

Anthocyanin-rich blackcurrant supplementation as a nutraceutical ergogenic aid for exercise performance and recovery: A narrative review

Mark E.T. Willems^{1,*}, Sam D. Blacker¹, Stefano Montanari², and Matthew D. Cook³

¹ University of Chichester, Institute of Applied Sciences, College Lane, Chichester, PO19 6PE, United Kingdom ² University of Northampton, Faculty of Arts, Science and Technology, Waterside Campus, University Drive, Northampton NN1 5PH, United Kingdom

³ University of Worcester, School of Sport & Exercise Science, Henwick Grove, Worcester WR2 6AJ, United Kingdom

* Correspondence: Mark Willems and m.willems@chi.ac.uk

Abbreviations: IL-6, interleukin-6; LIST, Loughborough intermittent shuttle test; Nrf2-Keap1, Kelch-like ECH-associated protein 1-nuclear factor erythroid 2-related factor 2; NZBC, New Zealand blackcurrant; TNF α , tumor necrosis factor alpha $\dot{V}O_{2max}$, maximum oxygen uptake.

Abstract

Athletes and physically active individuals consume sports nutrition supplements to enhance 1 competitive sport performance and exercise recovery. Polyphenols have emerged as a promising 2 area of research with application for sport and exercise nutrition due to affecting physiological 3 mechanisms for exercise performance and recovery. The anthocyanin is a polyphenol that can be 4 abundantly present in dark-colored fruits, berries and vegetables. Anthocyanins and anthocyanin-5 induced metabolites will provide antioxidant and anti-inflammatory effects. The focus in this 6 narrative review is on the observations with intake of anthocyanin-rich blackcurrant supplements 7 on *whole-body* exercise performance and exercise recovery. This review included a total number 8 9 of 17 studies with a randomized placebo-controlled cross-over design (10 studies on performance

and 8 on recovery effects) and 1 with a randomized placebo-controlled parallel group design 10 (recovery effects). Among the performance studies, 6 studies (60%) reported positive effects, 3 11 studies (30%) reported no significant effects and 1 study (10%) reported a mixed outcome. Among 12 the recovery studies, 7 studies (78%) reported positive effects, 1 study (11%) reported no 13 significant effects and 1 study (11%) reported a negative effect. Studies with intake of supplements 14 made from New Zealand blackcurrants (dose: 1.8 to 3.2 mg·kg⁻¹ and 105 to 315 mg of 15 anthocyanins, acute to 7-day intake) have provided meaningful (but not always consistent) effects 16 on continuous and intermittent exercise performance tasks (i.e. rowing, cycling and running) and 17 markers for exercise recovery. A mechanistic understanding for the beneficial exercise effects of 18 anthocyanins for athletes and physically active individuals is still limited. Future work requires a 19 better understanding of the specific types of anthocyanins and anthocyanin-induced metabolites 20 and their effects on altering cell function that can enhance exercise performance and recovery. 21

Keywords: blackcurrant; anthocyanins; sports nutrition; exercise performance; exercise recovery

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23 Summary

Studies with New Zealand blackcurrant extract have provided meaningful effects for exercise with
 different duration and intensities and exercise recovery.

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27 Introduction

Tissues of higher plants contain the flavonoid compound anthocyanins (1). Anthocyanins are anthocyanidins aglycones with incorporation of one or more carbohydrates. The diversity in chemical structures of the anthocyanidins aglycones allowed the identification of hundreds of

anthocyanins (2). In higher plants, the anthocyanins contribute to the color variety of berries and 31 fruits (2), and offer protection against environmental stresses (3). For humans, the presence of the 32 anthocyanins in the leaves, the seeds, the berries and the fruits make them readily available for 33 consumption. Humans consume primarily the anthocyanidins cyanidin, delphinidin, malvidin, 34 pelargonidin, peonidin and petunidin (4). In Europe, for example, intake of total anthocyanidins 35 for men and women were 64.88 (SE 1.86) and 44.08 (SE 2.45) mg·day⁻¹ (4). The evidence for the 36 health-related effects of anthocyanin intake is growing, where benefits have been shown to include 37 a reduced risk for cardiovascular disease and type 2 diabetes [for reviews see e.g. (5, 6, 7)]. 38 However, no dietary guidelines exist yet for the amount of intake of anthocyanins as part of a 39 healthy diet. In fact, among the thousands of flavonoids, an intake recommendation of 400-600 40 $mg \cdot day^{-1}$ only exists for flavan-3-ols, due to reported cardio-metabolic health implications (8). 41 Existing and future research on the effects of the intake of anthocyanins in humans [with focus on 42 beneficial health effects [e.g. (9)] will eventually provide the evidence to support intake 43 44 recommendations for anthocyanins.

For the blackcurrant, of the 15 anthocyanins present, cyanidin-3-O-glucoside, cyanidin-3-45 O-rutinoside, delphinidin-3-O-glucoside and delphinidin-3-O-rutinoside make up more than 97% 46 47 of the total anthocyanin content (10). However, different fruits and berries have their own unique anthocyanin composition (11). For anthocyanins, the low plasma bioavailability [e.g. (12)] 48 49 strongly indicates that the numerous anthocyanin-induced metabolites are causally linked with 50 providing the health effects (13). The health-related effects of anthocyanin intake are thought to be due to providing antioxidant, anti-inflammatory and immunomodulatory effects (14, 15). In 51 support, the intake of anthocyanins (~35 mg of chokeberry anthocyanins daily for 4 weeks) can 52 53 enhance the endogenous antioxidant system (16). However, note that the antioxidant capacity of

the individual anthocyanins contributes to the total antioxidant capacity relative to the weight of 54 the berry (11). The potential of plant compounds to enhance the antioxidant capacity of human 55 tissues as well as inhibition of the exercise-induced inflammatory response suggest the ergogenic 56 potential for applications in sport and exercise. Such application has been shown, for example, for 57 some of the flavan-3-ols in green tea extract with the ability to affect fat metabolism [for a review 58 59 see (17)]. The ability of skeletal muscle tissue to enhance cellular antioxidant defense may limit exercise-induced fatigue (18), and enhance exercise performance (19). However, it was only in the 60 study by Matsumoto et al (12) in which first observations were provided of fatigue-lowering 61 responses in humans in a non-exercise study after intake of blackcurrant anthocyanins. Following 62 an acute intake of 17 mg·kg body weight⁻¹ of blackcurrant anthocyanins, there was an increase in 63 left forearm blood flow using near infrared spectroscopy during typing activity and changes in 64 maximum total hemoglobin in the trapezius after maximal voluntary contractions after the typing 65 (12). In addition, an intake for 2 weeks of 7.7 mg·kg body weight⁻¹ tended to lower the muscle 66 activity (i.e. lower EMG root mean square) during intermittent typing work, suggestive of a 67 reduction in muscle fatigue (12). The observations by Matsumoto et al (12) seemed not to have 68 been recognized for some years and only in the last decade, many studies have addressed the 69 70 efficacy of blackcurrant anthocyanin intake on the physiological, cardiovascular and metabolic responses during exercise as well as the potential to affect exercise recovery. 71

In this narrative review, the focus will be on the studies that provided experimental evidence for the efficacy of anthocyanin-rich blackcurrant supplements (not whole food) to enhance *whole-body* exercise performance and recovery. Studies on effects in muscle groups will not be considered [e.g. (20, 21)]. Studies with combined intake of supplements including anthocyanin-rich blackcurrant and conference proceedings will not be considered. For the purpose

of this review, exercise performance is considered a task completion that may provide competitive 77 advantage, e.g. a faster running sprint time, cycling time-to-exhaustion or cycling time-trial. 78 Recovery is considered the observable physiological, metabolic and functional phenomena after 79 completion of an exercise task, so not solely an exercise performance task during the recovery 80 phase. Animal and *in-vitro* studies will only be considered for the purpose of our understanding of 81 82 the potential causal mechanism by the intake of anthocyanins for the exercise performance and exercise recovery effects in humans. We will consider the strengths and the limitations of the 83 experimental studies in humans and highlight the substantial gaps that still exist in our 84 understanding of the optimal dosing strategy and the mechanisms for whole-body exercise 85 performance and recovery effects by intake of anthocyanin-rich blackcurrant. As the first studies 86 on the effects of anthocyanin intake examined post-exercise effects, the review will cover first the 87 studies on recovery and subsequently the studies on the exercise performance effects. Observations 88 from studies with clinical cohorts will only be covered when they allow insight into the mechanism 89 90 for the exercise and recovery effects. It is not within the scope of this narrative review to provide detailed commentary on the metabolism of anthocyanin-induced metabolites and whole-body 91 physiological mechanisms underpinning the performance enhancing and exercise recovery effects. 92 93 With the information available, the literature has provided meaningful observations with primarily intake of anthocyanin-rich supplementation made from New Zealand grown blackcurrant. New 94 95 Zealand grown blackcurrant has higher levels of anthocyanins compared to non-New Zealand 96 grown blackcurrant (22). The available evidence obtained with studies on the effects of anthocyanin-rich blackcurrant will justify future work on the intake of a variety of anthocyanin-97 rich natural supplements to advance the field of sport and exercise nutrition (23, 24). 98

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100 Early evidence on the effect of intake of anthocyanins on exercise recovery in humans

The required time for the functional and physiological recovery from exercise-induced effects, e.g. 101 structural muscle damage, muscle soreness, muscle dysfunction, oxidative stress and 102 inflammation, can take days to weeks. The occurrence of these exercise-induced effects will 103 depend largely on the intensity and duration of the exercise, particularly when the exercise was of 104 105 an unaccustomed nature (25, 26). In a physical exercise training program, the exercise-induced oxidative stress and the inflammatory response post-exercise contribute to the physiological 106 adaptation processes [e.g. (27) and for a review see (28)]. In addition, adaptations from physical 107 training can include an enhanced endogenous antioxidant system (29). Therefore, regular intake 108 of polyphenols (including anthocyanins) in the diet is a non-exercise nutritional means for 109 enhancing the endogenous antioxidant system (30). An enhanced endogenous antioxidant system 110 is beneficial for coping with exercise-induced oxidative stress. One of the first studies to examine 111 the effects of chronic intake of anthocyanins on exercise-induced oxidative stress was with 112 chokeberry juice (16). Chokeberry juice is composed of up to 98.7% of cyanidin glycosides and 113 consist of cyanidin-3-O-galactoside, cyanidin-3-O-glucoside, cyanidin-3-O-arabinoside and 114 cyanidin-3-O-xyloside (31). Pilaczynska-Szczesniak et al (16) dosed 19 male elite rowers 115 116 (members of the Polish rowing team) with chokeberry (Aronia Melanocarpa L.) juice (3 x 50 mL per day) for 4 weeks. The chokeberry juice in the study contained 23 mg of anthocyanins per 100 117 118 mL. Four weeks intake of the chokeberry juice reduced levels of thiobarbituric acid reactive 119 substances, a measure of lipid peroxidation, 1 minute and 24 hours post-exercise following an incremental rowing protocol, providing support for enhancement of the antioxidant defense system 120 and therefore enhanced recovery (16). The enhanced endogenous antioxidant system by 121 122 polyphenol intake or exercise is due to the Kelch-like ECH-associated protein 1-nuclear

factor erythroid 2-related factor 2 (Nrf2-Keap1) system (32, 33). Evidence for the activation of the 123 Nrf2-Keap1 system by chokeberry, however, remains absent from the literature, but is present for 124 example for raspberry (primarily containing cyandin-3-O-glucoside) in human HepG2 cells (34). 125 It is surprising that considering the dark-blue colored chokeberry to be a very rich source of 126 polyphenols with anthocyanins (35), no studies with chokeberry intake in humans have provided 127 128 exercise performance-enhancing effects (36). It is possible that some anthocyanin-rich berries may provide beneficial effects for exercise recovery without a performance-enhancing effect. One of 129 the key messages of the present review is, therefore, that future work needs to address the 130 specificity of the anthocyanins or combination of anthocyanins that can be effective for both 131 exercise recovery and performance or those single or combination of anthocyanins that only seem 132 to have either recovery or performance effects. Studies with such aims have not been considered 133 or started in humans. In the C57BL/6 mouse model of polygenic obesity, for example, diets that 134 were supplemented with different berries provided different metabolic effects, e.g. differences in 135 both mitochondrial respiration and the dissipation of the mitochondrial proton gradient in adipose 136 tissue (37), and fasting glucose (38). Studies in humans on the effects of single anthocyanins on 137 physiological, metabolic, cardiovascular and exercise performance responses are absent. In 138 139 addition, many reviews on the effects of polyphenols in humans have not clearly recognized the importance of the potential differences in effects by intake of different combinations of 140 141 anthocyanins [e.g. (39, 40)]. In the following section, we will consider the evidence for the intake 142 of anthocyanin-rich blackcurrant for exercise recovery.

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144 Anthocyanin-rich Blackcurrant and Exercise Recovery

The recovery from the occurrence of exercise-induced muscle fatigue and potential muscle injury 145 of habitual exercise training sessions will require normally not more than a few days. Athletes in 146 preparation for competitive endurance events (e.g. marathon running) will have adopted tapering 147 strategies to optimize recovery from the progression in training volume. However, during physical 148 preparatory training or busy competitive schedules, an enhanced exercise recovery would benefit 149 150 the athletes for undertaking subsequent exercise training sessions and competition. Studies with bioactive nutritional compounds that have antioxidant and anti-inflammatory properties provided 151 experimental evidence to accelerate the recovery from exercise-induced muscle fatigue and muscle 152 injury. Early studies focused on effects of antioxidant delivering ability of vitamins E and C [for a 153 review see Evans et al (41)]. More recently, strong and abundant experimental support has emerged 154 for the effectiveness of anthocyanin-containing tart cherry supplementation on exercise recovery 155 providing anti-inflammatory effects. Tart cherry contains primarily the anthocyanins cyanidin-3-156 glucosylrutinoside and cyanidin-3-rutinoside, i.e. ~ 42% and 35% of total anthocyanins [e.g. (42)]. 157 In a systematic review and meta-analysis on tart cherry supplementation (43), small beneficial 158 effects were reported after strenuous exercise for muscle soreness (effect size: -0.44), sprint time 159 (effect size: -0.32), C-reactive protein (effect size: -0.46) and interleukin-6 (effect size: -0.35), 160 161 moderate effects for muscle strength (effect size: -0.78) and muscular power (effect size: -0.53) and large effects for jump height (effect size: -0.82). 162

In studies on the effects of intake of blackcurrant on exercise recovery, meaningful effects have been reported for the recovery from different exercise modalities that had variation for exercise duration and intensity (**Table 1**). As far as we know, the first study to examine the exercise recovery effects with intake of blackcurrant was done by the New Zealand Institute for Plant and Food Research Ltd (44). Lyall et al (44) examined the exercise recovery effects by the intake of

120 mg of blackcurrant anthocyanins before and after 30 min of indoor rowing at 80% $\dot{V}O_{2max}$ in 168 a recreationally active cohort (5 females, 5 males) with a broad age range (37 to 63 yrs, mean±SD: 169 48±3 yrs). Blackcurrant lowered protein carbonyl levels 30-min after exercise that were normally 170 elevated by ~40% by the indoor rowing at 80% $\dot{V}O_{2max}$ and indicative of oxidative stress. The 171 effect was of short duration as blackcurrant had no effect on plasma protein carbonyl levels at 1, 172 173 2 and 24 hr during recovery, but observations on IL-6, TNF α and creatine kinase were indicative of lower inflammation and reduced muscle damage. In the study by Lyall et al (44), the dosing 174strategy was not justified. However, based on the dosing information, intake of 120 mg of 175 blackcurrant extract was effective within 30 min, suggesting not only fast bioavailability of 176 anthocyanins and anthocyanin-induced metabolites [e.g. Costello et al (45) for presence over 6 hr 177 and Czank et al (46) for 48 hr] but maybe also rapid physiological antioxidative stress effects. 178 However, the potential effects of the many metabolites, e.g. protocatechuic acid, vanillic acid and 179 gallic acid (45, 46), on the alteration of *in-vivo* cell function are not known. In addition, Czank et 180 al (46) identified 24 metabolites and observed substantial interindividual differences in recovery 181 rate (15.1% to 99.3%) of a total of 25 ¹³C-labeled compounds that consisted of ¹³C₅-cyanidin-3-182 glucoside and the 24 labeled metabolites. The distribution, metabolism and excretion of the 183 184 anthocyanin-induced metabolites is beyond the focus of this narrative review. As far as we know, no information is available on the plasma availability of anthocyanins and parent metabolites by 185 186 different intake strategies of blackcurrant over a long period of time [see Kalt et al (47) for a study 187 with intake of blueberry juice]. In addition, more understanding is needed for the role of the gut microbiome on the plasma availability of anthocyanins and parent metabolites [for reviews see 188 (48, 49)]. In a subsequent study by the New Zealand Institute for Plant and Food Research Ltd, 30 189 190 min of indoor rowing at 70% $\dot{V}O_{2max}$ in healthy individuals reduced plasma protein carbonyl levels

not at 0 hr but 2 hr during recovery (compared to 0 hr) with 0.8 and 1.6 mg \cdot kg⁻¹ blackcurrant (50). 191 Thus, studies show inconsistent observations on plasma protein carbonyl levels as a marker of 192 oxidative stress after exercise with intake of blackcurrant (44, 50). Another marker of oxidative 193 stress, i.e. the lipid oxidation product malondialdehyde was reduced 2 hr after 30 min of indoor 194 rowing at 70% $\dot{V}O_{2max}$ in healthy individuals with similar efficacy with acute (1 hr before) and 5 195 weeks daily intake of 3.2 mg·kg⁻¹ (~ 240 mg) of blackcurrant anthocyanins (51). In addition to the 196 evidence of enhanced recovery with markers of oxidative stress, Lyall et al (44) also observed 197 blunting of the rise in creatine kinase levels 24 hr after exercise, an indication that blackcurrant 198 199 affects the symptoms of exercise-induced muscle damage. This was observed in a study by Hunt et al (52) in which 12 days of daily intake of 105 mg of blackcurrant anthocyanins in extract form 200 (8 days prior and 4 days following exercise) reduced muscle soreness and creatine kinase levels 201 during the recovery from 4x15 maximal concentric and eccentric contractions of the biceps brachii 202 muscle. However, no enhanced functional recovery was shown in Hunt et al (52). In contract, 203 muscle soreness and countermovement jump variables were not affected by intake of blackcurrant 204 anthocyanins (7-days prior and 2 days after with 210 mg anthocyanins per day) following a half-205 marathon run in recreationally runners (n=20, 8 females) (53). In addition, no effect on muscle 206 207 soreness was reported after eccentric squatting in healthy participants (n=24, 6 females) with intake of blackcurrant nectar (2x per day for 8 days with ~ 370 mg anthocyanins per day) but with 208 lower creatine kinase responses (54). In Perkins et al (55), the absolute lactate levels declined faster 209 210 during recovery from an intermittent high-intensity running protocol in recreationally active male team sport players following a 7-day intake of 105 mg of blackcurrant anthocyanins in extract 211 form. Faster decline for absolute lactate levels during recovery was also shown in the 20-min after 212 213 completion of a 16.1 km time trial (56). However, the recovery phase in the blackcurrant conditions

in Perkins et al (55) and Cook et al (56) were initiated with higher lactate levels suggesting a 214 potential role for the mass action effect. In a cycling study by Murphy et al (57), the time to 215 complete a 4 km time trial following 10-min of active recovery after a 4 km time trial was not 216 enhanced. With the information available, studies on effects of New Zealand blackcurrant extract 217 have not provided convincing evidence for enhanced endurance performance during a short 218 219 exercise recovery period. In addition, it remains unclear whether the potential enhanced exercise recovery by intake of New Zealand blackcurrant is beneficial for non-endurance exercise tasks. 220 Athletes will only benefit from enhanced exercise recovery when it would enhance subsequent 221 competitive sport performance or allowing enhanced adaptation from subsequent physical training 222 sessions. In the next section, we will focus on the effects of intake of blackcurrant on *whole-body* 223 exercise performance, i.e. continuous endurance exercise and intermittent exercise. 224

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226 Anthocyanin-rich Blackcurrant and Exercise Performance

Exercise performance is dependent upon multiple intrinsic (e.g. physiological and morphological 227 components) and extrinsic factors (e.g. motivation, sleep and nutritional practices) [for a 228 comprehensive review see (58)]. Competitive athletes are keen consumers of performance-229 230 enhancing nutritional ergogenic aids (59). The performance enhancing effects by the traditional supplements caffeine, creatine, β -alanine, sodium bicarbonate, dietary nitrate and glycerol are 231 232 recognized (60), with the enhancing effects related to the intensity and duration of the exercise 233 modality [e.g. for a review on caffeine (61)]. Anthocyanins have emerged as a performanceenhancing nutritional aid (24). This may be linked with the known potency to scavenge active 234 oxygen species, with first *in-vivo* evidence in the liver of rats (62). At that time, there was also the 235 236 concern for a role for reactive oxygen species affecting mechanisms to provide higher peripheral

muscle fatigue (63). However, it needs to be noted that there is no convincing evidence for an antioxidant *free radical* scavenging effect by intake of anthocyanins in *in-vivo* contracting human skeletal muscle. Nevertheless, postponing in a meaningful way the peripheral (and central) fatigue mechanisms by physical training modalities or different traditional and non-traditional nutritional supplements (e.g. blackcurrant supplementation) has the potential to enhance exercise performance.

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244 Whole-body continuous endurance exercise

Many studies, primarily from the University of Chichester (United Kingdom), have shown 245 enhanced exercise performance effects for a variety of exercise tasks but with some inconsistency 246 in the findings (Table 2). In Cook et al (56), first observations were provided for the effectiveness 247 of New Zealand blackcurrant extract (7x105 mg anthocyanins day⁻¹) on a 16.1 km ergometer 248 cycling time trial in trained male cyclists (n=14, $\dot{V}O_{2max}$: 53±6 mL·kg⁻¹·min⁻¹). To be included in 249 the study, participants had to cycle 8-10 hours a week in addition to having a personal best time 250 for a 16.1 km under 30 min. The non-paid cohort of trained male cyclists in Cook et al (56) had 251 two full familiarizations as part of the study. Full familiarization is a methodological necessity that 252 is required to minimize or exclude task learning effects and even more essential for participants 253 unfamiliar with an exercise task (64). More than one full familiarization may be essential to avoid 254 the variation in the performance of unfamiliar tasks even for a trained cohort. In Cook et al (56), 255 eleven participants had an increase in 16.1 km cycling time trial performance with a cohort 256 observation of an increase in time of 2.4% (placebo: 1722±131 s, New Zealand blackcurrant 257 extract: 1678±108 s). The enhanced performance time of 2.4% was similar to what has been 258 observed with acute intake of beetroot juice (0.5 L with 6.2 mmol of nitrate) for a cycling time 259

trail of 16.1 km (i.e. 2.7% increase) in competitive male cyclists (n=9, $\dot{V}O_{2max}$: 56.0±5.7 mL·kg⁻ 260 ¹·min⁻¹) (65). The study by Lansley et al (65) also had two full familiarizations. A higher enhanced 261 15 km cycling performance time of 4.6% was observed with 6 days intake of Montmorency cherry 262 powder (257 mg·day⁻¹ of anthocyanins) in trained male cyclists (n=8 and two full familiarizations) 263 264 (66). The early work with 7-day dosing with New Zealand blackcurrant extract raised the question whether there may be an effect by the last dose on the day of testing. Recent work on the dosing 265 time before exercise with Montmorency cherry indicated that ~90 min before was better for 266 enhanced 15 km cycling time trial performance than ~30 min and ~150 min before (67). In 267 Montanari et al (68), an acute intake of 315 mg of anthocyanins in male and female cyclists (fully 268 familiarized two times, n=34, VO_{2max}: 57±5 mL·kg⁻¹·min⁻¹, 8 females), 120 min before enhanced 269 performance for the 16.1 km cycling time trial, but only in the slower cyclists (i.e. >1400 s during 270 the familiarizations). It is possible that the 80% positive response rate to intake of blackcurrant in 271 Cook et al (56) was related to the cohort being considered slow cyclists according to Montanari et 272 al (68). It needs to be noted also that the study by Montanari et al (68) was a home-based study 273 during Covid lockdown in which participants were informed that the acute 16.1 km cycling 274 performance effects of two different products were tested. This approach is uncommon in sports 275 nutrition research in which a randomized, placebo-controlled, cross-over design remains the gold 276 standard. Nevertheless, in Montanari et al (68) was evidence that for some athletes, beneficial 277 cycling performance-enhancing effects can be obtained with acute intake of New Zealand 278 blackcurrant extract. Interestingly, a role for aerobic fitness level was also shown for nitrate 279 loading with lower increases in plasma nitrate in those with high $\dot{V}O_{2peak}$ and less improvement in 280 3-km field running time trial (69). Therefore, we cannot exclude that anthocyanin-induced 281

282 283 metabolite availability by intake of New Zealand blackcurrant contributes to interindividual responses (and potentially non-responses) in enhancement of exercise performance.

In trained male runners (n=16, $\dot{V}O_{2max}$: 55±6 mL·kg⁻¹·min⁻¹), an acute intake of 315 mg 284 anthocyanin-rich New Zealand blackcurrant extract enhanced 5 km treadmill running performance 285 286 by 2.8% (placebo time: 1346.33 ± 124.44 s) with 88% of the participants responding (70). Future work is required to examine whether higher acute dosing is required to enhance the overall 287 response rate in performance studies. In addition, it is not known whether prolonged dosing is 288 289 required for the faster cyclists (<1400 s for a 16.1 km cycling time trial) in the study by Montanari et al (68), and whether a dosing strategy for anthocyanin-rich New Zealand blackcurrant can exist 290 that provides a 100% meaningful response for performance enhancement in all participants. For 291 292 caffeine, for example, a role for genetics is apparent for the interindividual response on cycling time trial performance [for a meta-analysis see Wang et al (71)]. For the ability of anthocyanins to 293 enhance exercise performance, there is no research on the potential role of genetics to explain 294 interindividual differences by intake of blackcurrant anthocyanins [see for example Miranda-295 Vilela et al (72) for effects of gene polymorphisms on response to intake of pequi-oil 296 supplementation]. Interestingly, a study on the effects of pomegranate in patients with biochemical 297 recurrence following treatment for prostate cancer showed ability to respond in those with the 298 manganese superoxide dismutase (a mitochondrial antioxidant enzyme) genotype (73). However, 299 non-genotype factors will also contribute to variability of responses. For example, in a study on 300 301 the dose (105 and 210 mg of blackcurrant anthocyanins) and time (acute, 4 and 7 days) response to intake of New Zealand blackcurrant extract the response for performance enhancing effects for 302 303 the 16.1 km cycling time trial was inconsistent (74). For this study, eleven visits were required including washout periods of at least two weeks resulting in completion times from 3 to 11 months 304

(74). It is possible that the time period to complete all testing allowed unwanted variation due to 305 changes in seasonal activity lifestyles of the participants. In addition, the study had consistent 306 morning testing for only 3 of the 13 participants (74). In a study by Boyett et al (75), trained male 307 cyclists (n=7) responded with a higher performance effect during morning testing for a 3-km 308 cycling time trial compared to evening testing with intake of caffeine (6 mg \cdot kg body weight⁻¹). 309 310 Future studies should address whether the time of day can affect the performance-enhancing potential of anthocyanin-rich New Zealand blackcurrant for trained athletes. In addition, the 311 observations on potential time-of-day effects would also inform our knowledge on the optimal 312 dosing strategy required for time-of-day competitive athletic events. In another running study, 313 Pastellidou et al (76) examined the effect of New Zealand blackcurrant extract (315 mg of 314 anthocyanins with 1-day preloading) on time-to-exhaustion running test at two different intensities 315 in recreationally active males (n=15, $\dot{V}O_{2max}$: 53.1±3.4 mL·kg⁻¹·min⁻¹). Time-to-exhaustion 316 exercise performance tests compared to time-trials are known to have high variation (i.e. > 10%) 317 (77). Nevertheless, two time-to-exhaustion tests, one at critical speed (finish time: 1540–2284 s) 318 and one at 110% of $\dot{V}O_{2max}$ (185-367 s) provided no cohort effects, but the authors suggested a 319 performance enhancing effect for 60% the participants by 10-20% (76). Only one study examined 320 the endurance performance enhancing potential of intake of 7 days of New Zealand blackcurrant 321 extract (210 mg per day) in a stressful environmental condition (normobaric hypoxia: ~15% of 322 oxygen, i.e. ~2500 m) and found no effect in trained male cyclists (n=11, age: 38 ± 11 y, $\dot{V}O_{2max}$: 323 47 ± 5 mL·kg⁻¹·min⁻¹) for a 16.1 km time trial (78). In addition, in trained male cyclists (n=10), 324 there was not convincing evidence for a performance-enhancing effect (7 days intake of 105 mg 325 anthocyanins per day) for a 4 km time trial (57). It is possible that the study was underpowered. 326

However, when a second 4 km time trail was performed, the total time for the two 4 km time trails was 0.82% faster (57).

There is an absence of exercise performance studies with female cohorts with intake of anthocyanin-rich blackcurrant [see Smith et al (60) for a call for inclusion of females in sports nutrition studies]. In the only study with performance testing of an outdoor 5-km run in trained female runners (n=23, age: 31 ± 8 years, $\dot{V}O_{2max}$: 49 ± 4 mL·kg⁻¹·min⁻¹), the intake daily over three weeks in a training block was a fruit drink concentrate (of unknown composition) mixed with blackcurrant extract providing 300 mg of anthocyanins and 15 mg vitamin C (79).

In summary, there is limited and not always consistent evidence for an endurance 335 performance enhancing effect of intake of New Zealand blackcurrant. The available observations 336 337 seem to indicate that there is no effectiveness for performance enhancement for relatively short continuous best effort endurance tasks. More work is needed on the required dosing strategies 338 (dose and time) with New Zealand blackcurrant for enhancing endurance performance in specific 339 female and male cohorts with different athletic endurance abilities (e.g. 5 km and half-marathon 340 runners) and various endurance exercise modalities (e.g. rowing and cross-country skiing). In 341 addition, future work is recommended to examine performance enhancement by intake of New 342 Zealand blackcurrant in combination with metabolomic approaches (80), that may support the 343 understanding of interindividual responses. 344

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346 Whole-body intermittent exercise

Many team sports require repeated high-intensity and maximal-intensity bouts of exercise, e.g. jumping in volleyball and repeated running sprints in football, field hockey and rugby sevens [e.g. (81, 82). The exercise-induced oxidative and inflammatory stress during repeated running sprints

is probably higher than the oxidative stress during continuous exercise [for a role of exercise 350 intensity on oxidative stress, see (83)]. The first study on the effects on repeated and incremental 351 high-intensity exercise by Perkins et al (55) showed substantial changes in treadmill running 352 performance with 7-day intake of New Zealand blackcurrant extract (105 mg anthocyanins per 353 day) in participants with experience in sports with high-intensity intermittent exercise (**Table 3**). 354 In short, participants performed stages with six repeated high-intensity treadmill running bouts of 355 19 s each (starting speed at 80% of the running speed at $\dot{V}O_{2max}$) with an active recovery of 15 s 356 357 and passive recovery of 60 s between the incremental stages to the point of voluntary exhaustion [for more details see Perkins et al (55)]. The protocol used in Perkins et al (55) was adapted from 358 Mukherjee and Shia (84) for the testing of running capability in soccer players. For the cohort, the 359 speed of the first running bout was 11.5 ± 5.7 km·h⁻¹ and the speed at exhaustion was 18.0 ± 1.2 360 $\text{km}\cdot\text{h}^{-1}$ with active recovery speeds 7.2±3.6 $\text{km}\cdot\text{h}^{-1}$. With the intake of New Zealand blackcurrant 361 extract, participants were able to have a larger number of running bouts (placebo: 32±4, 362 blackcurrant: 35±6, P=0.02). In addition, the distance that was covered during the high-intensity 363 treadmill running bouts was increased by 10.8% (placebo: 2572±421 m, blackcurrant: 2849±570 364 m, P=0.024). Such effectiveness for New Zealand blackcurrant extract for high-intensity treadmill 365 running bouts justifies future work whether there is application in *real-world* competitive team 366 sports settings [e.g. (85)], in addition to providing meaningful performance effects in elite athletes 367 (86). 368

The effect of New Zealand blackcurrant extract (7-day of 105 mg anthocyanins per day) was also examined in the performance of the Loughborough intermittent shuttle test (LIST) (87), a test mimicking also the physical demands of football. The LIST consists of 5 x 15-min blocks with distance running at set speeds and 9 to 10 maximal 20 m sprints. It was only in the final two

blocks (i.e. after 45 min of exercise) that the effectiveness of New Zealand blackcurrant extract 373 became apparent with reduced slowing of the maximal sprint times (87). This may indicate that a 374 level of fatigue [see Daab et al (88) for peripheral and central fatigue during the LIST] is required 375 for meaningful effectiveness of intake of New Zealand blackcurrant to enhance exercise 376 performance. However, on completion of the 5 x 15 min blocks, no effect was observed for a time 377 378 to exhaustion running task (87). This may indicate that the effectiveness of New Zealand blackcurrant extract to enhance exercise performance in a fatigued state may be task-dependent. 379 Studies by Godwin et al (89) and Potter et al (90) also seem to confirm that some level of fatigue 380 is required for New Zealand blackcurrant to enhance exercise performance. New Zealand 381 blackcurrant extract (7-day intake of 210 mg anthocyanins per day) became only effective after 382 the 4th sprint in trained youth football players during the running based anaerobic sprint test. 383 However, in the same study, New Zealand blackcurrant extract had no effect in recreationally 384 active football players during the running based anaerobic sprint test (89). In Potter et al (90), a 385 trend (P=0.062) for a larger hang time and enhancement of sports climbing performance was 386 reported but potential methodological and analytical issues were raised [for a critique of the study 387 see (91)]. 388

As far as we know, the only cycling study with intermittent exercise was performed by Paton et al (92) in which effects of acute blackcurrant drink intake (300 mL containing 155 mg of anthocyanins, 80 mg L-theanine, 50 mg pine bark extract, 7.7 g carbohydrate) were examined in well-trained male cyclists (n=12, age: 39.5 ± 11.4 y, $\dot{V}O_{2peak}$: 4.71 ± 0.61 L·min⁻¹) for 8 x 5 min bouts of maximal cycling (with 2 min active recovery). No effects were observed for the blackcurrant drink (92). It is possible that a higher acute dosage or chronic dosing is required to obtain effectiveness, as was observed in Montanari et al (68), albeit for 16.1 km cycling performance in faster cyclists. Nevertheless, Paton et al (92) was the first study as well to examine acute effects
by intake of an anthocyanin-rich blackcurrant drink during high-intensity intermittent exercise.
Therefore, more work is required to optimize the dosing strategy for acute intake of blackcurrant
anthocyanins to affect intermittent exercise performance.

400

401 **Conclusions and Future Directions**

Intake of anthocyanins in the studies with extracts and powder made from New Zealand 402 blackcurrant have provided meaningful effects for whole-body exercise performance for 403 continuous and intermittent exercise models and exercise recovery. Fruit-derived polyphenols are 404 now recognized by the Australian Sports Commission with emerging potential as a performance 405 enhancing nutritional aid. However, the sheer diversity of berry- and fruit-derived polyphenols 406 including the numerous anthocyanins will provide the academic community with an enormous 407 challenge to establish optimal evidence-based dosing strategies in sports nutrition. Many 408 anthocyanin-rich berries, and therefore many combinations of naturally existing anthocyanins, 409 remain unexplored regarding the efficacy for recreationally active individuals and athletes. Dosing 410 studies with manufactured single or specific multiple anthocyanins with application for athletes 411 412 are likely to remain too costly to examine for effectiveness, at least in the short term. It is expected that it will take decades for the field of anthocyanin in application for sports nutrition to provide 413 414 the evidence on the dose and optimal combination of specific anthocyanins to establish maximal 415 efficacy for exercise performance and recovery. The question remains whether the blackcurrant anthocyanins cyanidin and delphinidin have established themselves as a winning combination with 416 application for sports nutrition. Time will tell! Future work on the efficacy of supplements with 417 418 natural combination of berry anthocyanins is warranted to establish its potential and usefulness for

- the contribution of natural berry and fruit sources as an ergogenic aid in sport and exercise
- 420 nutrition. In addition, future work should address also the efficacy and safety of combined intake
- 421 of long-term intake of anthocyanins and other recognized sports nutrition supplements.
- 422

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Data described in the manuscript is available from the published sources considered in the narrative review.

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Anthocyanin-rich blackcurrant supplementation as a nutraceutical ergogenic aid for exercise performance and recovery: A narrative

review

Mark Willems

Table 1. Summary of studies in humans examining the effects of intake of blackcurrant anthocyanins on exercise recovery. NZBC, NewZealand blackcurrant.

Source	Cohort	Design	Dosing strategy	Exercise task	Primary recovery
					outcomes with NZBC
Lyall et al	5 females, 5 males,	double-blind,	240 mg NZBC	30 min of rowing at	↓ plasma carbonyl
2009 (44)	age: 48±2.5 years,	placebo-controlled,	anthocyanins (120 mg	80% VO _{2max}	levels (0 h post-
	recreationally active	randomized, cross-	before and after		exercise, ↓ creatine
		over	exercise)		kinase (24 h post-
					exercise)
Hurst et al	healthy individuals,	double-blind,	1 x 0.8, 1.6, or 3.2	30 min of rowing at	lower post-exercise (0
2019 (50)	n=32, age range: 20 –	placebo-controlled,	mg⋅kg ⁻¹ of NZBC	70% V0 _{2max}	hr) heart rate with 0.8
	60 years	randomized,	anthocyanins		and 1.6 mg·kg ⁻¹
		parallel			blackcurrant, no effect
					on post-exercise
					lactate, ↓ plasma
					carbonyl levels (2 h
					post-exercise with 0.8
					and 1.6 mg·kg ⁻¹
					blackcurrant

Hurst et al	healthy individuals,	double-blind,	acute (1 hr before) and	30 min of indoor	\downarrow of malondialdehyde
2020 (51)	n=32, age range: 20 –	placebo-controlled,	5 weeks daily intake	rowing at 70%	2 hr post exercise with
	60 years	randomized,	of 3.2 mg·kg ⁻¹ (~ 240	$\dot{V}O_{2max}$	acute and chronic
		parallel	mg) of NZBC		intake
			anthocyanins		
Hunt et al	healthy non-resistance	double-blind,	each day 105 mg	4×15 repetitions	↓ muscle soreness at
2021 (52)	trained individuals,	placebo-controlled,	NZBC anthocyanins	of maximal	24 and 48 hrs post-
	NZBC: n=14, 10	randomized,	in extract form for 12	concentric and	exercise, \downarrow creatine
	women, age: 24±2	parallel	days	eccentric	kinase at 96 hrs post-
	years); placebo: n=13,			contractions of the	exercise
	9 women, age: 23±2			biceps brachii	
	years			muscle in the	
				dominant arm	
Costello et al	healthy individuals,	double-blind,	each day 210 mg	outdoor half	↑ urine IL-6 at 48 hr
2020 (53)	NZBC: n=10, 4	placebo-controlled,	NZBC anthocyanins	marathon race	post-exercise
	women, age: 30±4	randomized,	in extract form for 9		
	years; placebo: n=10, 4	parallel	days		
	women, age: 29±7				
	years				
Hutchison et	healthy individuals,	double-blind,	each day 2x ~369 mg	eccentric knee	\downarrow creatine kinase at 48
al 2016 (54)	blackcurrant: n=8, 7	placebo-controlled,	of blackcurrant	extensions (3×10)	and 96 hrs post-
	women, age: 19.5±0.3		anthocyanins (country	sets at 115% of 1-	exercise, ↓ plasma IL-

	years; placebo: n=8, 6	randomized,	unknown) in drinks	repetition	6 levels at 24 hr post-
	women, age: 20.9±0.9	parallel	for 8 days	maximum	exercise)
	years				
Perkins et al	13 men, recreationally	double blind,	105 mg NZBC	progressive high-	faster decline in blood
2015 (55)	active, age: 25±4 years	placebo-controlled,	anthocyanins in	intensity,	lactate for 30-min
		randomized, cross-	extract form for 7	intermittent	post-exercise
		over	days	treadmill running	
Cook et al	14 men, cycling 8-10	double blind,	105 mg NZBC	16.1 km cycling	faster decline in blood
2015 (56)	hr per week, age:	placebo-controlled,	anthocyanins in	time trial	lactate for 20-min
	38±13 years	randomized, cross-	extract form for 7		post-exercise
		over	days		
Murphy et al	10 men, cyclists, age:	double blind,	105 mg NZBC	2 x 4 km cycling	no change in time for
2017 (57)	30±12 years	placebo-controlled,	anthocyanins, in	time trial with 10	the 2 nd 4 km cycling
		randomized, cross-	extract form for 7	min in between	time trial
		over	days	with active	
				recovery	

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Table 2. Summary of studies in humans examining the effects of intake of blackcurrant anthocyanins on whole-body continuous exercise
performance. NZBC, New Zealand blackcurrant.

Source	Cohort	Design	Intake	Exercise task	Main outcomes
Cook et al	14 men, cycling 8-	double blind, placebo-	105 mg NZBC	16.1 km cycling time	2.4% faster time
2015 (56)	10 hr per week, age:	controlled, randomized,	anthocyanins in extract	trial (laboratory	
	38±13 years	cross-over	form for 7 days	testing)	
Montanari	34 cyclists (8	double blind, placebo-	acute intake of 315	16.1 km cycling time	1.3% faster time in
et al 2023	women), age: 38±7	controlled, randomized,	NZBC anthocyanins in	trial (home-based	slower cyclist
(68)	years	cross-over with	extract form	testing)	(>1400 seconds for
		participants informed			16.1 km)
		that 2 different			
		blackcurrant products			
		were tested			
Moss et al	trained male runners,	double blind, placebo-	acute intake of 315	5 km treadmill	2.7% faster times
2023 (70)	n=16, age:	controlled, randomized,	NZBC anthocyanins in	running	
	26±5 years	cross-over	extract form		
Montanari	13 male cyclists,	double blind, placebo-	105 mg and 210 mg	16.1 km cycling time	inconsistent effects
et al 2020	age: 39±10 years	controlled, randomized,	NZBC anthocyanins in	trial (laboratory	with 210 mg
(74)		cross-over with dose	extract form for 7 days	testing)	NZBC
		effects			anthocyanins

			with testing on day 1, 4		
			and 7		
Pastellidou	15 males,	double blind, placebo-	315 mg NZBC	treadmill running to	no cohort effect
et al 2021	recreationally active,	controlled, randomized,	anthocyanins extract	exhaustion at 110%	
(76)	age: 24.4±3.6 years	cross-over	form for 2 days	of $\dot{V}O_{2max}$	
Willems et	11 male cyclists,	double blind, placebo-	210 mg NZBC	16.1 km cycling time	no cohort effect
al 2019	age: 38±11 years	controlled, randomized,	anthocyanins extract	trial (laboratory	
(78)		cross-over	form for 7 days	testing) in	
				normobaric hypoxia	

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Table 3. Summary of studies in humans examining the effects of intake of blackcurrant anthocyanins on whole-body intermittent exercise with different intensities high intensity and maximal intensity exercise performance. NZBC, New Zealand blackcurrant.

Source	Cohort	Design	Intake	Exercise task	Main outcomes
Perkins et al	13 men,	double-blind, placebo-	105 mg NZBC	progressive high-	increase in number of
2015 (55)	recreationally active,	controlled, randomized,	anthocyanins in	intensity, intermittent	high-intensity
	age: 25±4 years	cross-over	extract form for 7	treadmill running	running bouts
			days		
Willems et al	13 men,	double-blind, placebo-	105 mg NZBC	Loughborough	reduced slowing of
2016 (87)	recreationally active,	controlled, randomized,	anthocyanins in	intermittent shuttle	the 20 m maximal
	age: 22±1 years	cross-over	extract form for 7	test	sprint in the final 15
			days		min block
Godwin et al	football players,	double-blind, placebo-	210 mg NZBC	running based	reduced slowing of
2017 (89)	recreationally active:	controlled, randomized,	anthocyanins in	anaerobic sprint test	sprint 5 in academy
	n=15, age: 20±1	cross-over	extract form for 7		players
	years; academy		days		
	(professional club):				
	n=9, age: 17±1 years				
Paton et al	12 well-trained male	double-blind, placebo-	acute blackcurrant	8 x 5 min maximal	no effect
2022 (92)	cyclists, age:	controlled, randomized,	drink intake (300	cycling	
	39.5±11.4 years	cross-over	mL containing 155		

	mg of	
	anthocyanins, 80	
	mg L-theanine, 50	
	mg pine bark	
	extract, 7.7 g	
	carbohydrate)	