL group and was also greater than the CJ group ($P < 0.05$). No URTS were reported in the CJ group whereas 50 % of runners in the PL group reported URTS at 24 h and 48 h post-Marathon. **CONCLUSIONS:** This is the first study that provides encouraging evidence of the potential role of Montmorency cherries in reducing the development of URTS post-Marathon possibly caused by exercise-induced hyperventilation trauma, and/or other infectious and non-infectious factors. [Dimitriou L, Hill JA, Jehnali A, Dunbar J, Brouner J, McHugh MP, Howatson G. Influence of a Montmorency cherry juice blend on indices of exercise-induced stress and upper respiratory tract symptoms following marathon running—a pilot investigation. *J Int Soc Sports Nutr.* 2015 May 11;12:22.]

2. **Montmorency tart cherry (*Prunus cerasus L.*) concentrate lowers uric acid, independent of plasma cyaniding-3-O-glucosiderutinoside.**

   Two doses (30 and 60 mL) of Montmorency tart cherry concentrate (MC) were used to investigate their impact on physiological indices of uric acid activity, inflammation and the bioavailability of the major anthocyanin (CYA-3-O-GluRut). Following MC supplementation plasma CYA-3-O-GluRut increased ($P < 0.05$), with a greater uptake in the 60 mL dose found at 1 h. Serum urate was decreased ($P < 0.001$) with a peak change (% of baseline) of 178 μmol·L−1 (36%) at 8 h; urinary urate excretion ($P < 0.05$) was increased, peaking at 2 h (178 μMol·mMol creatinine−1 [250%]). Serum hsCRP ($P < 0.001$) was decreased with peak decrements of 3.19 mg·L−1 (29%). These data show that MC impacts upon the activity of uric acid and lowers hsCRP, previously proposed to be useful in managing pathological conditions such as gouty arthritis; the findings suggest that changes in the observed variables are independent of the dose provided. [Bell P, et al. Montmorency tart cherry (*Prunus cerasus L.*) concentrate lowers uric acid, independent of plasma cyaniding-3-O-glucosiderutinoside. *Journal of Functional Foods.* 2014;11:82-90.]

3. **Randomized double-blind crossover study of the efficacy of a tart cherry juice blend in treatment of osteoarthritis (OA) of the knee.**

   OBJECTIVE: To assess the efficacy of tart cherry juice in treating pain and other features of knee osteoarthritis (OA). METHODS: 58 non-diabetic patients with Kellgren grade 2-3 OA were randomized to begin treatment with cherry juice or placebo. Two 8 oz bottles of tart cherry juice or placebo were consumed daily for 6 weeks with a 1 week washout period before switching treatments (crossover design). Western Ontario McMaster Osteoarthritis Index (WOMAC) scores and walking times were recorded prior to and after each treatment period. Additionally, plasma urate, creatinine and high sensitivity C-reactive protein (hsCRP) were recorded at baseline, after the first treatment period and after the second treatment period. Acetaminophen was allowed as a rescue drug and self reported after each treatment period. Treatment effect was examined with repeated measures analysis of variance (ANOVA) using an intention-to-treat (ITT) analysis. RESULTS: There were five withdrawals during the cherry juice treatment (four adverse events (AEs)) and seven withdrawals during the placebo treatment (three AEs). WOMAC scores decreased significantly ($P < 0.01$) after the cherry juice treatment but not after the placebo treatment ($P = 0.46$); differences between treatments were not significant ($P = 0.16$). hsCRP declined during the cherry juice treatment vs placebo ($P < 0.01$). The decline in hsCRP was associated with WOMAC improvement ($P < 0.01$). Walking time, acetaminophen use, plasma urate and creatinine were unaffected by treatments. CONCLUSIONS: Tart cherry juice provided symptom relief for patients with mild to

moderate knee OA, but this effect was not significantly greater than placebo. Tart cherry juice lowered hsCRP levels and this effect was associated with improved WOMAC scores. [Schumacher HR, Pullman-Mooar S, Gupta SR, Dinnella JE, Kim R, McHugh MP. Randomized double-blind crossover study of the efficacy of a tart cherry juice blend in treatment of osteoarthritis (OA) of the knee. *Osteoarthritis Cartilage.* 2013 Aug;21(8):1035-1041.]

4. **Cherry consumption and decreased risk of recurrent gout attacks.**

OBJECTIVE: To study the relationship between cherry intake and the risk of recurrent gout attacks among individuals with gout. METHODS: We conducted a case-crossover study to examine the associations of a set of putative risk factors with recurrent gout attacks. Individuals with gout were prospectively recruited and followed up online for 1 year. Participants were asked to provide the following information regarding gout attacks: the onset date of the gout attack, symptoms and signs, medications (including antigout medications), and exposure to potential risk factors (including daily intake of cherries and cherry extract) during the 2-day period prior to the gout attack. We assessed the same exposure information over 2-day control periods. We estimated the risk of recurrent gout attacks related to cherry intake using conditional logistic regression. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated. RESULTS: Our study included 633 individuals with gout. Cherry intake over a 2-day period was associated with a 35% lower risk of gout attacks compared with no intake (multivariate OR 0.65 [95% CI 0.50-0.85]). Cherry extract intake showed a similar inverse association (multivariate OR 0.55 [95% CI 0.30-0.98]). The effect of cherry intake persisted across subgroups stratified by sex, obesity status, purine intake, alcohol use, diuretic use, and use of antigout medications. When cherry intake was combined with allopurinol use, the risk of gout attacks was 75% lower than during periods without either exposure (OR 0.25 [95% CI 0.15-0.42]). CONCLUSION: These findings suggest that cherry intake is associated with a lower risk of gout attacks. [Zhang Y, Neogi T, Chen C, Chaisson C, Hunter DJ, Choi HK. Cherry consumption and decreased risk of recurrent gout attacks. *Arthritis Rheum.* 2012 Dec;64(12):4004-4011.]

5. **Pilot Studies of Cherry Juice Concentrate for Gout Flare Prophylaxis.**

The management of gout involves treating pain and inflammation associated with acute flares and lowering the uric acid pool. A challenge associated with the successful management of gout is an increased risk of acute flares after initiation of urate-lowering therapy (ULT). Prophylactic anti-inflammatory therapy is recommended to prevent flares and foster compliance with urate lowering therapy. The aim of our studies was to assess

whether use of cherry juice concentrate is useful for gout flare prophylaxis. We report the results of three studies using cherry juice concentrate for gout prophylaxis. The first is a randomized controlled study comparing the use of cherry juice concentrate versus pomegranate juice concentrate for flare prophylaxis. The second is a retrospective study evaluating flare prophylaxis when cherry juice concentrate was taken over a 4 month period or longer. Lastly, a third study evaluating the effect of cherry juice concentrate compared with pomegranate juice concentrate on secretion of interleukins by human monocytes exposed to monosodium urate (MSU) crystals in vitro. Ingesting cherry juice concentrate reduced the incidence of flares in gout patients regardless of whether or not they were treated with ULT. The number of flares was further reduced by cherry juice ingestion in patients receiving ULT than in patients not on ULT. We did not find a significant change in serum urate levels from baseline following intake of the cherry juice concentrate for 4 months or longer. Thus, cherry juice concentrate was most likely contributing to a reduction in flares via anti-inflammatory actions. We found cherry juice concentrate to inhibit in vitro secretion of IL-1β by up to 60%. In conclusion, our studies suggest that, consumption of cherry juice concentrate for a period of 4 months or longer, reduces acute gout flares, via anti-inflammatory actions such as inhibition of IL-1β secretion. Large long-term randomized controlled trials are needed to further evaluate the usefulness of cherries and cherry juice concentrate for gout flare prophylaxis. [Schlesinger N, Rabinowitz R, Schlesinger M. Pilot Studies of Cherry Juice Concentrate for Gout Flare Prophylaxis. *J Arthritis*. 2012;1:1.]

6. **Cherry juice targets antioxidant potential and pain relief.** Strenuous physical activity increases the risk of musculoskeletal injury and can induce muscle damage resulting in acute inflammation and decreased performance. The human body's natural response to injury results in inflammation-induced pain, swelling, and erythema. Among sports medicine physicians and athletic trainers, the mainstays of urgent treatment of soft tissue injury are rest, ice, compression, and elevation (RICE). In order to reduce pain and inflammation, anti-inflammatory agents such as non-steroidal anti-inflammatory drugs (NSAIDs) act on the multiple inflammatory pathways, which, although often very effective, can have undesirable side effects such as gastric ulceration and, infrequently, myocardial infarction and stroke. For centuries, natural anti-inflammatory compounds have been used to mediate the inflammatory process and often with fewer side effects. Tart cherries appear to possess similar effectiveness in treating the inflammatory reaction seen in both acute and chronic pain syndromes encountered among athletes and non-athletes with chronic inflammatory disease. This article reviews the antioxidant and anti-inflammatory effects of tart cherries on prevention, treatment, and recovery of soft tissue injury and pain. [Kuehl KS. Cherry juice targets antioxidant potential and pain relief. *Med Sport Sci.* 2012;59:86-93.]

a. This study demonstrated that tart cherries are able to modulate the inflammatory pathways without producing negative side effects seen with NSAIDs. Tart cherries are effective in all stages of soft tissue injuries and the resulting acute or chronic pain.

7. **Cherry juice targets antioxidant potential and pain relief.**

   Strenuous physical activity increases the risk of musculoskeletal injury and can induce muscle damage resulting in acute inflammation and decreased performance. The human body's natural response to injury results in inflammation-induced pain, swelling, and erythema. Among sports medicine physicians and athletic trainers, the mainstays of urgent treatment of soft tissue injury are rest, ice, compression, and elevation (RICE). In order to reduce pain and inflammation, anti-inflammatory agents such as non-steroidal anti-inflammatory drugs (NSAIDs) act on the multiple inflammatory pathways, which, although often very effective, can have undesirable side effects such as gastric ulceration and, infrequently, myocardial infarction and stroke. For centuries, natural anti-inflammatory compounds have been used to mediate the inflammatory process and often with fewer side effects. Tart cherries appear to possess similar effectiveness in treating the inflammatory reaction seen in both acute and chronic pain syndromes encountered among athletes and non-athletes with chronic inflammatory disease. This article reviews the antioxidant and anti-inflammatory effects of tart cherries on prevention, treatment, and recovery of soft tissue injury and pain. [Kuehl KS. Cherry juice targets antioxidant potential and pain relief. *Med Sport Sci.* 2012;59:86-93.]

8. **Effect of tart cherry juice (Prunus cerasus) on melatonin levels and enhanced sleep quality.** BACKGROUND: Tart Montmorency cherries have been reported to contain high levels of phytochemicals including melatonin, a molecule critical in regulating the sleep-wake cycle in humans. PURPOSE: The aim of our investigation was to ascertain whether ingestion of a tart cherry juice concentrate would increase the urinary melatonin levels in healthy adults and improve sleep quality. METHODS: In a randomised, double-blind, placebo-controlled, crossover design, 20 volunteers consumed either a placebo or tart cherry juice concentrate for 7 days. Measures of sleep quality recorded by actigraphy and subjective sleep questionnaires were completed. Sequential urine samples over 48 h were collected and urinary 6-sulfatoxymelatonin (major metabolite of melatonin) determined; cosinor analysis was used to determine melatonin circadian rhythm (mesor, acrophase and amplitude). In addition, total urinary melatonin content was determined over the sampled period. Trial differences were determined using a repeated measures ANOVA. RESULTS: Total melatonin content was significantly elevated ($P < 0.05$) in the cherry juice group, whilst no differences were shown between baseline and placebo trials. There were significant increases in time in bed, total sleep time and sleep efficiency total

($P < 0.05$) with cherry juice supplementation. Although there was no difference in timing of the melatonin circardian rhythm, there was a trend to a higher mesor and amplitude. CONCLUSIONS: These data suggest that consumption of a tart cherry juice concentrate provides an increase in exogenous melatonin that is beneficial in improving sleep duration and quality in healthy men and women and might be of benefit in managing disturbed sleep. [Howatson G, Bell PG, Tallent J, *et al.* Effect of tart cherry juice (Prunus cerasus) on melatonin levels and enhanced sleep quality. *European journal of nutrition*. 2012;51(8):909-916.]

   a. In this study, tart cherry juice was shown to have beneficial effects on sleep and melatonin levels. Tart cherry demonstrated significant increases in sleep quality, sleep duration and time spent in bed.

9. **Anti-diabetic effect of cherries in alloxan induced diabetic rats.**

   Diabetes mellitus (DM) is a metabolic disorder in the endocrine system resulting from a defect in insulin secretion, insulin action or both of them. Adverse side effects of chemical drugs for treatment of diabetes persuaded the using of medical plants. Cherry as a traditionally used plant for treatment of diabetes, is packed with powerful plant pigments called anthocyanins. They give cherries their dark red color and are one of the richest antioxidant sources which lower the blood sugar and bear other beneficial health effects. The purpose of this study is to evaluate the effect of ethanolic extract of cherry fruit on alloxan induced diabetic rats. In this study 36 Male Wistar rats, body weight of 150-200gr were divided into 6 groups. Diabetes was induced by intra peritoneal injection of 120 mg/kg Alloxan. The duration of the cherries treatment was 30 days in which single dose of extracts (200mg/kg) were oral administered to diabetic rats. Blood glucose levels were estimated with glucometer before treatment, 2h and 1- 4 weeks after administration of extracts. Treatment with extracts of the cherries resulted in a significant reduction in blood glucose and urinary microalbumin and an increase in the creatinine secretion level in urea. Extract of this plant is useful in controlling the blood glucose level. Cherries appear to aid in diabetes control and diminution of the complications of the disease. Some relevant patents are also outlined in this article. [Lachin T, Reza H. Anti-diabetic effect of cherries in alloxan induced diabetic rats. *Recent Pat Endocr Metab Immune Drug Discov.* 2012 Jan;6(1):67-72.]

10. **The effect of 100% tart cherry juice on serum uric acid levels, biomarkers of inflammation and cardiovascular disease risk factors.** Gout is a common inflammatory arthritis and is a risk factor for CVD and mortality. Obesity, a co-morbidity, is strongly correlated with hyperuricemia, a precipitating factor. Tart cherry juice (TCJ) has been used by some for gout for decades based largely on anecdotal evidence. In this randomized, placebo-controlled crossover study, we tested in

overweight and obese participants the effect of TCJ on serum uric acid (sUA), biomarkers of inflammation and risk factors for CVD. Ten participants (38.1 ± 12.5 yr; BMI 32.2 ± 4.6; 5 obese, 5 overweight) consumed 8 oz/d of either 100% TCJ or placebo beverage, for 4 weeks each with a 2 week intervening washout period. Baseline sUA levels were 289.3±23.1 uM (4.9±0.4 mg/dL) and 278.4±25.0 uM (4.7±0.4 mg/dL) for placebo and TCJ groups, respectively, and r=0.37 when sUA was compared with BMI. Although normouricemic, 70% (7/10) of participants displayed reduced sUA, 20% (2/10) displayed slight increases and 10% (1/10) remained unchanged after TCJ consumption. The erythrocyte sedimentation rate (ESR), an indicator of chronic inflammation, was significantly ($p<0.05$) lower with TCJ treatment than with the placebo control. We also observed marked reductions in TNF-alpha and monocyte chemotactic protein (MCP-1), both inflammatory markers. TCJ also significantly reduced mean serum triglycerides from 168 to 139 mg/dL in those that started the trial with TCJ. We also noted a significant reduction in VLDL and, as expected, the TG/HDL risk ratio. Collectively, these pilot data suggest that 100% TCJ may reduce sUA levels, biomarkers of inflammation and risk factors for CVD. [Martin KR, Bopp J, Burrell L, Hook G. The effect of 100% tart cherry juice on serum uric acid levels, biomarkers of inflammation and cardiovascular disease risk factors. *The FASEB Journal*. 2011;25:339.2]

a. Tart cherries have been used to control the symptoms of gout for several decades but little scientific evidence has been available on the actual efficacy. This study demonstrated that tart cherries can help reduce serum uric acid levels, decrease serum triglycerides (and TG/HDL risk ratio), decrease erythrocyte sedimentation rate (higher rates present in chronic inflammation) and reductions in the inflammatory markers TNF-alpha and monocyte chemotactic protein.

11. **Influence of tart cherry juice on indices of recovery following marathon running.**

This investigation determined the efficacy of a tart cherry juice in aiding recovery and reducing muscle damage, inflammation and oxidative stress. Twenty recreational Marathon runners assigned to either consumed cherry juice or placebo for 5 days before, the day of and for 48 h following a Marathon run. Markers of muscle damage (creatine kinase, lactate dehydrogenase, muscle soreness and isometric strength), inflammation [interleukin-6 (IL-6), C-reactive protein (CRP) and uric acid], total antioxidant status (TAS) and oxidative stress [thiobarbituric acid reactive species (TBARS) and protein carbonyls] were examined before and following the race. Isometric strength recovered significantly faster ($P=0.024$) in the cherry juice group. No other damage indices were significantly different. Inflammation was reduced in the cherry juice group (IL-6, $P<0.001$; CRP, $P<0.01$; uric acid, $P<0.05$). TAS was ~10% greater in the cherry juice than the placebo group for all post-supplementation measures ($P<0.05$). Protein carbonyls was not different; however, TBARS was lower in the cherry juice than the placebo at 48 h ($P<0.05$). The cherry juice appears to provide a viable means to aid recovery following

strenuous exercise by increasing total antioxidative capacity, reducing inflammation, lipid peroxidation and so aiding in the recovery of muscle function. [Howatson G, McHugh MP, Hill JA, Brouner J, Jewell AP, van Someren KA, Shave RE, Howatson SA. Influence of tart cherry juice on indices of recovery following marathon running. *Scand J Med Sci Sports*. 2010 Dec;20(6):843-852.]

12. **Effects of a tart cherry juice beverage on the sleep of older adults with insomnia: a pilot study.**

    This study ascertained whether a proprietary tart cherry juice blend (CherryPharm, Inc., Geneva, NY, USA) associated with anecdotal reports of sleep enhancement improves subjective reports of insomnia compared to a placebo beverage. The pilot study used a randomized, double-blind, crossover design where each participant received both treatment and placebo for 2 weeks with an intervening 2-week washout period. Sleep continuity (sleep onset, wake after sleep onset, total sleep time, and sleep efficiency) was assessed by 2-week mean values from daily sleep diaries and disease severity by the Insomnia Severity Index in a cohort of 15 older adults with chronic insomnia who were otherwise healthy. The tart cherry juice beverage was associated with statistically significant pre- to post-treatment improvements on all sleep variables. When compared to placebo, the study beverage produced significant reductions in insomnia severity (minutes awake after sleep onset); no such improvements were observed for sleep latency, total sleep time, or sleep efficiency compared to placebo. Effect sizes were moderate and in some cases negligible. The results of this pilot study suggest that CherryPharm, a tart cherry juice blend, has modest beneficial effects on sleep in older adults with insomnia with effect sizes equal to or exceeding those observed in studies of valerian and in some, but not all, studies of melatonin, the two most studied natural products for insomnia. These effects, however, were considerably less than those for evidence-based treatments of insomnia: hypnotic agents and cognitive-behavioral therapies for insomnia. [Pigeon WR, Carr M, Gorman C, Perlis ML. Effects of a tart cherry juice beverage on the sleep of older adults with insomnia: a pilot study. *J Med Food.* 2010 Jun;13(3):579-583.]

13. **Efficacy of tart cherry juice in reducing muscle pain during running: a randomized controlled trial.**

    BACKGROUND: Long distance running causes acute muscle damage resulting in inflammation and decreased force production. Endurance athletes use NSAIDs during competition to prevent or reduce pain, which carries the risk of adverse effects. Tart cherries, rich in antioxidant and anti-inflammatory properties, may have a protective effect to reduce muscle damage and pain during strenuous exercise. This study aimed to assess the effects of tart cherry juice as compared to a placebo cherry drink on pain among runners in a long distance relay race. METHODS: The design was a randomized,

double blind, placebo controlled trial. Fifty-four healthy runners (36 male, 18 female; 35.8 +/- 9.6 yrs) ran an average of 26.3 +/- 2.5 km over a 24 hour period. Participants ingested 355 mL bottles of tart cherry juice or placebo cherry drink twice daily for 7 days prior to the event and on the day of the race. Participants assessed level of pain on a standard 100 mm Visual Analog Scale (VAS) at baseline, before the race, and after the race. RESULTS: While both groups reported increased pain after the race, the cherry juice group reported a significantly smaller increase in pain (12 +/- 18 mm) compared to the placebo group (37 +/- 20 mm) ($p < .001$). Participants in the cherry juice group were more willing to use the drink in the future ($p < 0.001$) and reported higher satisfaction with the pain reduction they attributed to the drink ($p < 0.001$). CONCLUSIONS: Ingesting tart cherry juice for 7 days prior to and during a strenuous running event can minimize post-run muscle pain. [Kuehl KS, Perrier ET, Elliot DL, Chesnutt JC. Efficacy of tart cherry juice in reducing muscle pain during running: a randomized controlled trial. *J Int Soc Sports Nutri.* 2010 May 7;7:17.]

14. **Relation of total antiradical activity and total polyphenol content of sweet cherries (*Prunus avium* L.) and tart cherries (*Prunus cerasus* L.)** In present study the quantification of total phenolics content (TPC), total antioxidant activity (TAA) and their relation in sweet and tart cherries were studied. Aqueous and pure polar solvents were used to compare the yield of present phenolic compounds in prepared extracts. The solubility of phenolics was the most effective in sweet cherry extracts with using of 50 % methanol and in tart cherry extracts with using of 50 % acetone. The yield of TPC of both tested cherry fruit extracts was higher with pure methanol in comparison to pure acetone. Substantial TPC assessed with Folin-Ciocealteu assay in tart cherry extracts were in range from 70.6±8.46 mg to 241.4±7.26 mg GAE/100 g FW. Extracts from lyophilised tart cherries (methanolic and water-acetone mixtures) contain in average 2-times higher amount of polyphenols than ethanol extracts. The DPPH antiradical efficiency values of the both tested fruit extracts were higher in extracts of tart cherries (from 5.4 to 9.9 % of inhibition of DPPH radical) when compared to those of sweet cherries (from 2.4 to 3.5 % of inhibition of DPPH radical). Total antioxidant activity (TAA) of sweet cherry extracts (using 70 % ethanol and with 70 % methanol) and of tart cherry extracts (with 50% methanol) depended on phenolics content. [Melichacova S, Timoracka M, Bystricka J, Vollmannova A, Cery J. Relation of total antiradical activity and total polyphenol content of sweet cherries (*Prunus avium* L.) and tart cherries (*Prunus cerasus* L.) *Acta agriculturae Slovenica*. 2010 Mar;95(1):21-28.]
    a. This study demonstrated that lyophilized tart cherry extracts were superior in polyphenol content than ethanol extracts. The antiradical value for tart cherries was also higher than sweet cherries.

15. **Tart cherry juice decreases oxidative stress in healthy older men and women.**

    Compared with young adults, older adults have significantly impaired capacities to resist oxidative damage when faced with acute stress such as ischemia/reperfusion. This impairment likely contributes to increased morbidity and mortality in older adults in response to acute trauma, infections, and the susceptibility to diseases such as atherosclerosis, cancer, diabetes, and Alzheimer's disease. Consumption of foods high in polyphenols, particularly anthocyanins, have been associated with improved health, but the mechanisms contributing to these salutary effects remain to be fully established. This study tested the hypothesis that consumption of tart cherry juice containing high levels of anthocyanins improves the capacity of older adults to resist oxidative damage during acute oxidative stress. In a double-blind, placebo-controlled, crossover design, 12 volunteers [6 men and 6 women; age 69 +/- 4 y (61-75 y)] consumed in random order either tart cherry juice or placebo (240 mL twice daily for 14 d) separated by a 4-wk washout period. The capacity to resist oxidative damage was measured as the changes in plasma F(2)-isoprostane levels in response to forearm ischemia-reperfusion (I/R) before and after each treatment. The tart cherry juice intervention reduced the I/R-induced F(2)-isoprostane response ($P < 0.05$), whereas placebo had no significant effect. The tart cherry juice intervention also reduced basal urinary excretion of oxidized nucleic acids (8-hydroxy-2'-deoxyguanosine, 8-hydroxyguanosine) ($P < 0.05$) but not urinary excretion of isoprostanes. These data suggest that consumption of tart cherry juice improves antioxidant defenses in vivo in older adults as shown by an increased capacity to constrain an oxidative challenge and reduced oxidative damage to nucleic acids. [Traustadóttir T1, Davies SS, Stock AA, Su Y, Heward CB, Roberts LJ 2nd, Harman SM. Tart cherry juice decreases oxidative stress in healthy older men and women. *J Nutr*. 2009 Oct;139(10):1896-1900.]

16. **Chemical profile and antioxidant capacities of tart cherry products.** The levels of anthocyanins and other flavonoids, as well as melatonin, in various tart cherry products (frozen and dried cherries, powders from individually quick frozen (IQF) cherry and juice concentrate) from two tart cherry cultivars, 'Montmorency' and 'Balaton' were analysed comparatively by HPLC and electrospray mass spectrometry (EMS). Our results show that the major anthocyanin compound in these two tart cherry cultivars is cyanidin 3-glucosylrutinoside, followed by cyanidin 3-rutinoside, cyanydin sophoroside, and peonidin 3-glucoside. Studies on antioxidant activities (total antioxidant status assay) of crude extracts of ten tart cherry products show that these products preserve their antioxidant capacities after processing and storage. We have also compared the antioxidant activities of several single constituents that are present in tart cherry. When TEAC (trolox equivalent antioxidant capacity) values were evaluated conceptually against the cherry phytochemical profile, cyanidin and its derivatives were found to be the significant contributors to the antioxidant systems of tart cherries. It was shown that

standard compounds with common aglycon moieties show similar antioxidant activities. [Kirakosyan A, Seymour EM, Urcuyo Llanes DE, Kaufman PB, Bolling SF. Chemical profile and antioxidant capacities of tart cherry products. *Food Chemistry*. 2009 July 1;115(1):20-25.]

a. In this study, the main anthocyanins in tart cherry were identified as cyanidin 3-glucosylrutinoside, cyaniding 3-rutinoside, cyanydin sophoroside and peonidin 3-glucoside. Various samples were taken of frozen cherries, dried cherries, quick frozen cherries and cherry juice concentrate. All of the tart cherry products still had high antioxidant levels despite processing and storage.

17. **Antioxidant properties of sour cherries (Prunus cerasus L.): role of colorless phytochemicals from the methanolic extract of ripe fruits.**

Many edible plant metabolites are known to be useful as cellular antioxidants. In the search for antioxidative chemicals from native fruits of the Campania region of Italy, Prunus cerasus L., an acidic cherry widely used for culinary purposes, has been studied. Fruit crude extracts (MeOH, EtOAc, and hexane) were submitted to an antioxidative screening using specific assay media characterized from the presence of highly reactive radical species (DPPH*, ABTS*+, O2*-, NO) or lipoperoxidation markers. The reducing power of the samples was also determined. It was observed that the most polar extracts in MeOH and EtOAc were able to exercise a massive and dose-increasing antioxidative capacity. The peculiar efficacy of the same extracts was revealed by investigating their protein and deoxyribose oxidation capacity. A preliminary analysis of total phenol, flavonoid, and anthocyanin contents together with biological screening data put the basis on P. cerasus fruit phytochemical investigation of methanolic extract. Twenty secondary metabolites were isolated and characterized by spectroscopic (especially 1D and 2D NMR) and spectrometric techniques. 1-(4-Hydroxyphenyl)-1,2-ethanediol-1,2-bis-1-O-beta-D-glucopyranoside (3), (4-hydroxy-3-methoxyphenyl)methanol-1-O-beta-D-gentiobioside (4), epicatechin-3-malate (14), and epicatechin-3-(1"-methyl)malate (15) were isolated for the first time. All of the compounds were evaluated for their radical scavenging activity on DPPH*, O2*-, and NO. Flavonoids and quinic acid derivatives were found to be the more antioxidative substances. {Piccolella S, Fiorentino A, Pacifico S, D'Abrosca B, Uzzo P, Monaco P. Antioxidant properties of sour cherries (Prunus cerasus L.): role of colorless phytochemicals from the methanolic extract of ripe fruits. *J Agric Food Chem.* 2008 Mar 26;56(6):1928-1935.]

18. **Efficacy of a tart cherry juice blend in preventing the symptoms of muscle damage.**

Background: Numerous antioxidant and anti-inflammatory agents have been identified in tart cherries. Objective: To test the efficacy of a tart cherry juice blend in preventing the symptoms of exercise induced muscle damage. Methods: This was a randomised, placebo

controlled, crossover design. Fourteen male college students drank 12 fl oz of a cherry juice blend or a placebo twice a day for eight consecutive days. A bout of eccentric elbow flexion contractions (2620 maximum contractions) was performed on the fourth day of supplementation. Isometric elbow flexion strength, pain, muscle tenderness, and relaxed elbow angle were recorded before and for four days after the eccentric exercise. The protocol was repeated two weeks later with subjects who took the placebo initially, now taking the cherry juice (and vice versa). The opposite arm performed the eccentric exercise for the second bout to avoid the repeated bout protective effect. Results: Strength loss and pain were significantly less in the cherry juice trial versus placebo (time by treatment: strength p,0.0001, pain p = 0.017). Relaxed elbow angle (time by treatment p = 0.85) and muscle tenderness (time by treatment p = 0.81) were not different between trials. Conclusions: These data show efficacy for this cherry juice in decreasing some of the symptoms of exercise induced muscle damage. Most notably, strength loss averaged over the four days after eccentric exercise was 22% with the placebo but only 4% with the cherry juice. [Connolly DAJ, McHugh MP, Padilla-Zakour OI. Efficacy of a tart cherry juice blend in preventing the symptoms of muscle damage. *Br J Sports Med.*2006;40:679-683.]

19. **Tart cherry anthocyanins inhibit tumor development in Apc(Min) mice and reduce proliferation of human colon cancer cells.** Anthocyanins, which are bioactive phytochemicals, are widely distributed in plants and especially enriched in tart cherries. Based on previous observations that tart cherry anthocyanins and their respective aglycone, cyanidin, can inhibit cyclooxygenase enzymes, we conducted experiments to test the potential of anthocyanins to inhibit intestinal tumor development in Apc(Min) mice and growth of human colon cancer cell lines. Mice consuming the cherry diet, anthocyanins, or cyanidin had significantly fewer and smaller cecal adenomas than mice consuming the control diet or sulindac. Colonic tumor numbers and volume were not significantly influenced by treatment. Anthocyanins and cyanidin also reduced cell growth of human colon cancer cell lines HT 29 and HCT 116. The IC(50) of anthocyanins and cyanidin was 780 and 63 microM for HT 29 cells, respectively and 285 and 85 microM for HCT 116 cells, respectively. These results suggest that tart cherry anthocyanins and cyanidin may reduce the risk of colon cancer. [Kang SY, Seeram NP, Nair MG, Bourguin LD. Tart cherry anthocyanins inhibit tumor development in Apc(Min) mice and reduce proliferation of human colon cancer cells. *Cancer Lett.* 2003 May 8;194(1):13-19.]
    a. This study used mice and human colon cancer cells to test the anthocyanins in tart cherry and their effects on tumor proliferation. Cyanidin, is one of the main anthocyanins in tart cherry and has been shown to mediate the COX pathways by inhibiting corresponding enzymes. Mice treated with cherry juice showed a significant reduction in tumor size and number. Reductions in proliferation were also seen in the human colon cancer cells.