Protective and Performance effects of anthocyanin supplementation

A review of the literature

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Attestation of Authorship

"I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor used artificial intelligence tools or generative artificial intelligence tools (unless it is clearly stated, and referenced, along with the purpose of use), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning"

- Finn Clearkin | 16/04/2024

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Abstract

There has been growing interest from both the general and sporting populations in natural occurring plant extracts and phytochemicals that might elicit physiological and ergogenic effects, such as anthocyanin. Anthocyanins are responsible for the natural pigments in the flowers, leaves, fruits, vegetables and tubers; such as blues, purples, reds and oranges. The main aim of this dissertation is to review the literature in order to determine 1) the protective and potential health benefits of anthocyanins; 2) the effects of anthocyanins on physiological responses, and the primary aim; 3) the impact of anthocyanin intake on physical performance and adaptations during exercise. This dissertation comprised five chapters involving both a narrative and systematic review. The narrative review revealed promising protective effects of anthocyanin with daily dosages <300mg assisting in the reduction in the effects of free radicals, oxidative stress and providing anti-inflammatory cytokines to assist in prevention and risk reduction of different types of non-communicable diseases, cancers and neurological degradation. Anthocyanin research has shown beneficial effects to improve recovery and assist in the reduction of exercise-induced oxidative stress. Anthocyanins have vasodilatory properties that can increase peripheral blood flow, which in addition to reducing damage caused by exercise and non-exercise oxidative stress, can assist in enhancing oxygen delivery, muscle metabolite removal, and substrate utilisation. The systematic literature review was performed using PubMed, Scopus, and SPORTDiscus, revealing 11 studies that examined the effects of anthocyanins on physical performance. The studies on berries, such as blackcurrants, showed promising results within a seven-day supplementation period with daily doses of 105mg providing more evidence than 210mg, and 315mg, dosages. There was a notable improvement in cycling performance and indications of performance-enhancing effects from blueberries and cherries as well. Overall, this dissertation offers valuable insights into the effects of anthocyanin consumption on human health, physiology, and exercise performance.

Chapter One

Introduction

The field of sports nutrition adopts research to inform and guide the evidence of nutrients and exercise performance (Kreider et al., 2010), which includes macronutrients: including carbohydrates, proteins, and fats (Singh, Kesharwani, & Keservani, 2017), and micronutrients: vitamin and minerals (Thomas, Erdman, & Burke, 2016). Macronutrients provide the body with energy and affect energy balance (Singh et al., 2017), whereas micronutrients assist in bodily processes, such as digestion, hormone production and brain function (Shenkin, 2006). Manipulating the diet effectively can support an athlete with their training, performance goals and body composition (Jeukendrup, 2017; Kreider et al., 2010). As competitive level increases, the training required to become successful often becomes more demanding, requiring athletes often explore interventions to help meet such demands and also to gain an advantage in their training and performance. Sports nutrition interventions are highly individualised based on the sport and type of athlete (Jeukendrup, 2017). General recommendations can be adjusted to accommodate an athletes individual nutritional needs, health, performance goals, physical characteristics (weight, shape, growth and body composition), food preferences and their responses to strategies undertaken (Thomas et al., 2016).

Over many decades, research has contributed to informing and refining recommendations for athletes based on optimal macronutrient and micronutrient intake to meet training and competition demands. Examples include increased carbohydrate consumption in conjunction with higher volume training, around 5-8g/kg per day depending on intensity (Kreider et al., 2010), increased protein intake equal or exceeding 1.4g/kg per day for physique or hypertrophy goals commonly seen in resistance training (Jäger et al., 2017), and manipulation of carbohydrate availability (low carbohydrate, high fat, LCHF) for promoting fat oxidation in endurance athletes (Burke, 2015; Evans, Cogan, & Egan, 2017). Similarly, micronutrients, consisting of vitamins and minerals that are essential for many cellular processes to support health, growth and reproduction also play a key role and have been investigated with regards to their need in varying sport contexts (Shenkin, 2008). Micronutrients also have their own respective daily recommended intake (RDI) to support physiological functions in the body. For example, Vitamin C; a water-soluble vitamin, which has antioxidant activity in the body. Most adults require 45mg per day to meet the RDI. A daily dosage of 200-1000mg per day of vitamin C, and even a daily dosage of 235mg per day of vitamin E, a fat-soluble vitamin, have both been used by athletes to reduce exercise-induced oxidative stress. There is an increased requirement to meet the demands of sports, such as vitamin D in winter sports and iron in some female athletes have supported the need for individual health and to promote training adaptations, even if minor, can help in competitive advantage (Beck, von Hurst, O'Brien, & Badenhorst, 2021).

While a food first approach to meeting training and competition demands is recommended and to meet nutrition requirements of an athlete, an athlete's diet needs to be varied to provide sufficient energy and other essential nutrients to fulfil their dietary needs adequately. However, not all athletes meet this requirement (Thomas et al., 2016). Athletes often seek the use of dietary supplements such as multivitamins, minerals, ergogenic aids, amino acids, sports foods and caffeine containing products for many reasons including to support training capacity, improve recovery, and to reduce deficiencies to ensure they meet energy demands (Ron J Maughan, King, & Lea, 2004). The prevalence of dietary supplement use in athletes is shown by Huang, Johnson, and Pipe (2006) in Atlanta at the 1996 Olympic games (n = 121M and n = 136F) and the 2000 Sydney Olympic games (n = 150M and n = 150F), 69% and 74% of athletes specified supplement use, most commonly, multivitamins and minerals. Whereas, Nieper (2005) reported that 62% of junior track and field athletes (n = 32) used supplements in the past three months with multivitamins and minerals used at the highest, with ergogenic aids, which improve performance by enhancing energy utilisation, production and efficiency, being used more by males than females, giving reasons such as increase health performance (45% vs 33%), immunity (40% vs 44%) and improving performance (25% vs 11%). Motivations behind supplement use often include; meeting abnormal demands of training or frequent competitions, benefitting performance; keeping up with team-mates or opponents, or have been recommended by coach, parent or other influential individual (Garthe & Maughan, 2018).

Dietary supplements should be utilised to fill a gap in the athletes diet and do not replace a balanced nutritional plan, rather, can work synergistically toward improving performance goals (Burke, 2017). With athlete and general population interest in dietary supplements on the rise, it is within our best interest to carefully research the efficacy of supplements to benefit both performance and general health. In general, dietary supplements can be put into categories, such as sports foods (gels, bar, drinks, protein powders), vitamins and minerals, herbals and botanicals and ergogenic aids, which can come in the form of liquid, powder or capsule (Garthe & Maughan, 2018). Supplement use by athletes is a very common method to support training and recovery, and to help enhance athletic performance. This has become a common practice with various supplements (Porrini & Del Bo', 2016). Dietary supplements such as shown in Table 1, have demonstrated effectiveness in field and laboratory conditions (Garthe & Maughan, 2018; Kreider et al., 2010; Porrini & Del Bo', 2016). The mechanisms of action and the evidence supporting their use varies with several influencing factors in different sports (Burke, 2017; Porrini & Del Bo', 2016). The most common supplements with strong evidence include sodium bicarbonate, β-alanine, caffeine, creatine and phosphate.

Table 1: Common supplements, dosing protocols and potential benefits in sport performance

Supplement	Mechanism	Protocol and dosing recommendations	Sports/Events	AIS Ranking Group[1]
Sodium bicarbonate (Burke, 2013; Carr, Hopkins, & Gore, 2011)	Temporarily increase levels of blood bicarbonate to acutely enhance extra-cellular (situated or occurring outside a cell or the cells of the body) buffering of efflux of H+ ion on the contracting muscle. Bicarbonate can reduce fatigue and pain associated with high intensity exercise in which there is a large production of H+ ions from anaerobic glycolysis	300mg/kg.bw Split doses @ 2-2.5hr pre-event/competition	High intensity events from 2-8mins Swimming, rowing, track, cycling Just below lactate threshold Cycling time trials, 5000-1000 running) Intermittent high intensity sports with prolonged efforts above lactate threshold (team sports/combat sports)	A
β-alanine (Blancquaert, Everaert, & Derave, 2015; Trexler et al., 2015)	Increases levels of carnosine (protein building block) to chronically enhance intra-cellular (occurring within the cells) buffering and also the buffering of the efflux of H+ ion on the contracting muscle involved in the exercise. Beta alanine aims to reduce fatigue that is associated with exercise where there is a large production of H+ ions from anaerobic glycolysis.	Loading : ≥200g taken over 4–10 weeks in split daily doses (e.g., 3 × 3.2 g/day for 4 week or 2 × 2.4 for 10 week). Maintenance: ~2 g/day	Acute/competition performance High intensity from 1-8 minutes Swimming, rowing, track and cycling Chronic enhancement of high intensity training may have long-term benefit to other events	A
Caffeine (Burke, 2008; Spriet, 2014)	Adenosine antagonist with effects on many body targets including central nervous system Promotes Ca^{2+} release from sarcoplasmic reticulum	3-6mg/kg.bw (total dose) Numerous protocols amongst pre-event, in longer events (peri-intake) and at end of events involving single or several intakes	High intensity from 1-8 minutes Swimming, rowing, track and cycling High intensity events lasting 10-60mins Intermittent high-intensity sports Team sports (field and court): racket sports and combat sports Endurance: Marathon, ultra endurance (ironman triathlon, cycling road races) Prolonged skill sports: Golf, shooting	A
Creatine monohydrate (Bemben & Lamont, 2005; Buford et al., 2007)	Increased phosphocreatine content enhancing capacity for repeated bouts of high-intensity exercise with brief recovery intervals which would otherwise provide inadequate recovery of PCr stores. Enhancement of glycogen storage and direct effect in muscle protein synthesis	5-7 day @20g/day in split doses or 2/3g day for 28 days Plus maintenance of 2-3g even up to 5g per day	Acute /competition performance Intermittent high-intensity sports Team sports (field and court), racket sports and combat sports Chronic enhancement of interval and resistance training	A

Phosphate (Buck, Wallman, Dawson, & Guelfi, 2013)	Increased buffering capacity, increased 2,3-diphosphoglycerate to increase dissociation of O2 into muscle and increase phosphate availability for ATP Synthesis	3-5g/day for 3-6 days Continuous dosage	High intensity from 2-8 mins Swimming, rowing, track, cycling Endurance events? Intermittent high intensity sport: Team sports and combat sports	C

[1](Australian Institute of Sport, 2022b)

In the realm of high-performance competition, significant risk factors exist. Competitive sports have long been governed by stringent regulations, which continuously expand to encompass a growing list of banned substances (Petróczi & Naughton, 2007). The risks to athletes within high performance sport with the use of supplements and sport food is that compliance to safety and regulation is typically voluntary (Australian Institute of Sport, 2022a). The result of this carries risk of adverse effects and health concerns, for example; 23,000 reports of emergency department visits associated with dietary supplement use occurred in United States of America hospitals in 2015 (Geller et al., 2015). While this number of cases can be considered minimal in regard to population and overall supplement use, risk and concern from supplement use can disrupt training and participation and so it is important for athletes to understand this to guide future supplementation use and consideration (Garthe & Maughan, 2018; Ronald J Maughan et al., 2018). Additionally, due to the possibility of unregulated and unreported substances within some supplements and sports foods, the risk of failing to meet the World Anti-doping Agency (WADA) rules, athletes should only use batch-tested products, although there still exists risk of doping violations within these products (Australian Institute of Sport, 2022a, n.d.).

Faced with the ever-increasing demands for gaining a competitive edge, athletes may opt to explore naturally occurring substances, such as plant-based supplements, in pursuit of performance advantages (Shaw et al., 2022). For example, the consumption of beetroot juice or extracts, known for their high nitrate content have been heavily researched in recent times and have shown to have strong physiological (Olsson, Al-Saadi, Oehler, Pergolizzi, & Magnusson, 2019), and performance benefits, in both health and sport contexts (Ormsbee, Lox, & Arciero, 2013; Wylie et al., 2013). This has influenced the research into different plant-based extracts which whilst supporting health function in the body through immunity, durability and vitality (Shenkin, 2006), are useful in exercise performance (Shaw et al., 2022), although are less researched.

The recent shift towards plant-based and antioxidant ergogenic aids have shown benefits in meta-analysis and in field measurements on athletic performance (D'Angelo, 2020; Jones, 2014; Somerville, Bringans, & Braakhuis, 2017). The focus on the effects of fruit and vegetables in athletes and physically active individuals has recently been directed to a class of polyphenol; flavonoid, and sub-class of flavonoids; anthocyanin (Fang, 2014). In particular providing health benefits in antioxidant and anti-inflammatory capacities, where oxidative stress and inflammation is elevated from high-intensity and high duration sport events (Davies, Quintanilha, Brooks, & Packer, 1982; McHugh, Connolly, Eston, & Gleim, 1999).

The main aims of this dissertation was to review the literature in order to determine 1) the protective and potential health benefits of anthocyanins; 2) the effects of anthocyanins on physiological responses, and the primary aim; 3) the impact of anthocyanin intake on physical performance and adaptations during exercise.

Research Questions

- What is the mechanism(s) by which anthocyanins act in the human body?
- What are the main health benefits of anthocyanins?
- How does anthocyanin impact physiological responses during and after exercise?
- Can anthocyanin supplementation enhance sport performance?

Dissertation Structure

This Master's dissertation is intended to examine the effects of anthocyanins in a physiological, exercise, health and sport context. To address these areas, the structure of the dissertation is presented as follows: Chapter One includes the introduction, which provides context and presents an overview of the area of sports nutrition, introduces supplement use, and the emergence of polyphenol and anthocyanin supplements from plant sources. Chapter Two incorporates a two-part literature review introducing the primary mechanisms of how anthocyanin is acting in the human body, its impact on health (part A) and its effect on the physiological responses and adaptation to exercise (part B). Chapter Three describes the systematic approach used to explore the literature with respect to assessing the effects of anthocyanin supplementation on sport performance. Chapter Four presents the results of the systematic review of the performance literature and the quality of research studies in this field. Finally, Chapter Five incorporates an overall discussion and conclusion, evaluating the findings of the performance effects of anthocyanins, including limitations and areas for future research in this field of study.

Chapter Two

Part A: The effect of anthocyanins on physiology in the human body

This section of the review aims to discuss anthocyanins with respect to their presence, structure and bioavailability. The role and benefits of dietary anthocyanin consumption, including their antioxidant activity, anti-inflammatory effects, prevention of cardiovascular disease (CVD), anti-diabetic activity, neuroprotective effects, gastrointestinal effect, and anti-cancer properties will also be reviewed.

Anthocyanins

Anthocyanins are the natural occurring water-soluble plant pigments, responsible for the natural pigments in flowers, leaves, fruits, vegetables and tubers; such as blues, purples, reds and oranges (de Pascual-Teresa, Moreno, & García-Viguera, 2010). In acidic conditions, anthocyanins can appear as red pigment, and in alkaline conditions, anthocyanins can appear as a blue pigment (Castañeda-Ovando, de Lourdes Pacheco-Hernández, Páez-Hernández, Rodríguez, & Galán-Vidal, 2009; Khoo, Azlan, Tang, & Lim, 2017). Anthocyanins are a part of the flavonoid family, which are a part of a larger group of antioxidants known as polyphenols (Mattioli, Francioso, Mosca, & Silva, 2020). An anthocyanin is formed when anthocyanidin (uncommonly known as aglycone) is glycosylated by the enzyme glucosyltransferase (Figure 1) (Khoo et al., 2017; Mattioli et al., 2020). Some common anthocyanidins include; cyanidin, pelargonidin, delphinidin, peonidin, petunidin and malvidin (Figure 2). The cyanidin form appears in the most abundance (Bendokas et al., 2020). Anthocyanins undergo breakdown and absorption throughout the gastrointestinal tract, however, are mainly absorbed in the distal bowel. These are then processed via human phase II metabolism in the liver, which creates hybrid microbial-human metabolites which increase the bioavailability of anthocyanins (Mattioli et al., 2020).

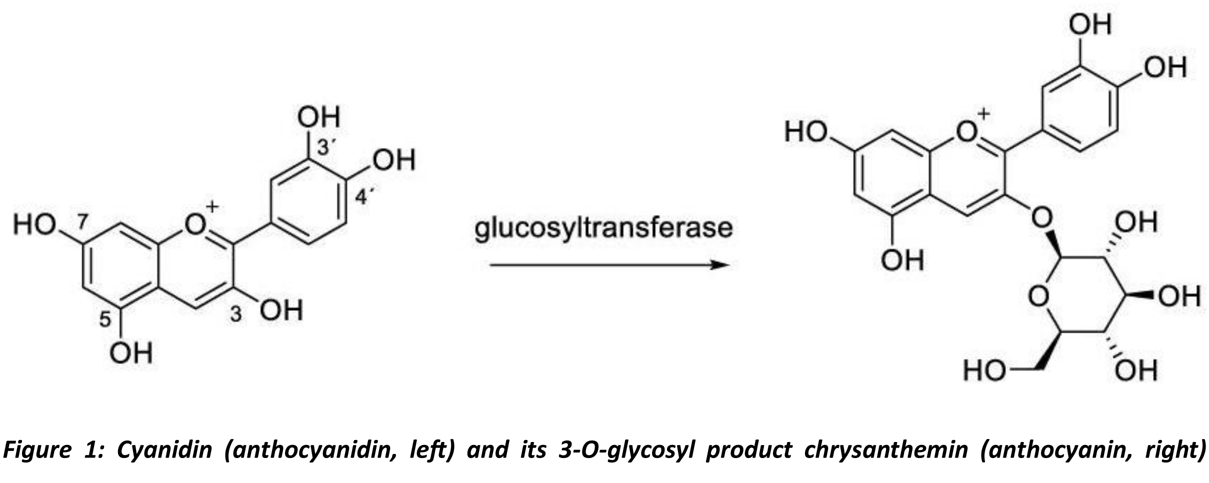
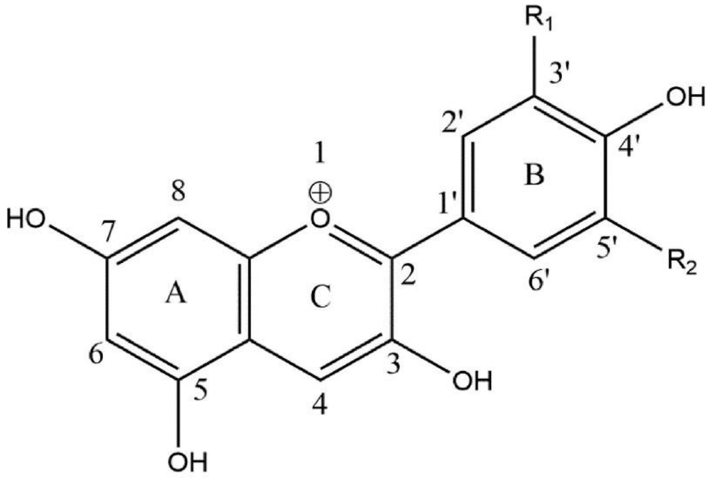


Figure 1: Cyanidin (anthocyanidin, left) and its 3-O-glycosyl product chrysanthemin (anthocyanin, right) derived from the enzymatic activity of glucosyltransferase (Mattioli et al., 2020)



R_1	R_2	Anthocyanin
H	H	Pelargonidin-3-glucoside
OH	H	Cyanidin-3-glucoside
OH	OH	Delphinidin-3-glucoside
OCH_3	H	Peonidin-3-glucoside
OCH_3	OH	Petunidin-3-glucoside
OCH_3	OCH_3	Malvidin-3-glucoside

Figure 2: General Structure of Anthocyanins and Glycosides types (Zhao et al., 2018)

Bioavailability

As with all nutrients, anthocyanins have differing bioavailability in the human body, meaning different quantities are absorbed depending on the type of food consumed. When consumed, as different plants have a variety of types of anthocyanin and at different concentrations, we see the bioavailability of these nutrients change. Furthermore, there may be inter-individual variations of absorption, namely, arising from an individual's gut microbiome (Eker et al., 2019; Hair, Sakaki, & Chun, 2021). Catabolism by the gut microbiome produces anthocyanin metabolites. Differing bacterial species in the gut microflora break down different anthocyanin into different metabolites which may either increase or decrease absorption (Eker et al., 2019). Interestingly, other research groups in both human and in vitro samples have highlighted a potential symbiotic relationship between anthocyanin and bacteria of the gut microbiota. Where following anthocyanin consumption, there has been an observed increase in beneficial bacteria in the gut microbiota, including *Bifidobacterium spp., Lactobacillus spp., or Actinobacteria*,. and have the potential to inhibit colonisation of harmful bacteria such as *Staphylococcus aureus* (Eker et al., 2019; Fang, 2014; Sun, Zhang, Zhu, Lou, & He, 2018; S. Vendrame et al., 2011). However, there is some research that supports partial degradation and absorption of anthocyanin metabolites, particularly of 4'-hydroxyhippuric acid and ferulic acid, in the upper gastrointestinal tract, before contact with the gut microbiota (Ludwig et al., 2015). Theoretically, variation in absorption based on individual gut microbiota could affect the absorption of anthocyanin metabolites, however, more research is required to confirm this correlation.

The stability and bioavailability of anthocyanins is widely influenced by factors such as pH of soil, ultraviolet (UV) exposure, temperature, thermal processing, climate, season and its structure (Khoo et al., 2017; Mattioli et al., 2020). Thermal processing of food damages cell walls, reducing the anthocyanin content of a food but concurrently increasing the accessibility and bioavailability of anthocyanins for absorption by the body (Eker et al., 2019). A barrier to the application of findings from many human studies is the potential impact of the food matrix on the absorption and bioavailability of anthocyanins, with the addition of the participants differing microbiome structure. With increasing evidence highlighting the importance of considering the impact of other dietary factors when analysing results in human studies (Eker et al., 2019; Ludwig et al., 2015). For example, one study found that absorption of anthocyanin from black currant juice compared to an aqueous citric acid solution of purified anthocyanins increased the absorption rate of anthocyanin in hyperlipidaemic rabbits (Nielsen, Dragsted, Ravn-Haren, Freese, & Rasmussen, 2003). The study suggested that the food matrix may increase bioavailability of anthocyanin. It is important to note that this was an animal study, so results are not readily applicable or transferrable to humans.

In contrast, a human study, investigating the link between anthocyanin absorption when consuming anthocyanin from blackcurrant juice in combination with rice cakes found there was no observed effect for absorption or excretion of anthocyanins. In this case, it was suggested that the rice cake slowed gastric emptying, therefore slowing absorption of anthocyanin in the intestine. There is scope for further research to identify ways that the food matrix interacts with absorption of anthocyanin from foods (Eker et al., 2019; Hair et al., 2021).

In human studies, foods containing primarily the delphinidin form of anthocyanin (blackcurrants and berries alike) showed largest improvements in metabolic and cardiovascular disease risk biomarkers (Davinelli, Bertoglio, Zarrelli, Pina, & Scapagnini, 2015). Current reviews have found that fruits like berries, currants, grapes and some tropical fruits have the highest concentration of anthocyanins, and the vegetables with the highest concentration of anthocyanins are leafy vegetables, grains, roots and tubers (Tena, Martín, & Asuero, 2020). In particular, berries, such as blueberries and blackcurrants have the highest content of anthocyanin. Whilst there is no known optimal intake of these micronutrients, blackcurrants contain between 130-460mg anthocyanin/100g fruit, in comparison to blueberries and blackberries, whilst still anthocyanin rich, contain comparably less anthocyanin (between 62-300mg anthocyanin/100g fruit) (A. Braakhuis, Somerville, & Hurst, 2020; de Pascual-Teresa et al., 2010). However, the high end of blackcurrants anthocyanin content comes from New Zealand blackcurrant extracts, New Zealand grown blackcurrants have shown to have higher concentrations of anthocyanins and other phytochemicals compared to blackcurrants grown in other countries. The believed reason for this likely the consequence of UV levels and longer sun exposure on sunny days in New Zealand as UV exposure is one of the biggest predictors of anthocyanin content (A. Braakhuis et al., 2020; Guo, Han, & Wang, 2008).

The antioxidant role of anthocyanins in the body

The role of anthocyanins within the body is primarily linked to their antioxidant properties, however, this is not their only role within the body. Research has also highlighted that anthocyanins play a key role in the gut microbiome by reducing pro-inflammatory gut bacteria and it has been postulated that anthocyanins hold nutrigenomic mechanisms such as altering regulation of genes involved in inflammation pathways (Chen, Xu, Sun, Jiang, & Bai, 2022). Anthocyanins undergo the process of neutralising or scavenging of free radicals (Tena et al., 2020). Free radicals are produced as a by-product of adenosine triphosphate (ATP) formation used to generate energy for use and storage of the human body cells, which is beneficial for immune responses and cellular functions. However, free radicals can overwhelm the ability of the human body to regulate them (Tungmunnithum, Thongboonyou, Pholboon, & Yangsabai, 2018). Free radicals can be formed endogenously through sources such as pollution, smoking, radiation, or pharmaceutical influence (Pham-Huy, He, & Pham-Huy, 2008). Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are a subset of free radicals and have similar effects to free radicals where an increased production can cause oxidative stress (Khoo et al., 2017; Tena et al., 2020). At base levels ROS and RNS are a by-product of ATP (Pizzino et al., 2017). Free radicals pilfer electrons from other molecules, altering the make-up of lipids, proteins and mitochondrial DNA, potentially damaging them and leading to oxidative stress; a trigger to a number of diseases, such as metabolic disorders, diabetes, atherosclerosis, cardiovascular disease, cancers and aging (Khoo et al., 2017). Antioxidants contain the electrons needed to neutralise the free radical, acting as a hydrogen atom donor or completing a single electron transfer, thus, stabilising the free radical. This makes anthocyanins the “switch” to disable a free radical, indirectly preventing harm or further damage to the human body (Pizzino et al., 2017).

Therapeutic effects of anthocyanins

In recent decades evidence-based research have shown the beneficial and protective effects of anthocyanins in fruits in the prevention of several diseases (Figure 3) (Cassidy et al., 2016; Fallah, Sarmast, Fatehi, & Jafari, 2020; Kalt et al., 2020; Rozita Naseri et al., 2018; Tena et al., 2020). This section will elaborate the beneficial effects of anthocyanin relating to different all-cause mortality, risk of disease and the prevention of chronic non-communicable disease (NCDs), consisting of various disease types including obesity, inflammation, diabetes, cardiovascular disease, neurological diseases and cancers.

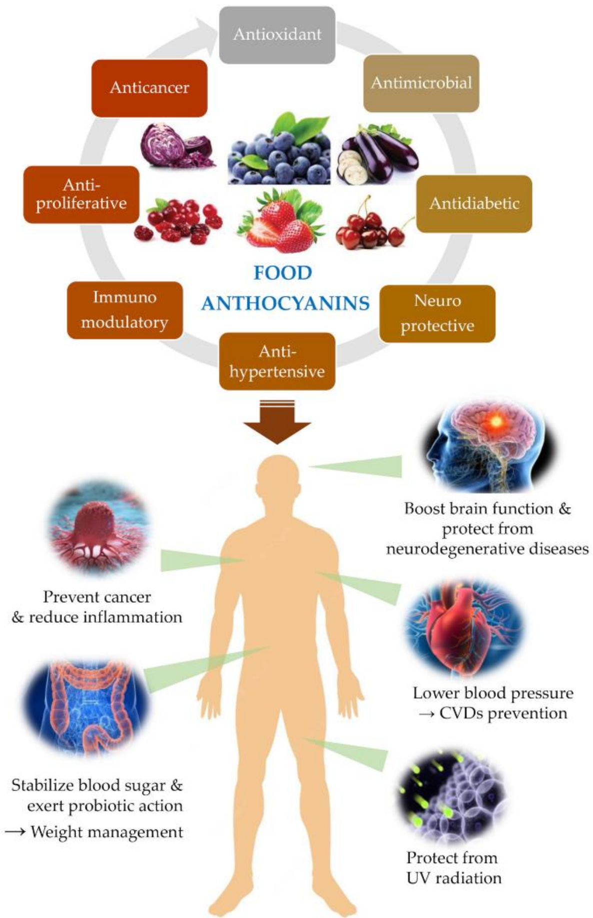


Figure 3 : Overview of major human protective effects associated to Anthocyanin consumption reported in the literature. Taken from Câmara et al. (2022)

Inflammation

As oxidative stress is harmful and may lead to serious outcomes in the pathogenesis and progression of many chronic NCDs, inflammation is also interrelated (Pizzino et al., 2017; Wang & He, 2018). Inflammation in its localised form is an immune response mechanism that protects the body from pathogens, damaged cells and toxicity (H. Lee, Lee, & Choue, 2013). In abundance, inflammation can become chronic, and damaging to the human body, which can also be seen as a precursor to many NCDs (Wang & He, 2018). Inflammation is inhibited by numerous factors, with the signalling pathways of nuclear factor kappa (NF-κB) being the primary influencer (Stefano Vendrame & Klimis-Zacas, 2015). The activation of NF-κB can stimulate the expression of numerous genes, leading to the production of diverse pro-inflammatory cytokines, including tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-1β (IL-1β), monocyte chemoattractant protein-1 (MCP-1), and C-reactive protein (CRP) (Ma, Du, Li, Yang, & Zhu, 2021; Stefano Vendrame & Klimis-Zacas, 2015; Wang & He, 2018).

In individuals who are overweight or obese, pro-inflammatory cytokines are significantly higher than adults with a healthy body mass index (BMI) and these cytokines circulate in higher quantities from a combination of energy surplus and fat accumulation (H. Lee et al., 2013). Increased adipose tissue mass is associated with increased , pro-inflammatory cytokines such as TNF-α, IL-6, and acute phase proteins, e.g.; CRP are significantly increased (Wang & He, 2018). Epidemiological studies have shown that anthocyanin has anti-inflammatory effects, improving a variety of disease risk factors linked with chronic low-grade inflammation such as insulin resistance, atherosclerosis, metabolic syndrome, cardiovascular disease, type II diabetes and even some cancers (Bendokas et al., 2020; Ma et al., 2021; Mattioli et al., 2020). This has been displayed in many randomised controlled trials. In a 8-week randomised control trial (RCT) with 63 overweight/obese subjects with a BMI <23 found that anthocyanin-rich black soybean testa extract significantly helped decrease inflammatory indictors of TNF-α and MCP-1, whilst also significantly decreasing abdominal fat in the experimental group (M. Lee, Sorn, Park, & Park, 2016). Similarly, a larger sample, longer duration 24-week RCT with purified anthocyanin capsules, recruited 150 aged adults found a significant decrease in serum high-sensitive C-creative proteins (hsCRP) and IL-1β, with no significant changes in TNF-α between the two groups (Y. Zhu et al., 2013). Meta-analysis indicated that dietary anthocyanins significantly decrease levels pro-inflammatory biomarkers, such as CRP, IL-6 and TNF-α and adiponectin, a circulating protein secreted from adipose tissues, has shown an significant increase in lab and human studies (Fallah et al., 2020; Shah & Shah, 2018). Adiponectin has been shown to have protective properties against inflammation, whilst regulating glucose levels, lipid metabolism and insulin sensitivity, through its anti-inflammatory, anti-fibrotic and antioxidant properties (Fallah et al., 2020; Khoramipour et al., 2021).

Chronic inflammation plays a significant role in the pathology of obesity and other associated NCDs, which includes CVD, insulin resistance and type II diabetes mellitus (T2DM) (García-Conesa et al., 2018). This is classified under the spectrum of metabolic syndrome, which all risk factors for the pathogenesis of these diseases are accentuated from inflammation and oxidative stress, leading to chronic conditions such as; hyperlipidaemia, hypertriglyceridemia, hyperglycaemia, and hypertension (Kassi, Pervanidou, Kaltsas, & Chrousos, 2011).

Cardiovascular disease

The role of anthocyanins is especially important in preventing CVD and myocardial infarction related to mortality (Tena et al., 2020), as cardiovascular disease is the biggest contributor to all-cause mortality in the world, with a significant burden on the healthcare systems in recent decades (Tran, Palfrey, & Welsh, 2021). The risk factors of CVD and heart related issues include, but not limited to: overweight/obesity, hypertension, abnormal lipids, atherosclerosis, and lifestyle factors due to inactivity, smoking, and low consumption of fruits and vegetables (Dahlöf, 2010). Anthocyanins have seen to demonstrate the improvement of vascular health and the prevention of endothelial stress, such as arterial stiffness, and atherosclerotic plaque (Mozos et al., 2021). Cardiovascular disease risk factors are often alleviated from the processes of nitric oxide (NO) in the body, where NO is an important determinant in cardiovascular health (Loscalzo & Welch, 1995). The antioxidant properties of anthocyanins increases the bioavailability and promotes the endogenous production of NO in the body (Festa, Da Boit, Hussain, & Singh, 2021). Polyphenols like anthocyanin have been shown to inhibit nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, an enzyme that reduces NO bioavailability and impairs NO vasodilation, reducing blood flow (Rodriguez-Mateos et al., 2014). NO is an integral molecule that has increased upregulation and minimises degradation from anthocyanins antioxidant properties, which is important in the regulation of endothelial homeostasis (Rodriguez-Mateos et al., 2013).

For example, in a 12-week RCT using purified anthocyanin supplements (320 mg/day anthocyanin), in people with hypercholesterolemia, significant improvements in lipoprotein markers, triglycerides (TG), blood pressure, and decrease in inflammation were observed (Y. Zhu et al., 2011). Similarly, a longer 24-week study by Y. Zhu et al. (2013), with an anthocyanin dose of 320 mg/day reported a significant decrease in low density lipoproteins (LDL)-cholesterol and significant increase in high density lipoprotein (HDL)-cholesterol between supplement and placebo (PL) groups, whilst also showing significant changes in LDL-cholesterol and HDL- cholesterol in the experimental group. In a 6-month randomised controlled trial with 115 subjects with metabolic syndrome, the consumption of one cup (364 mg/day anthocyanin) of a blueberry-extract, a half-cup (182 mg/day anthocyanin) and an identical placebo were compared. Vascular health remained unchanged in the half-cup group, whereas the one-cup group significantly improved in vascular function and lipid profiles, which may indicate a dose-response manner of anthocyanins exceeding 300 mg/day (Curtis et al., 2019).

Contradictory to the aforementioned studies, D. Li, Zhang, Liu, Sun, and Xia (2015) observed significant decreases in LDL, triglycerides, and an increase in HDL compared to placebo at a much lower dosage of 160 mg/day anthocyanins. In a 24-year cohort study, ischemic stroke and non-fatal myocardial infarction (MI) was associated with higher intake of fruit-based anthocyanin intake (Cassidy et al., 2016). A metanalysis of 17 randomised controlled trials showed that anthocyanins significantly improve lipid profiles [TG: mean difference (MD)= -9.16, p= 0.149; LDL: MD= -8.86, p= 0.098; HDL: MD= 1.67, p= 0.053] and inflammatory biomarkers (TNF-α: MD = −1.98, p= 0.975; IL-6: MD = 1.17, p= 0.825; hs-CRP: MD = 0.164, p= 0.569, 95% CI) (Shah & Shah, 2018),Another metanalysis of 99 RCTs concluded that the consumption of anthocyanin significantly decreased systolic (MD= −1.56, p= 0.000) and diastolic blood pressure (MD= −1.42,p= 0.000) regardless of individuals health status (García-Conesa et al., 2018).

Type 2 Diabetes Mellitus

Under the overarching body of metabolic syndrome, insulin sensitivity and type two diabetes mellitus (T2DM) are extremely prevalent in recent decades (Desroches & Lamarche, 2007; Kolovou, Anagnostopoulou, Salpea, & Mikhailidis, 2007). T2DM is a major contributor to other metabolic diseases and conditions such as renal damage, CVD, strokes and even premature death (García-Conesa et al., 2018). T2DM is generally caused by a combination of insulin resistance and changes in beta-cell (β-cell) function, the body's cells also often do not recognise that insulin is present, resulting in high blood glucose levels (R. Naseri et al., 2018). Some researchers found that dietary anthocyanin in berries acted as inhibitors for carbohydrate digestive enzymes, by competing with carbohydrates and inhibiting α-glucosidase due to the similar structure of β-linked maltose and glucosyl groups on the anthocyanin aglycones which help control glucose homeostasis and potentially reducing the post prandial rise in blood glucose levels (Z. Li et al., 2023; McDougall & Stewart, 2005). Further research is required to confirm this correlation.

One clinical trial conducted by Nikbakht et al. (2021) tested the efficacy of anthocyanin supplementation on diabetes-associated inflammatory biomarkers, biochemical and physical parameters and dietary inflammatory scores were calculated from three-day diet recalls. This 4-week study included a total of 40 participants between the ages of 25-75 years of age and was further split into three groups; healthy (n=14), T2DM (n=12), and at-risk of T2DM (n=14) with all dosed 320 mg/day anthocyanin. The at-risk group were selected if they possessed at least three metabolic syndrome conditions within the categories of obesity, high lipid profiles and elevated fasting glucose levels. While there were no significant changes in BMI, waist height ratio or anthropometric data in any group, fasting blood glucose levels were significantly reduced in the at-risk of T2DM group after the anthocyanin intervention. The at-risk T2DM group also had a significant reduction in LDL cholesterol levels, however, lowered total cholesterol did not reach a level of statistical significance. Interestingly, Nikbakht et al. (2021), observed a significant reduction in some pro-inflammatory biomarkers; interleukin-6, interleukin-18, and tumour necrosis factor-α in the T2DM group suggesting that inflammation plays an important role in the development of T2DM and diabetes risk factors. Dietary analysis highlighted a significantly higher carbohydrate, total fat and mono-unsaturated fat intake in the at-risk of T2DM group compared to healthy individuals. Additionally the T2DM group had higher protein, total fat, saturated fat, mono-unsaturated fat and total cholesterol intake than the healthy group. This research indicates that anthocyanin supplementation may have a beneficial impact on some diabetes-associated inflammatory biomarkers and other diabetes-associated biochemical factors. Limitations of study includes the small sample size and the concurrent anti-inflammatory dietary patterns followed by participants which may have increased the anti-inflammatory effect of the anthocyanin supplement. Further research with larger sample populations would be beneficial to create meaningful and applicable data for public health related intervention.

Compared to earlier work by Yang et al. (2017) who, in a 12-week RCT, assessed a larger sample size population of 138 (intervention; n = 76, PL; n= 62) 40-75 year old participants with prediabetes or early diabetes and reported that a purified dosage of 320 mg/day anthocyanin significantly reduced glycated haemoglobin (HbA1c) from baseline measures and LDL-C showed a significant between group reduction compared to placebo, indicating a in favour of anthocyanin for glycaemic control and affect in lipid profile. However this was the only larger population sample size study assessing anthocyanin, further studies with larger sample size and study duration are necessary to confirm the findings of this research.

Neurological

Anthocyanins have also been utilised in the treatment of neurodegenerative disease such as Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (as a general term: dementia), within but not limited to the aging population (Fatima, Mehendale, & Reddy, 2022; Mattioli et al., 2020).

Worldwide, more than 55 million people have dementia, with an estimate of 10 million more diagnosed each year, these statistics highlight increasing concern around prevalence of neurological conditions (WHO, 2023). Oxidative stress and inflammation is a major influencing factor of the impairment of neurological function and the increased aging of the brain (Hassan, Noreen, Rehman, Kamal, & da Rocha, 2022). It is believed that the brain has low antioxidant defence mechanisms compared to other organs, so the addition of the antioxidant and anti-inflammatory properties of anthocyanin containing fruits and vegetables can be important in the slowing of cognitive decline and prevention of neurological diseases and conditions (Winter & Bickford, 2019). Numerous studies have shown the antioxidant properties of anthocyanins through the scavenging of free radicals, ROS and RNS (de Pascual-Teresa et al., 2010; Kalt et al., 2020; Khoo et al., 2017; Tena et al., 2020). In addition to the damage caused by oxidative stress and inflammation on the brain, other damaging processes such as excitotoxicity, and the disruption of calcium homeostasis can cause damage to the brain, spinal cord, and the imbalance of overall protein homeostasis, which leads to neuronal death and their associated signalling networks, ultimately resulting in neurological and cognitive decline (Hassan et al., 2022; Winter & Bickford, 2019). Excitotoxicity is unique to neurons, in which excitatory stimuli can cause neurons to experience a massive influx of calcium, mitochondrial disruption and damage of plasma membranes, which can ultimately lead to neuronal death (Winter & Bickford, 2019). Maintaining calcium homeostasis is important to prevent neuronal death and in-vitro and in-vivo research has shown promising results in anthocyanin treatment, especially berry-fruits on the function of hippocampal neurons (Badshah, Kim, & Kim, 2015; Subash et al., 2014), which are responsible for learning, emotions and memory (Wheeler et al., 2015), displaying increases in intracellular calcium levels in response to neurotoxic agents (Badshah et al., 2015; Subash et al., 2014; Winter & Bickford, 2019). For example, Lin, Gong, Song, and Cui (2017) saw improvements in visual and audible memory at 3 months, but not 6 months in a study of 122 older adults with a low dose of anthocyanin (1.35, 2.7, and 7mg /day, respectively), showing that dose-manner response over chronic periods may still improve cognitive function. Whereas, Dodd, Williams, Butler, and Spencer (2019) demonstrated no significant improvement on cognitive performance healthy older adults following the consumption of blueberries (508 mg anthocyanin) in 2 and 5 hours post consumption, although cognitive function of the adults improved in both 2 and 5 hour tasks compared to a control group, but this did not reach a level of statistical significance. More recently, work from Wood et al. (2023) has demonstrated significant differences in memory task in a RCT between groups after a 12-week wild blueberry (302 mg anthocyanin) consumption with 61 healthy older adults. This may suggest that a single dose of anthocyanin may have protective effects on cognition, but dosing regardless of amount in greater dosing periods may provide consistent protective effects, beneficial to neurological health. To the researchers knowledge there are no meta-analyses or systematic reviews on the neurological benefits of anthocyanin consumption, so it is still unclear of the how beneficial anthocyanin consumption is for the betterment of neurological health, and further human research is needed to establish a clear link.

Cancer

Anthocyanins have also seen promising results in the treatment and prevention of certain cancers. The antioxidant properties of anthocyanins have preventative measures in the formation of cancerous tumours, it is proposed that anthocyanins increase the production of ROS, which induce cell DNA damage. Oxidative stress can cause gene cell damage and leading to gene mutation (Chen et al., 2022). Anthocyanins antioxidant properties can prevent damaged cells from occurring and preventing the subsequent transformation of these cells by gene mutation in tumour formation (Lin et al., 2017). Anthocyanins can also inhibit angiogenesis, the formation of new blood vessels which supply blood to tumours, through downregulation of metalloproteinases which is crucial in tumour growth and metastasis of tumours (Chen et al., 2022). Anthocyanins also modulate cellular signalling pathways that contribute to the carcinogenic properties of cell-cycles. They are involved in inhibiting cell proliferation and promote of apoptosis (programmed cell death) which can inhibit the growth of cancer cells (Chen et al., 2022; Lin et al., 2017). In particular, the glycoside delphinidin, has been shown to inhibit anti-apoptotic genes through its antioxidant and cytotoxic effects, leading to apoptosis of prostate cancer cells (Jeong et al., 2016). In a metanalysis of 44 articles, breast cancer treatment with anthocyanins have been reported for their chemoprotective properties in breast carcinogenic tissue. It is postulated that the anthocyanins, especially from fruits containing delphinidin, suppress the expression of matrix metalloproteinases (MMP-2 and MMP-9) in tumour growth and metastases by inhibiting the modulation pathways of cell proliferation and decreasing NF-κB anti-inflammatory activation in the cells that promote carcinogenesis due to their antioxidant nature (W. Li, Peng, Zhaojie, & Wei, 2022). Li et al., (2022) goes on to state that anthocyanins are promising candidates as an alternative or as an adjuvant therapy, however mentioning that bioavailability plays an important role, where acylated anthocyanins such as fruit have better absorption than nonacylated anthocyanins, such as vegetables and plants. Better understanding of anthocyanin bioavailability may help provide proper efficacies on dose response and chronic effect of this compound-based use in cancer or preventative cancer treatment.

Summary

The accumulation of evidence suggests a synergistic effect between the forms of anthocyanin and their attributed health benefiting properties. Oxidative stress has a significant impact on the pathogenesis of many diseases and conditions, in which anthocyanins with their antioxidant properties pose a possible benefit by scavenging free radicals, inhibit and reducing the damaging processes of ROS and RNS. The above research has indicated that anthocyanin intake or supplementation may reduce inflammation and decrease pro-inflammatory biomarkers. This has a role in reduction in of HbA1c in Type two Diabetes Mellitus, increased blood flow in cardiovascular disease, promotion of apoptosis and suppression of tumour growth in cancer. Anthocyanin use also holds an antioxidant effect which has been shown to slow cognitive decline by improving the brains antioxidant defence. It may also have a role in improving cognitive performance. It is important to acknowledge that the positive effects of anthocyanins may also be mediated through pathways other than the antioxidant pathways. This includes the gut microbiome and the nutrigenomic pathway, which may explain the variable results in the research to date. Further research is required regarding the effects of antioxidants and how these could be applied in humans to support health and wellness and prevention or treatment of some of these conditions. Research with anthocyanin across metabolic and non-communicable diseases indicates a significant link to daily dosages ≥300 mg/day in health benefits, even in high doses, anthocyanins and anthocyanin extracts have displayed no negative effects (Fairlie-Jones, Davison, Fromentin, & Hill, 2017; Tian et al., 2021). However, with the evidence from the above-mentioned studies may bring forth the need for further research assessing anthocyanin intake between 200-300 mg/day and may provide further indication and better understanding for future dosing recommendations.

Part B: Physiological effects during exercise

Anthocyanins, known for their antioxidant and inflammatory properties, have created significant interest in their health benefits and has been largely researched in the past decade. The observed health benefits have motivated research in exercise physiology performance and recovery contexts (Cook & Willems, 2019; Kimble, Jones, & Howatson, 2023). While the exact mechanisms of how anthocyanins affect physiological responses is not fully understood, research in many areas of athleticism is ongoing, with several proposed and promising benefits to exercise arising from anthocyanin. This section will consider the acute and chronic physiological responses of anthocyanin consumption, as well as its impact on markers of recovery.

Cardiovascular responses

Supplementation of anthocyanin extracts can influence cardiovascular alterations, by vasodilation of blood vessels and increased peripheral blood flow (Cook & Willems, 2019; Somerville et al., 2017). One of the earliest use of anthocyanin consumption, with blackcurrant, observed performance enhancing benefits was assessed by Matsumoto et al. (2005), who investigated the effect on forearm peripheral blood flow in an two-week intervention, dosing with blackcurrant, although dosage was not mentioned specifically. Matsumoto et al., were able to show that following venous occlusion, blackcurrant intake increased forearm blood flow by 22% and reduced muscle stiffness and fatigue from typing. Left forearm was assessed with near-infrared spectroscopy (NIRS), which indicated an increase in peripheral blood flow. Enlargement of femoral artery was observed in a study by Cook, Myers, Gault, and Willems (2017) who assessed seven days of 210mg anthocyanin blackcurrant supplementation on submaximal quadriceps muscle isometric contraction. No main differences in the isometric contraction performance test were observed but, the enlargement of the femoral artery was coupled with cardiovascular alterations in a decrease in overall systolic ($F(1,96) = 41.41$, $p < 0.001$) and diastolic ($F(1,96) = 35.27$, $p < 0.001$) blood pressure, with an increase in cardiac output and stroke volume. With no changes in HR. This could indicate potential mechanism for performance with anthocyanin consumption.

Increased blood flow to the working muscles could support the notion of an potential increase in exercise, observed in low to moderate intensity endurance performance (Cook, Myers, Gault, Edwards, & Willems, 2017; Cook, Myers, Blacker, & Willems, 2015; Strauss, Willems, & Shepherd, 2018), with an increase in time-trial by 2.4% cycling and an observed 10.6% increase in total distance in high intensity running trials (Cook et al., 2015; Perkins, Vine, Blacker, & Theodorus Willems, 2015). Mechanisms are proposed that anthocyanins can influence the ability to increase the production of nitric oxide (NO) in the body, (Rodriguez-Mateos et al., 2014; Rodriguez-Mateos et al., 2013). The function of NO is regulating endothelial function, through the inhibition of NADPH – an enzyme that reduces NO bioavailability. This process decreases arterial stiffness and provides vasodilation for the blood vessels allows for an increased peripheral blood flow capacity attributed to anthocyanin consumption (Rodriguez-Mateos et al., 2014). The increased blood flow is important within recovery of tissue and nutrient delivery to the muscles and organs (Byrne, Twist, & Eston, 2004). Anthocyanins and NO have a positive effect on cardiovascular health and adaptation. They cause an increased peripheral blood flow which improved the removal of muscle metabolic by-products and promote an increase in substrate delivery to muscle and organs during exercise (Curtis et al., 2019; D'Angelo, 2020).

Metabolic responses

Muscle metabolites such as lactate, are a by-product of moderate to vigorous intensity exercise, is greatly improved when influenced by vasodilatory properties of anthocyanin. The greater blood flow to the exercising muscle would accelerate lactate clearance, thus contributing to lower blood lactate levels (Loscalzo & Welch, 1995; Manach, Scalbert, Morand, Rémésy, & Jiménez, 2004; Marafon et al., 2022). As lactate build up in the muscles affects performance and contributes to muscle fatigue, the ability to clear lactate more efficiency will increase an athletes lactate threshold, crucial to cardiovascular endurance, and an athletes capacity to endure higher intensity exercise for a longer duration, and also provide less fatigue in high-intensity exercise (Rodriguez-Mateos et al., 2014). Seen in cycling endurance and running time-trials (Brandenburg & Giles, 2019; Cook et al., 2015; Perkins et al., 2015). Increased vasodilation and blood flow allows for better substrate delivery and utilisation for muscle.

Energy metabolised during exercise is derived from lipids (such as; plasma free fatty acids and intramuscular triglycerides),glucose (such as; plasma glucose and muscle glycogen), and is dependent on the intensity of exercise performed. For lower intensity exercise (<45% VO_{2max}), the main substrate used are fats (lipids) and for higher intensity exercise, (>85% VO_{2max}) the main substrate used are carbohydrates (glucose) (Ramadoss, Stanzione, & Volpe, 2022).

Another proposed mechanism of improved substrate utilisation was described in a randomised control-crossover trial from Cook, Myers, Gault, Edwards, et al. (2017), who tested the effect of a seven-day blackcurrant anthocyanin intake and on fat oxidation and mitochondrial function. This study demonstrated a dose-response effect from supplementing seven-days of 600-900mg (~210 and ~315 mg anthocyanins) daily NZBC with a 22% and 24% greater fat oxidation than the placebo trial when cycling for 120-min at 65% VO_{2max}. Additionally Strauss et al. (2018), indicated a 27% increase in fat oxidation in 120-minutes of cycling (65% VO_{2max}) in female subjects with an anthocyanin dosage of 210mg/day. Similar to Cook et al. (2015), who also indicated a 27% fat oxidation increase in a 16.1km cycling time-trial (NZBC: 1678 ± 108, PL: 1722 ± 131 s) in male subjects with 105mg/day of anthocyanin. Anthocyanins antioxidant properties aim to help reduce exercise-induced oxidative stress and reduce mitochondrial damage, allowing for better enhancement of the mitochondria, which supports energy metabolism better by providing muscle cells with more efficient and faster nutrient delivery, decreasing heart rate and supporting the notion that anthocyanin might increase the rate that fat and even carbohydrate (glucose) is oxidised during exercise (Achten & Jeukendrup, 2004). This has been shown to promote potential benefits in maximal sprinting ability measures and provide increases in respiratory exchange rate (RER) (Perkins et al., 2015; M. E. T. Willems, Cousins, Williams, & Blacker, 2016). In a study by Cook et al, assessing maximal ramp testing, where the substrate utilised in the tests shift from fat oxidation to a carbohydrate oxidation at higher intensities, showing significant trend for RER being lower compared to placebo trials at 45%, 55% and 65%VO_{2max} ($P = 0.066$; $P = 0.120$; $P = 0.043$, respectively) (Cook et al., 2015). Research has indicated that anthocyanin consumption can show improvements in mitigating oxidative stress that impair NO and mitochondrial functions, improving cardiovascular performance, and influencing training adaptations(Cook, Myers, Gault, Edwards, et al., 2017; Cook et al., 2015; Perkins et al., 2015; Rodriguez-Mateos et al., 2014; M. E. Willems, Myers, Gault, & Cook, 2015). This adaptation improves exercise performance by allowing for more blood volume with less resistance, decreasing blood pressure, decreasing the risk of hypertensive states and improving overall cardiovascular health (Dahlöf, 2010; Mattioli et al., 2020).

One key response highlighted in the literature relating to long-term daily anthocyanin consumption and exercise is the reduction of adipose tissue. Adipose tissue promotes increased inflammatory cytokines and oxidative stress (D'Angelo, 2020; Khoramipour et al., 2021). There is some research that suggests anthocyanin intake can improve insulin sensitivity and glycaemic control (Castro-Acosta, Lenihan-Geels, Corpe, & Hall, 2016), which could be a promising factor for optimisation of muscle glucose uptake in exercise. Anthocyanins inhibitory functions for carbohydrate digestive enzymes may indirectly promote the use of fat as an energy source over glucose metabolism (Burke, 2015; Castro-Acosta et al., 2016). Insulin resistance has been shown to have a positive correlation with VO_{2max} (DiMenna & Arad, 2018), and it has been hypothesised that mitochondrial function is compromised in insulin resistance (Wahl, Scalzo, Regensteiner, & Reusch, 2018; Whillier, 2020). Since anthocyanin has properties that alleviate oxidative stress and damage from ROS and RNS, anthocyanin use may reduce mitochondrial impairments from insulin resistance and also assist oxygen delivery through its vasodilatory properties (McDougall & Stewart, 2005; Whillier, 2020). Anthocyanin use shows promise in exercise related interventions targeting glycaemic control. Additionally, research has noted daily anthocyanin consumption alongside daily exercise decreases the risk of pathogenesis of NCDs through action of anthocyanin’s antioxidant defence mechanisms (Subash et al., 2014; Tena et al., 2020).

Recovery and inflammation post exercise

Research shows that the effects of anthocyanin supplementation, both over a period of seven-days and in chronic consumption, can have an ergogenic effect to metabolically improve blood flow, improve recovery, enhance endothelial function and promote increased adaptations to exercise (Byrne et al., 2004; Rodriguez-Mateos et al., 2014; Rodriguez-Mateos et al., 2013; Tena et al., 2020). Through the antioxidant and anti-inflammatory properties of anthocyanins negating the effect of oxidative stress, ROS and RNS from exercise or lifestyle factors, researchers have observed a reduction in biomarkers such as creatine kinase and an improvement in overall quality of life (Tena et al., 2020). Alongside this is the reduction of inflammation in the brain which can reduce risk factors of cognitive decline and advanced aging, promoting better neurological response to exercise (Mee-Inta, Zhao, & Kuo, 2019; Seo, Heo, Ko, & Kwak, 2019). While regular moderate to vigorous exercise daily has been linked to numerous health benefits, including lowering the risk of many chronic diseases, such as cardiovascular disease and type 2 diabetes mellitus, and some types of cancers, as well as improving neurological health (Chen et al., 2022; R. Naseri et al., 2018; Tena et al., 2020; Winter & Bickford, 2019), intense and prolonged bouts of exercise have shown to increase the production of free radicals, RNS and ROS in the skeletal muscle, as well as a pathological responses of inflammation (Jackson, Vasilaki, & McArdle, 2016). Excessive levels of oxidative stress caused by free radicals, RNS and ROS is detrimental to cells, resulting in muscle damaging mechanisms such as lipid peroxidation, damage to mitochondrial membrane integrity, and damage to the endoplasmic and sarcoplasmic reticulum (Davies et al., 1982; McHugh et al., 1999). However, this can also assist in the adaptation and growth process of muscle building following exercise. Antioxidant use may blunt this physiological adaptation and reduce the response to exercise (Cook & Willems, 2019). An intake threshold may need to be considered, for example vitamin C intake in higher dosages of >1000mg per day may blunt training adaptation through limiting mitochondrial biogenesis and the possibility of altering cardiovascular function, but 200mg per day may be sufficient to reduce oxidative stress and provide health benefits without impairing training adaptations (A. J. Braakhuis, 2012).

Post-exercise recovery strategies are important as the less time needed to recover after training and exercise allows for improved adaptation and greater responsiveness to intense and higher volume training (Kimble et al., 2023). A meta-analysis and systematic review of 25 studies on the effect of fruit as a recovery strategy from the effects of exercise-induced muscle damage (EIMD), which encompasses delayed onset muscle soreness (DOMS), impaired power and strength of the muscles, which have negative consequences of training and recovery (Byrne et al., 2004). This review reported that berries had the largest effect in alleviating and preventing the effects of EIMD (Doma, Gahreman, & Connor, 2021). Berries are rich in anthocyanins, and their antioxidant properties may provide further assistance to alleviate exercise induced oxidative stress (Zafra-Stone et al., 2007), such examples as assisting in lowering the formation of lipid peroxides and the damage of lipid peroxidation. Lipid peroxides have been shown to attack polyunsaturated fatty acid (PUFAs), damaging to the integrity of mitochondrial and endoplasmic reticulum membranes. This damage impairs the functions of these membranes and leads to cell proliferation (Cobley, Close, Bailey, & Davison, 2017; Davies et al., 1982).

Mitochondrial damage can result in decreased ATP production. ATP is important in the anaerobic lactic and anaerobic glycolytic energy systems, so a reduction in ATP results in a decrease in performance of moderate to high intensity bouts of exercise (Baker, McCormick, & Robergs, 2010). Oxidative stress can impair mitochondrial function, which leads to a reduction in ATP production (Davies et al., 1982; McHugh et al., 1999). This releases pro-apoptotic and pro-inflammatory cytokine (CRP, IL-6 and TNF-α) and the activation of cell death pathways. Loss of mitochondrial function can also enhance ROS production, which further increases oxidative stress (Ma et al., 2021). Anthocyanins, which have shown anti-inflammatory properties can help reduce mitochondrial decline and can activate cell apoptosis through "bim" pathways and exert potential anti-cancer effects (Ma et al., 2021; Zhang et al., 2020).

Endoplasmic reticulum (ER) is vital in assisting with muscle protein synthesis (MPS), which is crucial to the repair and adaptation of muscle tissue (Marafon et al., 2022). Sarcoplasmic reticulum (SR) is a network of specialised, smooth endoplasmic reticulum, responsible for the regulation of calcium ions (Ca^{2+}), storage and release, which is directly involved in the control of relaxation and contraction of muscle myofibril, which influences muscle function directly (Nusier, Shah, & Dhalla, 2021). ER and SR synergistically support recovery of muscle tissue and enhancing cell function, however oxidative stress caused by exercise can disrupt these complex structures, damaging their integrity (McHugh et al., 1999). Mechanical stress induced from exercise can cause an increase in intracellular proteins to flow into the blood, such as creatine kinase (CK), effecting the regulation of Ca^{2+} and function of MPS, and leading to results including cell apoptosis or autophagy, which has a negative impact on muscle recovery and adaptation (Duhamel, Green, Sandiford, Perco, & Ouyang, 2004; McHugh et al., 1999; Nusier et al., 2021). Muscle contraction and relaxation impairment further leads to muscle fatigue and weakness (McHugh et al., 1999). The antioxidant properties of anthocyanin and their anti-inflammatory responses to stimuli could alleviated stress on the complex tissue involved in muscle cells (Alam et al., 2021). However, more research is needed to confirm this.

Summary

In conclusion, the research exploring anthocyanin use before, during and after exercise is growing. The main evidence supporting anthocyanin consumption improving exercise performance is its ability to improve peripheral blood flow, improve NADPH and boost NO production, this will assist in enhancing oxygen delivery, muscle metabolite removal, and increased fat oxidation. These processes could potentially assist the working muscles and serve to enhance athletic performance. Additionally anthocyanin is important in the recovery of muscles, to reduce the effects of exercise induced oxidative stress and to reduce the degradation of the complex muscle tissue structures. However, more research, specifically long-term research, is required to make meaningful connections and associations.

Chapter Three

Methods

Search Strategy for identification of studies

A systematic literature search was conducting of the following electronic bibliographic databases: PubMed, Scopus and SPORTDiscus on the impact of anthocyanin on physical performance. The main search terms used were “anthocyanin” AND “athletes” OR “anthocyanin” AND “sport” AND “performance”. This was carried out following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines (Page et al., 2021), which helped improve the integrity of this review. The results from the electronic database search and the titles and abstract of each study were initially screened during the electronic search to exclude irrelevant studies and duplicates, as well as proving the full-text readings. Furthermore, the reference list of retrieved literature reviews was manually searched to find potential articles to include in the review. The search for published studies was performed by the main researcher/author (FC) and the results were independently screened by a co-researcher (AK), and disagreements were resolved through mutual discussions between them.

Study Selection

The inclusion criteria were as follows: 1) Randomised control trials OR reviews; 2) Trained adult participants (>3 hours training per week/minimum 2 years training in selected sport); 3) Average age ≥18 years; 4) consumed supplement included anthocyanin-rich food or extract (black grape, blackberry, blackcurrant, blueberry, cherry, chokeberry, elderberry, plum, pomegranate, raspberry, red wine, strawberry or other red/blue/purple berries where anthocyanin content was reported] given before exercise (administration could continue afterwards) (Manach et al., 2004; Pérez-Jiménez, Neveu, Vos, & Scalbert, 2010); 5) Compared against placebo or suitable control; 6) Single or double-blind in study design; 7) Performance measured with clear performance outcomes (such as time-trial, time to exhaustion and/or a functional quantified metric).

Exclusion criteria: 1) Participants aged <18 years; 2) Anthocyanin product taken alongside another intervention type (might be some conditions in this) 3); Smokers or diseased participants; 4) Animal or in-vitro studies; 5) No appropriate control or reference groups.

Chapter Four

Results

Description of selected studies

The search results, presented in Figure 4, identified a total of 156 articles related to the selected search descriptors. From the 156 articles, 59 of them were removed because they were duplications and a further 2 that were irrelevant to the search criteria. From the remaining 69 articles, 5 meta-analysis' and 12 reviews were removed. From the 52 articles assessed for their eligibility, 41 were removed because they did not meet the inclusion criteria and were unrelated to the impact of anthocyanin on physical performance. A review of the references lists of published work was also screened but provided no additional literature. Overall, a total of 11 studies were included in the performance-focussed systematic review.

Quality assessment of the identified studies

The screening of papers was performed by the primary researcher (FC) along with the inclusion and exclusion process of randomized control trials. In Table 1, the results of the Physiotherapy Evidence Database (PEDro) scale evaluation are presented individually (Moseley, Elkins, Van der Wees, & Pinheiro, 2020). In total, the PEDro scale consists of 11 items encompassing external validity (item 1), internal validity (items 2 to 9), and statistical reporting (items 10 to 11). 1) Eligibility criteria and source, 2) Random allocation, 3) Concealed allocation, 4) Baseline comparability, 5) Blinding of participants, 6) Blinding of therapists, 7) Blinding of assessors, 8) Adequate follow-up (>85%), 9) Intention-to-treat analysis, 10) Between-group statistical comparisons, 11) Reporting of point measures and measures of variability. Items are rated yes or no according to whether the criterion are clearly satisfied in each study. Items 2-11 are included in the score and each score is based on a quality rating: <4 are considered 'poor', 4 to 5 are considered 'fair', 6 to 8 are considered 'good' and 9 to 10 are considered 'excellent' (Cashin & McAuley, 2020).

Study characteristics

Among the performance focussed studies included in this systematic review, the samples were composed on an average 13.2 ± 2.8 individuals, ranging from 8 to 18 subjects, and the mean age of participants ranged from 19.7 ± 1.6 to 38 ± 13 years (Table 2). The information extracted from the records identified: study source (including authors and year of publication), study design, anthocyanin administration (dose and timing), sample size, characteristics of the participants (training status and sex), and performance outcomes of the intervention. Based off the PEDro quality assessment of the

11 articles, 5 articles had a quality score of 'excellent' and 6 had a quality score of 'good'. Of the 5 studies that provided an 'excellent' score based of the PEDro Scale, the difference between these studies compared to the studies in this systematic review that scored a 'good' was primarily due to either their lack of adequate follow-up or compliance within the participants and lack of baseline comparisons. Compliance of 85% or more was exhibited in those with a higher score. The criterion that baseline data of the study was presented was not met in 6 studies.

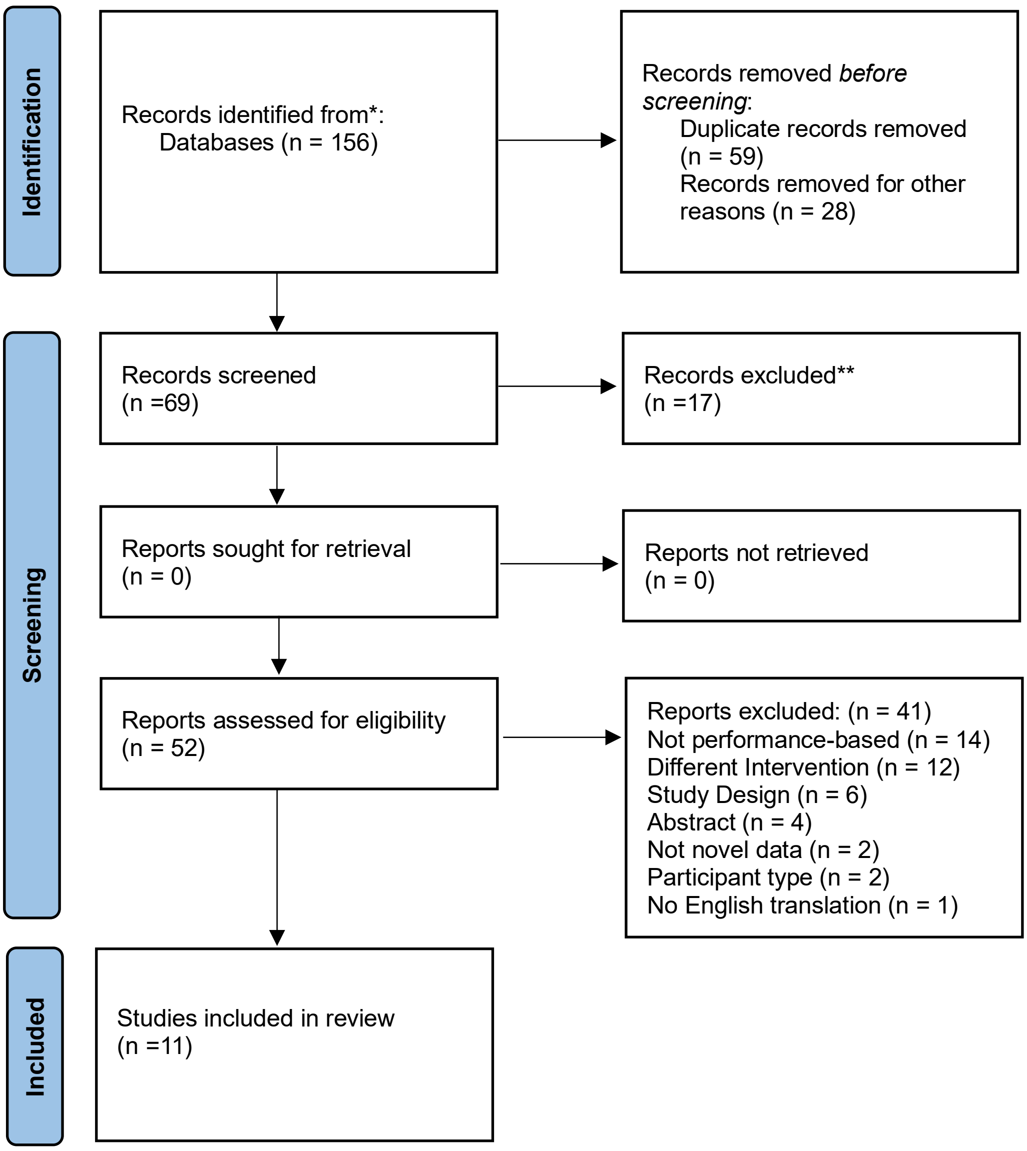


Figure 4: PRISMA flow diagram; selection of studies

Table 2: Quality Assessment of Performance Studies using PEDro scale

Study	ECS	RA	CA	BC	BP	BT	BA	AF	ITTA	BGC	PMV	Score	Quality
(Brandenburg & Giles, 2019)	✓	✓	X	X	✓	✓	✓	✓	✓	✓	✓	8/10	Excellent
(Cook et al., 2015)	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	9/10	Excellent
(Fryer et al., 2020)	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	9/10	Excellent
(Fryer et al., 2021)	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	9/10	Excellent
(Morgan, Barton, & Bowtell, 2019)	X	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	9/10	Excellent
(Moss, Brindley, Enright, Highton, & Bott, 2023)	✓	✓	X	X	✓	✓	✓	X	✓	✓	✓	7/10	Good
(Murphy, Cook, & Willems, 2017)	✓	✓	X	X	✓	✓	✓	X	✓	✓	✓	7/10	Good
(Pastellidou et al., 2021)	✓	✓	X	X	✓	✓	✓	X	✓	✓	✓	7/10	Good
(Perkins et al., 2015)	✓	✓	X	X	✓	✓	✓	X	✓	✓	✓	7/10	Good
(Potter et al., 2020)	✓	✓	X	X	✓	✓	✓	X	✓	✓	✓	7/10	Good
(M. E. T. Willems et al., 2016)	✓	✓	X	X	✓	✓	✓	X	✓	✓	✓	7/10	Good

Abbreviations - AF: Adequate follow-up (>85%), BA: Blinding of assessors, BC: Baseline comparison, BGC: Between-group comparison, BP: Blinding of participants, BT: Blinding of therapists, CA: Concealed allocation, ECS: Eligibility criteria and source, ITTA: Intention-to-treat analysis, PMV: Point measure and variability, RA: Random allocation.

Review Results

Provided in this review are 11 studies, in which running, cycling and rock climbing were assessed (Table 3). Running performance was assessed within five studies, two studies included an acute dosing protocol, with the main performance outcomes of time-trials providing one significant improvement in a 5-km run. Three running performance trials included a seven-day dosing protocol with an improvement in total distance and time-to-exhaustion trials. Three studies assessed cycling performance where the mean improvement was 2.7% for performance trials between 4km and 16.1km. Three studies utilised forearm grip protocols for assessing rock climbing performance with improvements in MVC for 60% and not 40%, with one study showing a 23% improvement in total hang time.

Table 3: Summary of the anthocyanin supplementation and sport performance studies (n=11) included in review

Study	Study Population	Study design and duration	Dosing Protocol (anthocyanin mg/day)	Dosage timing before exercise	Performance protocol	Outcomes measure	Outcomes (between/within group)
(Brandenburg & Giles, 2019)	N = 14 Healthy runners Age: 31.3 ± 10.3	RCT Cross-over 2 days or 4 days	24 g Blueberry powder (336 mg ANC per serving) 3 x a day (T:1008 mg/day) 2DAYS OR 4DAYs	Not specified	8-km time-trial (TT) and counter-movement vertical jump (CMVJ)	TT CMVJ	Within group: TT: ↔ CMVJ: ↔
(Cook et al., 2015)	N = 14 healthy men Age: 38 ± 13 years	RCT Cross-over 7 days	1x BC capsule (105 mg ANC)	2 hours	30min cycling; 3x10min stages at 45%, 55%, 65% VO_{2max}, followed by a 16.1-km time-trial	TT	Between group TT: ↑* ($p = 0.027$)
(Fryer et al., 2020)	N = 12 intermediate rock climbers Age: 26 ± 6	RCT Cross-over 7 days	2x BC capsules (210 mg ANC)	2 hours	Isometric forearm muscle contraction time-to-exhaustion muscle volitional capacity @ 40%	TTE MVC	Between group: TTE: ↔ MVC: ↔
(Fryer et al., 2021)	N = 12 Intermediate and advanced rock climbers Age: 25 ± 4	RCT Cross-over 7 days	2x BC capsules (210 mg ANC)	2 hours	Isometric forearm muscle contraction time-to-exhaustion muscle volitional capacity @ 60%	TTE MVC	Within group: TTE: ↓* ($p < 0.001$) MVC: ↔ Between group: TTE ↔ MVC: ↔

(Morgan et al., 2019)	N = 8 Male competitive cyclists Age: 19.7 ± 1.6	RCT Cross-over 7 days	6 x Montmorency cherry capsules (257 mg ANC)	60 minutes (3 pills consumed)	15-km time-trial	TT	Between groups: TT: ↑* 4.6 ± 2.9% (P <0.05)
(Moss et al., 2023)	N = 16 trained male runners Age: 26 ± 5	RCT Cross-over Acute 1-day	3 x BC capsule (315 mg ANC)	2 hours	5-km time-trial followed by 10-min at lactate threshold	TT	Between group: TT: ↑* ($p = 0.001$)
(Murphy et al., 2017)	N = 10 male cyclists Age: 30 ± 12	RCT Cross-over 7 days	1 x BC capsule (105 mg ANC)	2 hours	2 x 4-km cycling time-trial	4-km (1st) 4-km (2nd)	Within groups: 4-km (1st): ↔ 4-km (2nd): ↔ Between groups: 4-km (1st): ↔ 4-km (2nd): ↔
(Pastellidou et al., 2021)	N = 15 recreationally active males Age: 24.4 ± 3.6	RCT Cross-over 7 days	1 x BC capsule (105 mg ANC)	Not specified	Running incremental step test	Critical power Distance TTE	Within group: Critical power: ↔ Distance: ↔ Between group: TTE: ↔
(Perkins et al., 2015)	N = 13 Active males Age: 25 ± 4	RCT Cross-over 7 days	1x BC capsule (105 mg ANC)	3 hours	Rapid ramp test (VO_{2max}), High intensity intermittent treadmill running test	Distance of HIIR Distance of RS	Between group: Distance HIIR: ↑* 10.6% ($p = 0.023$) Distance RS: ↑* 10.8% ($p = 0.024$)

(Potter et al., 2020)	N = 18 Male sport climbers Age: 24 ± 6	RCT Cross-over 7 days	2x BC capsules (210mg ANC)	Not specified	Time to exhaustion , pull-ups (PU), total climbing time (TCT) and handgrip strength (HS)	TTE PU TCT HS	Within group: TCT: ↑ 31.7 ± 11.6s TCT: ↑ 23% Between group: TTE ↑* (p = 0.062) PU: ↔ HS: ↑
(M. E. T. Willems et al., 2016)	N = Thirteen males Age: 22 ± 1	RCT Cross-over 7 days	1 x BC capsule (105mg ANC)	3 hours	5 × 15 min blocks with intermittent 15-m maximal sprints, interspersed by moderate and high-intensity running, and TTE	15-m sprint time average (15-m AV) TTE Vertical jump (VJ) power	Between group: 15-m AV:↔ TTE: ↔ VJ Power: ↔

Abbreviations - ANC: Anthocyanin, AV: Average, BC: Blackcurrant, CMVJ: Counter-movement vertical jump, ES: Effect size (using Cohen's d), HIIR: High-intensity intermittent running, HS: Handgrip strength, HT: Hang time, m: Meters, PU: Pull-ups, RCT: Randomised control trial, RS: Repeated sprints, s: Seconds, T: Total, TCT: Total climbing time, TT: Time-trial, TTE: Time-to-exhaustion, VJ: Vertical jump, **↔:** No change **↓:** Decrease**, ↑:** Improvement/increase

*: indicates a significant change ($p < 0.05$)

Chapter Five

Discussion

The present study represents an analysis and evaluation of the effects of dietary anthocyanin intake on physiology and athletic performance from the available literature that considers anthocyanin dosages, time, performance outcomes and study duration. The primary aim of this review of the literature is to investigate the impact of anthocyanin intake on physical performance and adaptations during exercise. The primary finding of this review indicated that anthocyanin results in significant increases in time-trial and time-to-exhaustion performance measures in running and cycling, though with mixed results within other high-intensity performance tests (Table 3). The proposed mechanisms behind anthocyanins ability to increase exercise performance include anthocyanins vasodilatory properties that can increase peripheral blood flow. This is likely caused by an enhanced endothelial function due to the upregulation of nitric oxide from consumption of anthocyanin containing fruits (Festa et al., 2021; Rodriguez-Mateos et al., 2013). Of the literature assessed in this study, anthocyanin containing berries, and in particular, blackcurrant displayed the most significant effects overall in performance markers as displayed in Table 3.

Research using blackcurrants as a means to improve exercise performance has been quite prevalent, but only in the past decade. Of the eleven studies in this review, nine used blackcurrants in their anthocyanin protocol, specifically, a New Zealand blackcurrant (NZBC) supplement that has higher anthocyanin content, with the total anthocyanin content in New Zealand blackcurrant juices ranging between 346 and 850 mg/100 mL, compared to 179–310 mg/100 mL for other varietals (Haswell, Ali, Page, Hurst, & Rutherfurd-Markwick, 2021), and approximately equivalent to 80 blackcurrants a day in the capsule, the anthocyanin content shows much higher bioavailability of anthocyanin when grown in New Zealand. The NZBC supplement consists of 300mg blackcurrant and 105mg of anthocyanin per capsule. According to the manufacturers (CurraNZ™, Health Currancy Ltd, Surrey, UK) each 300 mg NZBC capsule contains 105 mg of anthocyanins, consisting of 35–50% delphinidin-3-rutinoside, 5–20% delphinidin-3-glucoside, 30–45% cyanidin-3-rutinoside, and 3–10% cyanidin-3-glucoside. Dosing varied between each study, with five studies using one capsule (105mg anthocyanin), three studies used two capsules (210mg anthocyanin) and one used three capsules (315mg anthocyanin) per day of their intervention period.

Acute anthocyanin dosing

Acute anthocyanin doses, defined for the purpose of this review as a single dose and up to four days of supplementation, have been shown to improve performance in time-trials. The most recent but shortest dosing duration protocol in the current analysis was a study by Moss et al. (2023) with 16 trained male runners. This study had the highest single day dosing protocol in this analysis with three NZBC capsules (315mg/day anthocyanin) consumed two hours before a 5-km running TT. Following this, there was a 10-min run at lactate threshold. Results indicated no improvements in metabolic and physiological response such as substrate oxidation, RER, lactate or heart rate but a significant 2.9% increase in 5-km running performance compared to placebo ($p = 0.001$; NZBC: 1,308.96 ± 122.36 s, PL: 1,346.33 ± 124.44 s, $d = −0.23$). Similarly, a recent study by S. Montanari, Blacker, and Willems (2023) also assessed the acute effect one-off dosing (315mg anthocyanin NZBC) on performance in a 16.1km cycle with male and female cyclists ($n = 34$). Interestingly, when categorised by performance ability, NZBC consumption resulted in a 20 s faster time in the 'slow' group ($p = 0.02$; NZBC: 1479 ± 83 s, 95% CI [1437, 1522 s]; PLA: 1499 ± 91 s, 95% CI [1452, 1546 s]), but no notable increase was observed in the 'fast' group. Physiological and metabolic responses were not measured in this study, so no conclusions can be drawn for the effect of blackcurrant anthocyanins intake on peripheral blood flow and potential of lactate clearance and substrate utilisation. However, the findings of this study could be applied to provide potential benefits to less-experienced cyclists to show minor but noticeable improvements in their endurance performance over a short period of time. These findings show insight into the benefits of acute dosage of NZBC supplementation.

Of the acute studies outlined in Table 2 that did not use blackcurrant supplements, was a study by Brandenburg and Giles (2019). They had the highest dosage of all the studies collated for the current review, at 1008mg/day of anthocyanin. In this study, 14 runners completed an 8-km TT, followed by counter-movement vertical jump (CMVJ) and depth jump test were measured with a supplementation protocol of a blueberry powder extract. Participants were split into placebo, 4 days (4DAYS) blueberry supplementation or 2 days of placebo followed by 2-days (2DAY) of blueberry supplementation groups. In a randomised control, crossover design, the groups consumed a 24g each blueberry extract packet, three times daily (336mg anthocyanin per packet) or identical placebo three times daily. Overall, for all groups no statistical differences were observed in the 8-km TT. However the results indicated that post-TT lactate was significantly lower in the 4DAY group than the 2DAY and placebo groups ($p = 0.038$), with a significant interaction observed in blood lactate responses to the 8-km TT ($p = 0.027$). In another study, blood lactate was significantly lower in the blueberry group (PL: 8.9 ± 2.7; Blueberries: 7.2 ± 1.9; $p = 0.02$) post 30-min running TT in normobaric hypoxia conditions (altitude >1200m) following a 4-day blueberry extract supplementation (Brandenburg & Giles, 2021), but not following TT. The supplementation protocol was in line with their previous work (2DAY and 4DAY interventions; 336mg anthocyanin daily) (Brandenburg & Giles, 2019). The lower blood lactate values in 4-day supplementation protocol were likely the result of increased lactate clearance and/or reduced lactate production due to anthocyanins vasodilatory properties (Rodriguez-Mateos et al., 2014). Similar to previous work, blueberry supplementation did not elicit in differences for TT times, and additionally other metabolic and physiological responses did not differ as well (Brandenburg & Giles, 2019). Overall, there is growing evidence to suggest that anthocyanins can be ergogenic when acute doses (1-4 days) are consumed with an effective dosage exceeding 300mg/day.

Chronic anthocyanin dosing

While short duration acute anthocyanin dosing periods have shown some performance benefits (Brandenburg & Giles, 2019, 2021; S. Montanari et al., 2023; Moss et al., 2023), analysis from this literature review indicates that several studies have adopted longer dosing durations >4 days and observed performance gains in a range of activities including cycling, running and activities that require speed, power and strength.

Cycling

Cook et al. (2015), conducted a randomised-control crossover trial and reported for the first berry-induced performance enhancing outcome. In this study, 14 healthy men completed a 16.1km time-trial on a cycle ergometer and a 2.4% average decrease in time-trial time was observed with NZBC supplementation (300mg blackcurrant containing 105mg of anthocyanin per capsule) taken for seven days compared to a placebo control. Alongside this, they also observed an increase in fat oxidation in participants that was 27% higher compared to placebo at 65% VO_{2max} during a 10-min cycling test, with no differences in heart rate and oxygen consumption. NZBC supplementation of 105mg anthocyanin for seven days has also shown a significant improvement in repeated 2 x 4-km cycling time trials, with a 0.82% decrease in time compared to placebo on the total time to complete the trials (PL: 771 ± 60 s, NZBC 764 ± 56 s, $p = 0.034$), with a slightly higher, although not significant difference in cadence and power output (wattage) on cycling ergometer (PL: 747 ± 138 W; NZBC 754 ± 140 W; $p = 0.095$). It was likely that the ergogenic effects of NZBC were observed in the second 4-km trial were due to the participants reduced fatigued state, though no effect was observed in metabolic or physiological responses (Murphy et al., 2017). Stefano Montanari, Şahin, Lee, Blacker, and Willems (2020) also observed time difference in repeated 3 x 16.1-km time trials over seven days, with 105mg and 210mg NZBC anthocyanin dosage. However, the time differences were only observed between day one and day four (D1: 1701 ± 163 s; D4: 1682 ± 162 s; 1.1% $p = 0.05$) of taking the 210mg anthocyanin supplement, but not after day four and no difference in metabolic and physiological responses were observed to help explain the observations.

When assessing changes in altitude on performance whilst supplementing anthocyanin, a randomised control cross-over trial by M. E. T. Willems, Şahin, Berendsen, and Cook (2019) assessed eleven trained males cyclists 16.1km cycling time following a 3 x 10 minute (45%, 55% and 65% VO_{2max}) steady state ride, after seven-days of 210mg/day NZBC intake. Assessment took place in a simulated normobaric hypoxic environment, with altitude conditions of ~2500 meters. However, no effect on physiology (blood glucose, lactate, heart rate, substrate oxidation, and respiratory exchange ratio) or cycling performance (NZBC: 1685 ± 99 s; PL: 1685 ± 92 s, P = 0.974) was observed compared to placebo. Compared to other plant-based supplements such as nitrate (beetroot extract) where a single dose provided a significant increase of 2.9% in TT performance compared to baseline (Baseline: 1716 ± 17 s; Beetroot (BR): 1664 ± 14 s, P = 0.006, CI 15.3 – 66 s) and an significant improvement compared to placebo (PL: 1702 ± 15 s, P = 0.021) (Katayama, Goto, Ishida, & Ogita, 2010). This study by Willems et al., also contradicts Cook et al. (2015) results on fat oxidation and TT performance despite having doubled the anthocyanin content. It could be speculated that hypoxia induced vasodilation is not influenced by the vasodilatory properties of anthocyanin from blackcurrants, however the mechanisms are not fully understood as research on the effect of anthocyanin intake in high altitude conditions is less prevalent.

Other anthocyanin containing fruits that have shown potential in improving cycling performance include cherries and blueberries. In this randomised control-crossover study eight trained cyclists, consumed in three Montmorency cherry capsules morning and night (six total capsules daily; 257 mg of anthocyanins/day) for seven days (Morgan et al., 2019). A 10-min steady state bout at 65% VO_{2max}, followed by a 15-km TT were assessed. Tart cherry supplementation significantly improved 15-km cycling performance by 4.6 ± 2.9% (74 ± 50 s) compared to placebo. Performance times were observed during the middle 5-km and final 5-km indicating a group performance which was consistent in all eight participants, ranging from a 9 second (0.6%) improvement to a 155 second (8.9%) improvement in one participant. Interestingly, this study also saw a dose-dependent increase of >8% like Cook et al. (2015) in the most improved participant. In contrast, a study using blueberry powder with higher anthocyanin content but for less days than the Morgan et al., study observed no improvements to 30-min cycling TT, but did observe increased lactate clearance (Brandenburg & Giles, 2021).

Running

For running performance, Perkins et al. (2015) was the first to assess the effects of daily NZBC supplementation (105mg anthocyanin) for seven-days, measuring high-intensity performance. 13 active males (25 ± 4 years) were examined in a treadmill running protocol consisting of a rapid ramp test to volitional exhaustion, and a high intensity intermittent running (HIIR) test to assess sprinting performance. Participants increased the number sprints (PL: 34 ± 4; NZBC: 35 ± 6) and increased total distance significantly by 10.6% (PL: 3871 ± 622 m; NZBC: 4282 ± 833 m; P=0.023), which incidentally significantly increased total distance covered by 10.8% (PL: 2572 ± 421 m; NZBC: 2849 ± 570 m, P=0.024) compared to placebo in the HIIR test. Additionally, there was no significant responses in the rapid ramp test between conditions for HR, oxygen uptake, blood lactate and rate of perceived exertion (RPE). HIIR testing results highlighted a high blood lactate trend at exhaustion by 15% ($p = 0.07$). This evidence provides promising effects of anthocyanin consumption on repeated sprinting performance of relevance to team sports.

M. E. T. Willems et al. (2016) investigated NZBC anthocyanin consumption in a study with 13 males, assessing the Loughborough Intermittent Shuttle Test (LIST) and vertical power, involved 5 x 15-min blocks with intermittent 15-m maximal sprints, with vertical jump testing after completion of two blocks, this protocol was used to simulate team sport activity, and participants ran until the required pace was no kept up with. Dosing with 105mg of anthocyanin for seven-days provided no effect on 15-m sprint time but reduced slowing of the fastest sprint between block one and five (PL: 0.12 ± 0.07 s; NZBC: 0.06 ± 0.12 s; $p < 0.05$) but no significant change to time-to-exhaustion (TTE) time but providing increases to 60% of the participants in this measure. However, there were no effect on HR and lactate responses. In addition to running performance Pastellidou et al. (2021) assessed 15 males running performance in an incremental step test with a seven-day NZBC (105mg anthocyanin) supplementation, with no significant performance responses in speed (PL: 12.1 ± 1.0 km/h; NZBC 11.9 ± 1.0 km/h, $p > .05$) and distance (PL: 918.6 ± 223.2 m; NZBC 965.2 ± 231.2 m, $p > .05$). However, there was an increase in distance observed in 60% of the participants. A dosage of 315 mg anthocyanin as well as 105mg anthocyanin both provided no effect to performance and substrate utilisation also provided no effect on TTE. Participants in this study did not have familiarisation trials, which could skew pre and post-test results. The timing of consumption of anthocyanin before performance measures was also not disclosed, thus these findings cannot be compared to those from Perkins et al., and Willems et al., who had their dosing protocol two hours before performance testing.

Power, speed and strength

Willems et al. (2016) observed a potential resistance to fatigue with NZBC anthocyanin consumption linked to vertical power, three maximal vertical jumps were tested approximately 10-15s after each block of running performance, indicating a slight trend of improved performance compared to placebo, indicating potential resistance to fatigue when supplementing NZBC, however not significant. Running is prevalent in many sports and some, including soccer and rugby incorporate many jumps, anthocyanin consumption may be beneficial to improve team sport performance over all spectrums, however more research assessing anthocyanin consumption on game-day performance needs to be done. NZBC was also tested in rugby players on sprint performance (Illinois agility test), seated medicine ball throw and handgrip strength – consistent actions performed in game (Leite et al., 2016; Vaz, Kraak, Batista, Honório, & Miguel Fernandes, 2021). Proving faster averages in sprint times (PL: 18.46 ± 1.44 s, 95% CI [17.59, 19.33 s]; NZBC extract: 18.15 ± 1.22 s, 95% CI [17.41, 18.88 s], d = −0.24 (small), p = 0.07), but no improvement in grip strength (PL: 50.1 ± 8.2 kg, 95% CI [45.1, 55.0 kg]; NZBC extract: 49.7± 8.4 kg, 95% CI [44.6, 54.8 kg], p = 0.74) and seated medicine ball (PL: 5.57 ± 0.58 m, 95% CI [5.22, 5.92 m]; NZBC extract: 5.47 ± 0.60 m, 95% CI [5.11, 5.83 m], p = 0.11). This indicates a trend of anthocyanin not affecting peak power and some strength markers.

Building on from earlier research by Matsumoto et al. (2005) who assessed the effects of anthocyanin blackcurrant consumption on forearm circulation and blood flow during typing, Potter et al. (2020) was one of the first to assess rock climbing performance following a seven-day NZBC 210mg/day anthocyanin supplementation. Eighteen sports climbers were assessed on climbing ability through, hang time, pulls ups, total distance and a time-to-exhaustion. The number of pulls did not significantly increase following NZBC but hang time did (p = 0.062) compared to placebo (PL: 29.3 ± 10.6 s; NZBC: 31.7 ± 11.6 s). Total climbing time was assessed three times each revealed a significant interaction ($F(2, 34) = 6.24$, $P = 0.005$, $\eta 2\ p = 0.27$, power = 0.87) with climbing time increasing by 23% across the three climbs with NZBC, but only 11% in the placebo group. NZBC indicated no significant effects in RPE and HR during the climbs, and lactate indicated lower levels of response during the climbs and in the repeated bouts of climbing. In the same year, Fryer et al. (2020) assessed 12 intermediate-level rock climbers who performed submaximal intermittent contractions at 40% maximal voluntary contraction (MVC) to volitional exhaustion, after a dosing of 210mg of anthocyanin. However, no significant effect on MVC was observed (p = 0.935) and TTE (p = 0.809), with no responses to blood flow with the NZBC dose compared with placebo. However the tissue saturation index (TSI), assessed via forearm NIRS of the dominant arm, was higher in the NZBC than placebo (PL:43 ± 8; NZBC; 50 ± 11 TSI%; p=0.007; Cohens' d=1.01), which could indicate improved blood flow. Fryer et al. (2021) then assessed MVC at 60% following NZBC capsules with 210mg of anthocyanin, NZBC provided no improvement in MVC (56.1 vs. 56.2 kg), but TTE did improve, indicating a main effect of time, but for both conditions (p <0.001), with additionally an improvement in oxidative capacity (PL: 14.4 ± 6.8; NZBC: 9.1 ± 4.2 s respectively; mean difference= 5.3, 95 CI % = 0.4–10.2 s; p = 0.036, d = 0.94) and TSI (p = 0.046) indicating a better blood flow response as well. This change provides a positive effect to higher intensity muscle contraction in rock climbing performance when supplementing NZBC. The research collated in this systematic review highlighted that anthocyanin is beneficial for enhancing peripheral blood flow and substrate utilisation. These outcomes may be protective in the context of metabolic syndrome, cardiovascular disease, hypertension and Type 2 Diabetes Mellitus. The practical applications of the research collated in this systematic review indicates a supplementation dosage in between 100mg and 310mg per day of anthocyanin can provide overall health benefits and ergogenic effects to performance mainly in the use of time-trials, time-to-exhaustion and help with muscle fatigue**.** Overall, more research is required to solidify the findings to date, and to quantify the effective dosage and timing for anthocyanin supplementation recommendations for athletes.

Limitations

The main limitation of this systematic review was the small sample, overall the number of studies that were accepted for review were small, the change from initial Boolean phrases searches to determine different study samples was large, and after checking for eligibility diminished it to just 11. Small sample size may introduce errors of interpretation and caution is advised within the practical applications of this review. The evidence provided does having some acknowledgement in the overall anthocyanin and performance research but may not be up to par when comparing this dissertation level systematic review to other researchers overall conclusions who have more experience, time and funds in this field of research.

Another limitation to this review was the overall consensus on what was interpreted as 'chronic' in this review, after method searching the literature that fit the criteria, it became consistent in supplementation protocols that a seven-day dosage period was the maximum time for dosing. For the purpose of this review, acute dosing consisted of single dose anthocyanin (Moss et al., 2023) and upwards to four days (Brandenburg & Giles, 2019), whereas chronic dosing consisted of anytime exceeding four days which the overall literature search including mostly seven-day protocol. In anthocyanin research for performance, more research is needed long-term, exceeding seven days to state a conclusion or benefit to chronic dosing of anthocyanin, and in particular New Zealand blackcurrant.

A limitation of the studies involved in this review is that is cannot be ruled out that some participants did not consume anthocyanin-based products in the 48-hr anthocyanin/polyphenol cessation periods of these performance protocols. Due to wide variety of anthocyanins in normal dietary intake participants may have consumed more than necessary anthocyanins, which could potentially skew the result. Additionally, some studies used dietary restrictions to reduce anthocyanin intake. There may be an overestimate in the effect, as removal of natural antioxidants from the diet might theoretically impair the natural processes of anthocyanins; therefore consumption of anthocyanin may only be increased to pre-restriction intake, whereas placebo remains in a depleted state.

Also, the washout periods differ in between the studies, for example, some studies incorporated a seven-day wash out period between each period of the crossover trial (Murphy et al., 2017; M. E. T. Willems et al., 2016), whereas most included a washout period of 14-15 days. In line with 1-month reported of a return to baseline of biochemical parameters and biomarkers of antioxidant status after 15-day washout (Alvarez-Suarez et al., 2014), which provides rationale for 14–15-day washout period with these studies. Having a washout period below this may skew the results as anthocyanin may be still circulating in the body from the supplement in the pre-test phase of a crossover trial.

Future considerations

There are several avenues for future research that would benefit the anthocyanin and sport performance literature base. Identifying the optimal dosage of NZBC or anthocyanin supplementation for physiological and performance gains is likely to require further research. The research from this review shows variable dosages and durations of supplementation between studies with some, but not all, leading to performance enhancement. The most positive increase was observed with an anthocyanin dosage of 105mg anthocyanin, following a dosage of 210mg, then a 315 mg dosing. However 315mg was only included once in Table 2 and in a single dose. More research is needed with the variety of dosages and future research should try and distinguish the optimum dosage and time needed for performance, an important factor in this review.

Additionally, as a seven-day supplementation of anthocyanin shows promise for exercise performance; future studies should look to determine larger time-trial and time periods assessing anthocyanin use in endurance performance testing, such as assessing endurance performance beyond 120-mins at 45% Future research in the long-term effects of using anthocyanin supplements, such as 4-week, 8-week or even 12-week supplementation periods may provide insight to competition preparation of anthocyanin in athletes. Future study of different types of training might need to be explored further than what is included in this review, in terms of team sports and a larger sport application to provide a probable conclusion on the efficacy of supplementing anthocyanin products, such as New Zealand blackcurrant supplements.

Finally, some researchers have reported that dietary anthocyanin in berries acted as inhibitors for carbohydrate digestive enzymes, by competing with carbohydrates and inhibiting α-glucosidase due to the similar structure of β-linked maltose and glucosyl groups on the anthocyanin aglycones which help control glucose homeostasis and potentially reducing the post prandial rise in blood glucose levels (Z. Li et al., 2023; McDougall & Stewart, 2005). This may have implications for athletes who consume high carbohydrate loads and should be considered when planning an athletes dietary pattern when considering anthocyanin supplementation. More research is required to further consolidate this finding.

Conclusion

In summary, there is evidence to suggest that consumption of anthocyanins prior to exercise can enhance athletic performance. The majority of performance benefitting studies to date have shown anthocyanin-containing New Zealand blackcurrant to be effective across a range of exercise durations and intensities. However, showing consistent evidence in increased cycling performance. The mechanisms for the improvement of exercise from anthocyanin consumption and subsequent results in blackcurrant consumption may result from increased peripheral blood flow, and subsequent antioxidant and anti-inflammatory properties of anthocyanins. However more research is needed with varying supplementation protocols, different performance trials and calibre of athletes in order to provide further evidence of anthocyanins ability to enhance performance in various contexts and sporting groups as well as the protective, health-related effects of anthocyanin supplementation.

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