The Effect of Black Chokeberry (Aronia melanocarpa) on Human Inflammation Biomarkers and Antioxidant Enzymes: A Systematic Review of Randomized Controlled Trials

Article *in* Nutrition Reviews · November 2024

DOI: 10.1093/nutrit/nuae143

CITATIONS
7

READS
90

5 authors, including:

Buse Sarıkaya
Amasya University
13 PUBLICATIONS **63** CITATIONS
SEE PROFILE

Ezgi Melody Kolay
EFAD
16 PUBLICATIONS **141** CITATIONS
SEE PROFILE

Merve Guney-Coskun
Istanbul Medipol University
27 PUBLICATIONS **181** CITATIONS
SEE PROFILE

Aslı Yiğit Ziolkowski
University of Life Sciences in Poznań
15 PUBLICATIONS **200** CITATIONS
SEE PROFILE

Systematic Review

The Effect of Black Chokeberry (*Aronia melanocarpa*) on Human Inflammation Biomarkers and Antioxidant Enzymes: A Systematic Review of Randomized Controlled Trials

Buse Sarıkaya, PhD [1,*], Ezgi Kolay, MSc [2], Merve Guney-Coskun, MSc [3], Aslı Yiğit- Ziolkowski, PhD [4], Şule Aktaç, PhD [5]

[1]Department of Nutrition and Dietetics, Faculty of Health Sciences, Amasya University, Amasya 05100, Turkey; [2]Dietitian, Independent Nutrition Reseacher, Istanbul 34000, Turkey; [3]Department of Nutrition and Dietetics, Faculty of Health Sciences, Medipol University, Istanbul 34810, Turkey; [4]Department of Biochemistry and Biotechnology, Poznan University of Life Sciences, Poznan 60-632, Poland; [5]Department of Nutrition and Dietetics, Faculty of Health Sciences, Marmara University, Istanbul 34854, Turkey
*Corresponding Author: *Buse Sarıkaya*, Department of Nutrition and Dietetics, Faculty of Health Sciences, Amasya University, İpekköy Yerleşkesi, 05100 Merkez/AMASYA, Turkey (buse.sarikaya@amasya.edu.tr).

Context: *Consuming antioxidant-rich foods has been associated with potential benefits in managing chronic diseases by reducing oxidative stress and inflammation.* ***Objective:*** *This systematic review aimed to evaluate the effects of Aronia melanocarpa (aronia berry or chokeberry) on human inflammation biomarkers and antioxidant enzymes.* ***Data Sources:*** *A systematic search was conducted across multiple databases, including PubMed, Scopus, Science Direct, and Web of Science, to identify relevant studies investigating the potential effects of aronia on human inflammation biomarkers and antioxidant enzymes between April 2022 and November 2023.* ***Data Extraction:*** *The selection of studies followed the PRISMA guidelines, data screening was conducted by 4 independent reviewers, and data extraction and risk-of-bias assessments were performed by 2 independent reviewers using the Cochrane Risk of Bias 2 tool.* ***Data Analysis:*** *A total of 1986 studies were screened, and 18 studies that met the inclusion criteria were included in a systematic review that investigated the anti-inflammatory effects of aronia on various health parameters. These studies primarily focused on the effects of aronia on cardiometabolic diseases, performance in sport, and other health parameters.* ***Conclusions:*** *This study examined the effects of Aronia intervention on human health outcomes using aronia juice, extract, or oven-dried powder for a period of 4 to 13 weeks. The primary health parameters considered were C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), interleukin-8 (IL-8), interleukin-10 (IL-10), interleukin-1ß (IL-1ß), superoxide dismutase (SOD), catalase (CAT), and reduced glutathione peroxidase (GSH-Px). The results showed that aronia had a beneficial effect on several inflammatory cytokines, including reductions in CRP, TNF-α and IL-6 concentrations, as well as elevated IL-10 levels. Moreover, positive changes have been observed in antioxidant enzyme systems, including; elevated SOD, GSH-Px and CAT activity. The findings of the presented studies provide evidence that Aronia melanocarpa may have beneficial effects on inflammatory markers.* ***Systematic Review Registration:*** *PROSPERO registration No. CRD42022325633.*

Key words: *antioxidants, Aronia melanocarpa, black chokeberry, inflammation.*

https://doi.org/10.1093/nutrit/nuae143

INTRODUCTION

Aronia melanocarpa, known as black chokeberry, belongs to the Rosaceae family and is originally from North America. It is widely cultivated as a nutraceutical in Poland, Germany, and Russia.[1] In addition, it is a low-maintenance crop that effectively repels pests, and it is consumed in European countries in the form of fruit juices, jams, jellies, and teas as part of the diet.[2] Aronia berries are black-purple, with a 6–13 mm diameter and a weight of 0.8–2 g. Among berries, aronia berries are widely recognized for their high polyphenol and bioactive content, which makes them an excellent source of antioxidants, and they are deemed to have numerous health benefits.[3,4] The aronia peel contains 73% of the anthocyanins, while the flesh contains 78% of the phenolic acids.[5] Notably, the European Food Safety Authority (EFSA) has confirmed the "antioxidant effects" health claim for aronia.[6]

Extensive research has been conducted on antioxidants in the last 20 years due to the discovery of the role of free radicals in the development of diseases.[7] Oxidative stress within the cell emerges due to the imbalance between reactive oxygen species (ROS) production and antioxidant defense systems.[8,9] Both oxidative stress and inflammation are central to the development and progression of several chronic diseases, including chronic obstructive pulmonary disease (COPD), diabetes, cardiovascular diseases (CVDs), neurodegenerative diseases, and cancer.[10] Chronic inflammation is characterized by increased production of pro-inflammatory cytokines IL-1ß, IL-6, IL-8, and TNF-α, and hepatic acute-phase proteins, e.g. C-reactive protein (CRP).[11,12]

Given their therapeutic value in the prevention and treatment of disease, plant-derived bioactive compounds have attracted significant interest in recent years. These compounds can be obtained from whole plants, plant extracts, or isolated components with complete phytochemical profiles.[13] Antioxidant compounds, including polyphenols, play a protective role by mitigating the harmful impact of ROS and subsequently prompting the upregulation of antioxidative enzymes such as catalase, superoxide dismutase, and glutathione peroxidase.[14] Polyphenols, more precisely anthocyanins, are responsible for the anti-inflammatory properties of berries, supporting their use in human diets and as dietary supplements.[15,16]

In aronia, the types of anthocyanins include cyanidin-3-galactoside, cyanidin-3-glucoside, cyanidin-3-arabinoside, and cyanidin-3-xyloside; types of phenolic acids include chlorogenic and neo-chlorogenic acids; types of flavanols include epicatechin and quercetin glycosides.[17–21] Proanthocyanidins specifically procyanidins constitute 40% of aronia berries' in vitro antioxidant activity, followed by anthocyanins (24%), hydroxycinnamic acids (18%), and epicatechin (11%).[22] Procyanidins are considered better antioxidants than their monomers.[23] Cyanidin and its glucosides, the primary anthocyanin components in aronia extracts, demonstrate extremely potent anti-inflammatory activity.[24] It has been reported that cyaniding-3-glucoside metabolites, the predominant anthocyanin species in aronia, promote a significant reduction in the inflammatory mediator proteins, including IL-6, in human vascular cells.[25]

It has been suggested that Aronia can help prevent the onset of chronic diseases, including diabetes, CVD, and immune system disorders.[26–28] Numerous studies have reported anti-inflammatory effects being associated with *Aronia melanocarpa*, which have been attributed to inhibition of the release of inflammatory cytokines.[29–32] Aronia extract has been shown to have an anti-inflammatory effect on endotoxin-induced uveitis in rats' eyes by suppressing TNF-α and blocking the expression of nitric oxide synthase (NOS).[31] According to a recent study conducted to assess the anti-inflammatory properties of aronia juice on human peripheral monocytes, aronia juice intake was shown to be associated with a significant improvement in immune system function by suppressing the release of pro-inflammatory cytokines such as IL-6, IL-8, and TNF-α,[29] and upregulating IL-10 production in mouse splenocytes.[16] A recent study by Jang et al proposed the use of the aronia bioactive fraction as a nutraceutical agent for suppressing airway inflammation. That study found that the fraction significantly decreased the mRNA expression of TNF-α, IL-6, IL-8, and IL-1β in lipopolysaccharide-stimulated human bronchial epithelial cells.[30] Zapolska-Downar et al (2012)[32] reported the anti-inflammatory and antioxidative properties of *Aronia melanocarpa* extract on human aortic endothelial cells. In addition to *in vivo and in vitro* studies, aronia berry has been reported to have an anti-inflammatory effect in human studies.[33–35] Collectively, these studies indicate that aronia, which has rich antioxidant content, can have a role in the prevention of diseases associated with chronic inflammation and oxidative stress.

Physical exercise is another condition that results in the release of ROS and oxidative stress. During exercise, the energy requirement can increase by 10 to 15 times compared with resting, thus increasing ROS production. Regular exercise can have beneficial and detrimental effects on the body, depending on the intensity, duration, and frequency.[36] Studies have demonstrated that increased oxygen consumption during exercise increases ROS production. The accumulation and

production of ROS and cytokines can positively and negatively affect the body.[37,38] As a negative impact, insufficient levels of antioxidants counteract the production of ROS during exercise, which can lead to oxidative stress.[39] Although humans have an adequate antioxidant defense system, it has been hypothesized that antioxidant supplementation can improve performance in individuals who exercise intensely.[36] It has been observed that antioxidant supplementation elevates both plasma and cellular antioxidant levels, thereby mitigating the oxidative stress response.[40,41] As anthocyanins possess antioxidant and anti-inflammatory properties that combat fatigue and promote recovery, berry supplementation is claimed to have ergogenic potential due to its ability to reduce oxidative stress.[42,43] Polyphenols may improve exercise performance by improving antioxidant capacity. However, the precise underlying mechanisms remain unclear and require further investigation.[44] Furthermore, the relative impacts of different sources of antioxidant supplements on reducing oxidative stress and pro-inflammatory cytokines remains uncertain.[38]

Despite growing animal studies on the health benefits of aronia, the limited number of systematic human studies on aronia focuses mainly on its lipid-lowering effects, glucose-lowering effects, and cardiovascular health effects[28,45,46] in athletes.[47] Concurrently, a significant gap exists in the systematic review literature for evaluating the anti-inflammatory effects of aronia in clinical studies. Therefore, conducting a systematic review that exclusively focuses on the anti-inflammatory effects of aronia in human randomized, placebo-controlled clinical trials can provide a critical understanding of this area. This systematic review aimed to synthesize the quantitative data on the aronia berry's anti-inflammatory effects from randomized, placebo-controlled clinical trials to summarize the currently available evidence on the potential anti-inflammatory effects of aronia.

METHODS

The protocol was registered in the "PROSPERO International Prospective Register of Systematic Reviews" (PROSPERO 2022 no. CRD42022325633).

Search Strategy

Four databases (PubMed, Web of Science, Science Direct, and Scopus) were searched for trials conducted with aronia and the effects of aronia on human inflammation markers and antioxidant enzymes between April 2022 and November 2023. The search strategy for the specific databases included the following index terms, titles, or abstracts: ([Inflammation markers OR antioxidant enzymes OR IL-6 OR TNF-α OR CRP OR IL-1ß OR IL-8 OR IL-10 OR CAT OR SOD OR GSH-Px] AND [Aronia OR black chokeberry OR *Aronia melanocarpa*] AND [human]). The research strategy for the databases has been provided as supplementary material.

Four reviewers (B.S., E.K., M.G.C., and A.Y.Z) independently screened one database each for this systematic review, and another reviewer (Ş.A.) resolved any discrepancies. This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Inclusion and Exclusion Criteria

Randomized controlled clinical trials that investigated the effect of black chokeberry on human inflammation biomarkers and antioxidant enzymes were considered for the review. The PICOS criteria were used to define the research question for the review. The inclusion criteria of the review were (1) human participants regardless of age, sex, and health status, (2) articles in the English language, (3) outcomes that measured at least one of the following: TNF-α, IL-6, IL-10, IL-8, IL-1 b, SOD, CAT, or GPx, and (4) short-term and long-term interventions that declared a quantitative or quantifiable aronia dose and form. Studies were excluded when (1) there was an in vivo design or they were conducted on animals, (2) observational and case studies, (3) the study language was other than English, and (4) aronia was mixed with other substances (Table 1).

Quality Assessment

After removing duplicates, 2 investigators screened the titles and abstracts of the articles to select the eligible studies, and any disagreements were resolved through discussion via consulting with other investigators. Two reviewers (B.S. and E.K.) independently evaluated the risk of bias for each included study using the Cochrane Risk of Bias Tool 2.0 (RoB2)[48] for randomized trials. In the case of randomized studies, the assessment encompassed (1) bias arising from the randomization process, (2) bias due to deviations from the intended intervention, (3) bias due to missing outcome data, (4) bias in the measurement of the outcome, and (5) bias in the selection of the reported results. For crossover studies, consideration was also given to the risk of bias arising from the duration of the intervention and carryover effects. Each domain underwent assessment and was categorized as having low risk of bias, high risk of bias, or some concerns regarding bias risk (Figure 1).

Table 1. PICOS Criteria for Inclusion and Exclusion of Studies

Parameter	Inclusion criterion	Exclusion criterion
Participant	Humans	In vitro, animals
Intervention	Aronia extract, juice, or oven-dry powder	Aronia combined with other ingredients
Comparison	Control group (received no intervention)	Any intervention
Outcomes	Inflammatory markers (CRP, IL-6, TNF-α, IL-8, IL-10, IL-1ß) and antioxidant enzymes (SOD, CAT, GSH-Px)	Studies without available data
Study design	Interventional trials (including randomized controlled trials, single-arm studies, parallel studies, 2-arm studies, and placebo-controlled studies)	Systematic reviews, meta-analyses, reviews

Abbreviations: CAT, catalase; CRP, C-reactive protein; GSH-Px, reduced glutathione peroxidase; IL, interleukin; SOD, superoxide dismutase; TNF-α, tumor necrosis factor alpha.

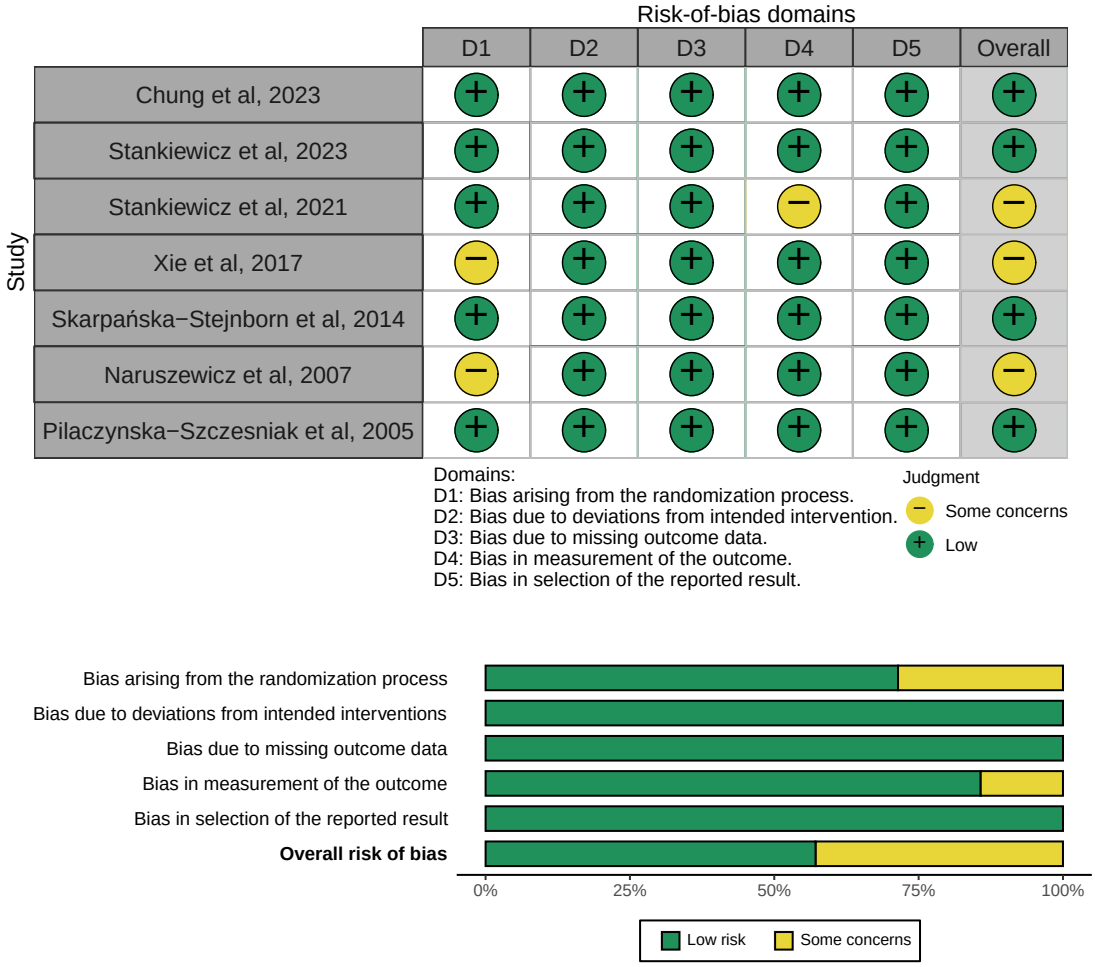

Figure 1. Assessment of Bias of the Randomized Studies According to the RoB 2 Tool[48]

The Risk Of Bias In Non-Randomized Studies of Interventions (ROBINS-I)[49] was used for the non-randomized study to assess the bias. In the case of non-randomized studies, the assessment encompassed (1) bias due to confounding (2) bias due to selection of participants (3) bias in classification of interventions (4) bias due to deviations from intended interventions (5) bias due to missing data (6) bias in measurement of outcomes (7) bias in selection of the reported result (Figure 2).

Risk of Bias Assessment

Seven out of the 18 studies were randomized controlled trials; 2 were crossover studies, while 9 were non-randomized. Randomized control trials were assessed in terms of risk of bias. The risk-of-bias assessment was visualized using the Robvis online tool.[50]

Most randomized controlled trials were associated with a low risk of bias, except for 3 studies, which were associated with some concerns about bias in the

outcome measurement. No clear information was provided regarding the assessors' awareness of the outcome of the intervention received. However, knowledge of the intervention probably did not influence the findings, since the researchers were blinded to the assignment of individuals to groups. For the nonrandomized studies, the overall risk of bias was assessed as follows: serious risk approximately 40%, critical risk approximately 25%, moderate risk approximately 25%, and low risk approximately 10%.

RESULTS

Study Selection

A total of 1986 studies were screened for inclusion in this systematic review. After the elimination process, a total of 18 studies were included. Figure 3 summarizes the study selection process, which included an assessment of articles based on title, abstract, and full text. None of the remaining studies included in our systematic review were randomized or employed a blind trial design. The participants in these studies were a diverse group, including healthy adults in 2 of the studies,[51,52] and hemodialysis patients with CVD risk in 1 study.[53] The remaining studies focused on patients with cardiometabolic risk,[34,35,53,57–60,62,63,65] sports-related research,[36,54–56,61] and healthy adults.[64]

Study Characteristics

The studies were performed internationally and encompassed the following countries: Poland ($n = 6$),[35,36,54–57] Serbia ($n = 6$),[52,53,58–61] Bulgaria ($n = 1$),[62] Finland ($n = 1$),[34] Denmark ($n = 1$),[63] Germany ($n = 1$),[51] South Korea ($n = 1$),[64] and the USA ($n = 1$).[65] The studies investigated cardiometabolic diseases ($n = 10$),[34,35,53,57–60,62,63,65] sports-related research ($n = 5$),[36,54–56,61] and healthy adults ($n = 3$).[51,52,64]

The types of aronia used in the interventions were aronia extract ($n = 10$),[35,51,53,54,57,58,61,63–65] aronia juice ($n = 8$).[34,36,52,55,56,59,60,62] and aronia juice and oven-dried aronia powder ($n = 1$).[34] The content of the aronia products used in the studies has been provided as supplementary material. The intervention periods were 12 weeks ($n = 6$),[52,54,59,61,62,65] 8 weeks ($n = 4$),[34,56,57,64] 4 weeks ($n = 5$),[36,51,53,58,60] 6 weeks ($n = 1$),[35] 7 weeks ($n = 1$),[55] and 13 weeks ($n = 1$).[63] Most of the studies had adult participants ($n = 14$). Three of the studies focused on individuals with metabolic syndrome (MetS),[53,57,58] and another 2 examined hypertensive patients;[34,60] additionally, 1 study focused on patients with type 2 diabetes,[59] 1 study involved individuals who had a medical history of myocardial infarctions (MIs),[35] 1 study involved hemodialysis patients with CVD risk,[53] 1 study involved former smokers,[65] and 1 study involved individuals who were classified as overweight.[62]

This systematic review found that only 3 CVD-related studies followed a nonrandomized, nonblind trial approach. Of the 5 sports studies analyzed, only 1 did not use a randomized or blinded trial design. All participants in these studies were athletes, including rowers ($n = 38$), football players ($n = 42$), and handball players ($n = 16$).

We examined the studies conducted with healthy adults in the health studies section (n = 3). Additionally, we included the study by Chung et al (2023)[64] that examined healthy adults after exercise (n = 70) while investigating healthy adult populations.

Anti-Inflammatory Parameters

Of 15 of the included studies, 10 investigated CRP,[34,35,53,57–60,62,63,65] 10 SOD,[36,51–53,57,61–65] 8 CAT,[51,53,57,61–65] 7 IL-6,[34,35,54–56,64,65] 6 GPx,[36,51,52,57,64,65] 4 TNF-α,[34,53,56,65] 2 IL-8,[34,65] 2 IL-10,[34,54] and 1 IL-1ß.[65]

Type of Aronia

Six of the 7 studies utilizing aronia extract used standardized products manufactured by companies. It was observed that 30 mL/day liquid extract was provided in 3 studies conducted in Serbia,[53,58,61] and commercially available products (300 mg/d and 255 mg/d) were used in 2 studies conducted in Poland.[35,57] A 6 g/day lyophilized extract was administered in a particular study, without specifying its content.[54] Regarding the form and dosage of supplementation, aronia anthocyanins ranged from 40 to 63.7 mg per 100 g or 100 mL.

All studies that involved juice consumption utilized commercially manufactured fruit juices. Both research studies conducted by Kardum et al (2014; 2015)[52,60] used the same brand of fruit juice, while 2 separate studies in Poland also supplied the same brand of juice. The juices exhibited varying anthocyanin contents, ranging from 23 to 172.7 mg per 100 mL. Individuals were exposed to anthocyanin amounts ranging from 34.5 to an impressive 330.6 mg/day of anthocyanin. Loo et al (2016)[34] indicated that 100 mL of juice was prepared from 106 g of aronia berries.

Key Results

Table 2 summarizes the study design, duration, subjects' characteristics, type and dose of aronia, and results from articles investigating the influence of aronia consumption on inflammation biomarkers and antioxidant enzymes.

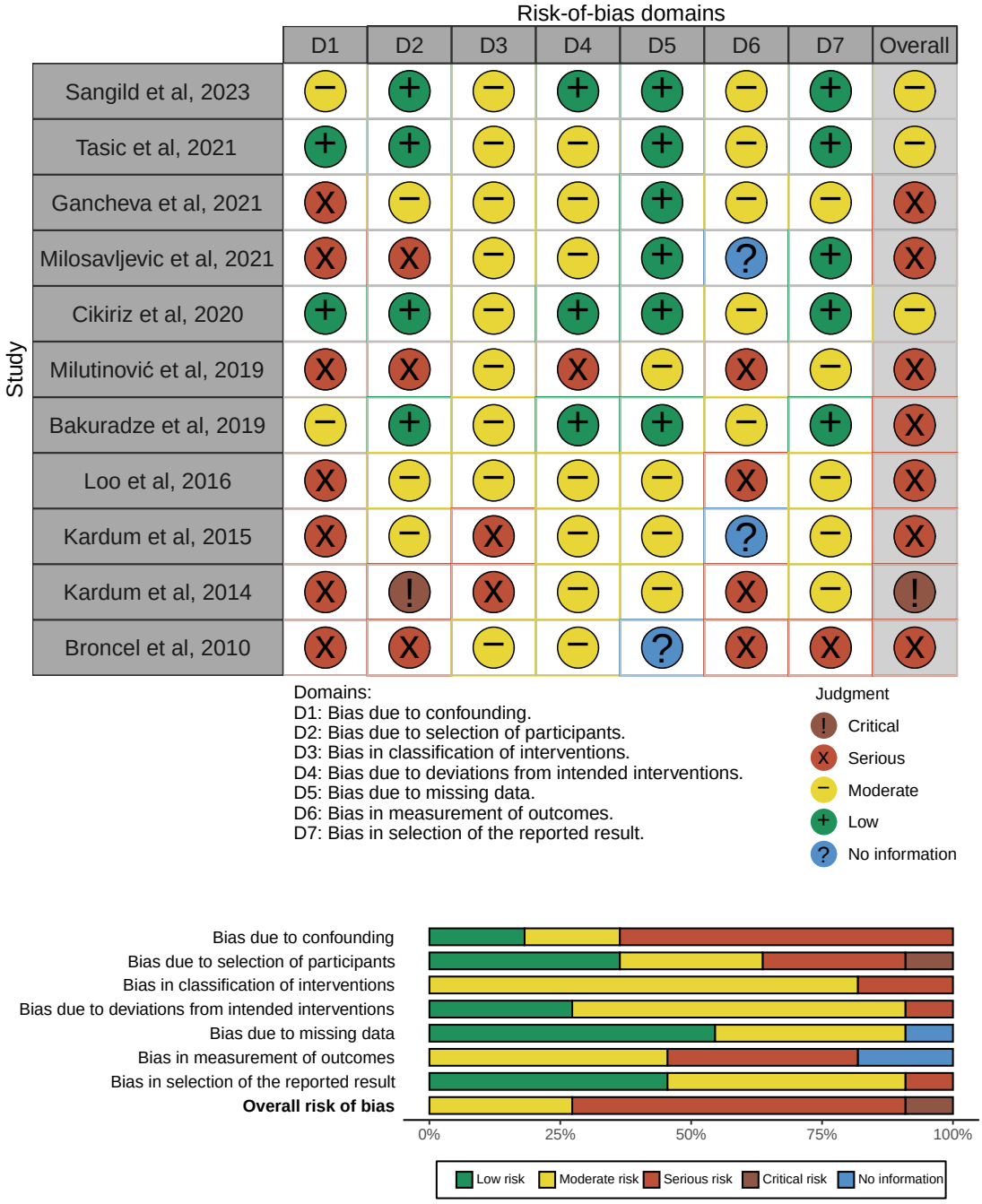

Figure 2. Assessment of Bias of the Non-Randomized Studies According to the ROBINS-I Tool[49]

DISCUSSION

Cardiometabolic Diseases

The systematic review indicated that *Aronia melanocarpa* demonstrated a mixed yet promising impact on reducing key inflammatory biomarkers in individuals with MetS, obesity, and cardiovascular risk. Despite some studies showing no significant changes in specific biomarkers, the aronia intervention consistently improved antioxidant enzyme activity, suggesting potential benefits in managing oxidative stress and inflammation across various cardiometabolic health conditions. The findings for the oxidative stress and inflammatory markers indicated the following: CAT, IL-1 β, IL-6, and IL-8 showed no change; IL-10 decreased; SOD showed no change or increased; CRP showed no change or decreased; hsCRP decreased or increased; TNF-α showed no change or decreased; and GPx increased or showed no change.

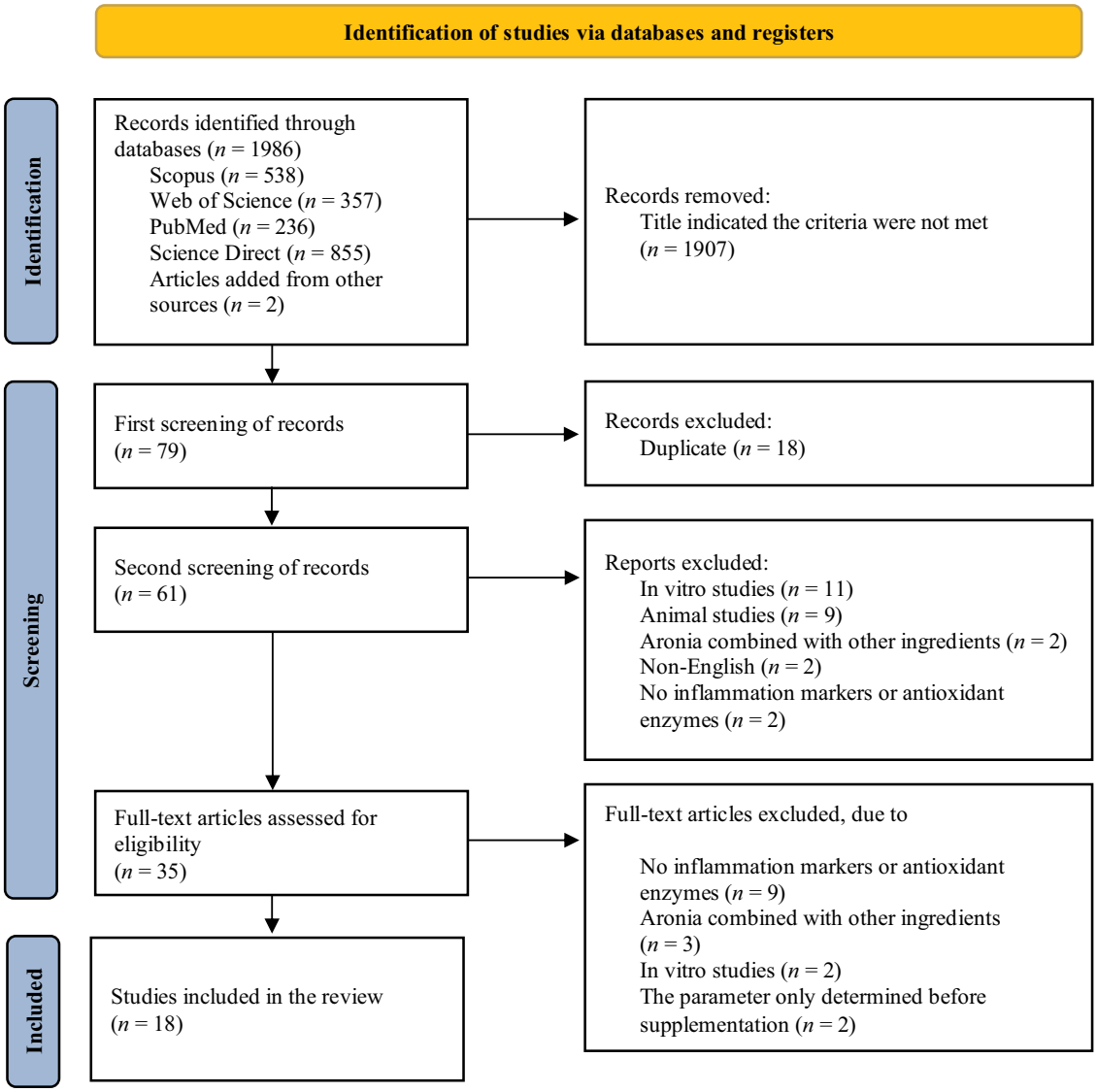

Figure 3. Flow Diagram of the Screening Process

Modifiable risk factors such as hypertension, dyslipidemia, poor glucose tolerance, obesity, and smoking, along with lifestyle factors such as an unhealthy diet and physical inactivity, contribute to the development of cardiometabolic diseases through their role in increasing oxidative stress.[66,67] A polyphenol-rich diet is recognized as having protective effects and it is considered that it may reduce the risk factors for cardiometabolic disorders through antioxidant processes or by regulating intracellular signaling pathways, hormones, and enzymes.[68–70] Even though the existing clinical studies have shown that *Aronia melanocarpa* extract or juice has beneficial properties on several risk factors for cardiometabolic disorders,[57–60,71] the precise influence of aronia on the inflammatory markers remains unclear.[46]

Foods and natural products with antidiabetic and lipid-lowering properties are of interest as an alternative to the use of drugs in preventing chronic inflammatory diseases due to a lower risk of drug interactions.[72,73] In a study examining aronia extract's effects on women with MetS, significant reductions in CRP levels were noted (from 5.8 ± 2.4 mg/L to 2.8 ± 0.6 mg/L, $P < .05$) following the intervention.[58] Conversely, the study by Broncel et al (2010)[57] found no significant change in CRP levels among MetS patients receiving aronia extract (3×100 mg/day) over an 8-week period. Broncel et al did, however, observe increased GPx activity, reduced erythrocyte CAT activity, and increased erythrocyte SOD levels after the same intervention period.[57] Similar to the studies with aronia, studies with other berries in individuals with MetS have reported mixed results regarding CRP levels.[74–76] In one study, individuals with MetS who consumed the acai beverage (325 mL twice daily) for 12 weeks showed small to

Table 2. Effect of Aronia Berry on Inflammatory Markers in Human Studies

Reference	Study design	Duration	Subjects	Sample Size		Age (year)	Aronia		Outcome	
				Test group	Control group		Type	Dose		
Cardiometabolic studies										
Sangild et al, 2023[63]	Parallel, 2-arm, PC, crossover	13 weeks	Hypercholesterolemic	51	44	47.7–51.9	Extract	150 mg/day	CRP CAT SOD	↔ ↔ ↔
Tasic et al, 2021[58]	Single-arm study	4 weeks	MetS, MF	143	NA	52.53	Extract	30 mL	CRP	↓
Gancheva et al 2021[62]	Parallel, 2-arm study	12 weeks	Overweight and obese, MF	11	11	51.9	Juice	150 mL/day	CRP CAT SOD	↓ ↔ ↑
Milosavljevic et al, 2021[53]	Single-arm study	4 weeks	Hemodialysis patients with CVD risk, MF	30	NA	62.93	Extract, (liquid form)	30 mL/day	TNF-α CRP CAT SOD	↔ ↔ ↑ ↔
Milutinović et al, 2019[59]	Single-arm study	12 weeks	Type 2 diabetic, MF	44	NA	56.3	Juice	150 mL/day	hs-CRP	↑
Xie et al, 2017[65]	Parallel, 2-arm, PC	12 weeks	Former smokers, MF	25	24	32.6	Extract	500 mg	IL-1β IL-6 IL-8 TNF-α CRP CAT GPx SOD	↔ ↔ ↔ ↔ ↔ ↔ ↔ ↔
Loo et al, 2016[34]	Parallel, 2-arm, PC, crossover	8 weeks	Hypertensive, MF	19	18	55.8	Juice + oven-dried powder	300 mL/day 3 g/day	IL-6 IL-8 IL-10 TNF-α hs-CRP	↔ ↔ ↓ ↓ ↔
Kardum et al, 2015[60]	Single-arm study	4 weeks	Hypertensive, MF	23	NA	47.5	Juice	200 mL/day	CRP	↓
Broncel et al, 2010[57]	Parallel, 2-arm, PC	8 weeks	MetS, MF	25	22	42–65	Extract	300 mg/day	CRP CAT SOD GPx	↔ ↓ ↑ ↑
Naruszewicz et al, 2007[35]	Parallel, 2-arm, PC	6 weeks	Patients after MI, MF	22	22	66	Extract	255 mg/day	hsIL-6* hsCRP**	↓ ↓
Sport studies										
Stankiewicz et al, 2023[54]	Parallel, 2-arm, PC	12 weeks	Football players, M	10	12	19.96	Extract Lyophilized	6 g/day	IL-6 IL-10	↓ ↑
Stankiewicz et al, 2021[55]	Parallel, 2-arm, PC	7 weeks	Football players, M	12	8	15.8	Juice	200 mL/day	IL-6	↔

(continued)

Table 2. Continued

Reference	Study design	Duration	Subjects	Sample Size		Age (year)	Aronia		Outcome	
				Test group	Control group		Type	Dose		
Cikiriz et al, 2020[61]	Single-arm study	12 weeks	Handball players, M	16	NA	20.26	Extract, (liquid form)	30 mL	CAT SOD	↑ ↓
Skarpańska-Stejnborn et al, 2014[56]	Parallel, 2-arm, PC	8 weeks	Rowers, M	10	9	20.5	Juice	150 mL/day	IL-6 TNF-α	↔ ↓
Pilaczynska-Szczesniak et al, 2005[36]	Parallel, 2-arm, PC	4 weeks	Rowers, M	9	10	21	Juice	150 mL/day	SOD GPx	↔ ↓
Studies of healthy individuals										
Chung et al, 2023[64]	Parallel, 2-arm, PC	8 weeks	Healthy adults after exercise	35	35	45	Extract	300 mg/day	IL-6, CAT GPx SOD	↔ ↔ ↑ ↔
Bakuradze et al, 2019[51]	Single-arm study	4 weeks	Healthy, M	10	NA	26.8	Extract, (liquid form)	50 mL/day	CAT GPx SOD	↔ ↔ ↓
Kardum et al, 2014[52]	Single-arm study	12 weeks	Healthy, F	25	NA	35.2	Juice	100 mL	GPx SOD	↑ ↑

Abbreviations: MF, male and female; F, female; M, male; PC, placebo-controlled; MetS, metabolic syndrome; MI, myocardial infarction; NA, not applicable; CRP, C-reactive protein; CAT, catalase; CVD, cardiovascular disease; SOD, superoxide dismutase; IL-1β, interleukin 1 beta; IL-6, interleukin 6; IL-8, interleukin 8; IL-10, interleukin 10; TNF-α, tumor necrosis factor alpha; GPx, glutathione peroxidase; hsIL-6, high-sensitivity interleukin 6; hsCRP, high-sensitivity C-reactive protein, ↔, no change; ↑, increased;↓, decreased.

moderate increases in exercise-induced CRP compared with a placebo group.[75] Another study[76] found no significant changes in fasting plasma high-sensitivity (hs)-CRP levels after MetS individuals consumed 50 g of freeze-dried blueberry powder daily for 8 weeks compared with a control group, while one study observed reduced hs-CRP levels in MetS individuals following consumption of approximately 400 g of fresh bilberries.[74]

In a further study, aronia juice supplementation in type 2 diabetic patients did not result in statistical changes in hs-CRP.[59] Similarly, in a study in which type 2 diabetic men and women were given 1500 mg of cranberry extract daily for 12 weeks, no significant change in CRP levels was observed.[77]

Following a 90-day intervention with 150 mg of aronia extract in hypercholesterolemic men, no statistically significant change was observed in their levels of SOD, CAT, or hs-CRP.[63] Furthermore, in studies involving adults with moderate hypercholesterolemia, consumption of 50 g/day of freeze-dried strawberries for 4 weeks did not result in significant changes in hs-CRP levels as compared with the control group.[78] Another study examining individuals with hypercholesterolemia reported inconsistent effects of wolfberry extract consumption on SOD and CAT activities, with minimal observed differences.[79]

Oxidative stress in hypertension causes dysfunction in the production of nitric oxide (NO), resulting in vasoconstriction and increased blood pressure caused by ROS in endothelial cells. Furthermore, there is a reduction in the availability of antioxidants.[80,81] In turn, dietary modifications and antioxidant supplementation are recommended for controlling blood pressure and vascular endothelial damage.[82] Loo et al (2016)[34] reported decreased concentrations of IL-10 and TNF-α but no changes in CRP, IL-6, or IL-8 levels after an 8-week intervention with 300 mL/day of aronia juice and 3 g/day of oven-dried powder in hypertensive patients. Correspondingly, another study found that, while CRP levels in hypertensive patients were reduced after 4 weeks of consuming 200 mL/day of aronia juice, this result was not statistically significant.[60] Other berry studies, partially supporting aronia studies, have shown similar mixed results.[83–85] A study in hypertensive men who consumed a daily mix of 640 mg of blueberries and black currants for 4 weeks observed no significant changes in hs-CRP, TNF-α, or IL-6 levels.[85] Additionally, postmenopausal women with hypertension who consumed blueberries for 8 weeks showed no significant changes in CRP levels, although SOD levels significantly increased at 4 and 8 weeks compared with baseline in both the blueberry and control groups.[84] However, middle-aged adults with elevated brachial blood pressure who consumed 500 mL/day of cranberry juice for 8 weeks showed that baseline CRP values might moderate treatment effects.[83]

Studies show that high-dose statin therapy reduces CVD mortality risk by decreasing CRP levels below 2 mg/L. Moderate doses combined with natural polyphenols are recommended as an alternative therapeutic approach. In patients with a history of MIs, 255 mg/day of aronia extract for 6 weeks was associated with significantly reduced hs-CRP ($P < .007$) compared with the placebo group.[35] Research on polyphenol-rich interventions in hemodialysis patients has shown their potential to mitigate oxidative stress and inflammation, which are common complications associated with the disease.[86,87] In a study that included 30 hemodialysis patients with at least one CVD risk, 30 days of standardized aronia extract intake was associated with increased CAT levels, while no significant change was observed in SOD, CRP, or TNF-α levels.[53]

Contrastingly, a study involving males with at least one CVD risk factor found no change in IL-6, TNF-α, or hs-CRP after 6 weeks of supplementation with a wild 25 g/day blueberry drink, compared with the control group.[88] In another study in individuals at risk of CVD, a 4-week intervention with 330 mL of bilberry juice resulted in decreased IL-6 and hs-CRP levels, but an increase in TNF-α levels.[89]

Analyses suggest that baseline inflammatory status may influence the effects of berry supplementation on specified CVD risk factors. Individuals with elevated CRP may be experiencing a greater physiological challenge that cannot be overcome with aronia juice bioactives alone.[83] In this regard, aronia berry juice could be beneficial before the onset of chronic diseases or in inflammatory status. A study by Tasic et al (2021)[58] included in this systematic review found that aronia supplementation led to a significant decrease in CRP levels, particularly in the group with elevated baseline CRP levels.

In obesity, the increase in visceral fat accumulation is associated with increased production of ROS, and prolonged oxidative stress results in a decrease in the activity of antioxidant enzymes, which increases the susceptibility of cells to oxidative damage.[90–92] Gancheva et al (2021)[62] researched overweight and healthy individuals who consumed aronia juice (50 mL) 3 times daily for 3 months. Aronia juice consumption reduced CRP levels and improved the antioxidant defense system by increasing the SOD activity in the overweight group.[62] In interventions ranging from 6 to 12 weeks for obese and overweight participants, studies with berries such as freeze-dried blueberry powder, freeze-dried strawberry beverages, and strawberry juice showed no effect on CRP levels.[93–95] However, cranberry juice interventions

were associated with reduced CRP levels in overweight and obese patients.[96,97]

Cigarette smoking leads to increased oxidative stress and inflammation, with studies showing elevated levels of precursor cytokines like IL-8, IL-1β, and IL-6 in smokers.[98] Additionally, former smokers experience impaired vascular and antioxidant function, highlighting the need for additional strategies to reduce their CVD risk.[65] Former smokers who consumed 500 mg of aronia extract for 12 weeks showed no statistical difference in inflammatory markers such as IL-6, TNF-α, and IL-1β or in the activity of antioxidant enzymes such as CAT, GSH-PX, SOD.[65]

Among the inflammatory markers, CRP, TNF-α, and IL-6 are particularly noteworthy, as they are believed to contribute to the development of insulin resistance and cardiometabolic diseases, which often feature low-grade inflammation.[99] Diminishing these markers through aronia supplementation could offer advantages in postponing and preventing cardiovascular issues.

Sport Studies

Studies evaluating the effects of aronia supplementation on athletes have generally focused on changes in oxidative stress and inflammation markers. The studies included in this review suggested that aronia supplementation may reduce oxidative stress and inflammation: IL-6 exhibited both decreases and no changes, IL-10 showed increases, CAT demonstrated increases, SOD displayed both decreases and no changes, TNF-α showed decreases, and GPx exhibited decreases. However, the results are conflicting.

Polyphenol supplements may enhance exercise performance by influencing oxidative stress and inflammation.[42,43] However, athletes must be cautious of interfering with these processes, especially during periods where adaptations to training are prioritized, as in pre-season. Aronia, rich in polyphenols, holds promise in influencing both the health and performance of athletes, including effects on redox status, exercise-induced inflammation, and exercise performance.

Due to its high polyphenol content, aronia has been the subject of numerous studies investigating its effects on biomarkers associated with exercise, sporting performance, and recovery, encompassing inflammatory status[54,56] and oxidative stress.[36,55,61] A recent systematic review of human clinical trials of aronia supplementation among athletes revealed its potential to alter the redox balance.[47] The results of a study that examined endogenous antioxidants found that after 4 weeks of consuming 150 mL of aronia juice, rowers exhibited lower GPx activity in samples collected 1 minute after the exercise test; in addition, SOD activity was reduced in samples obtained during a 24-hour recovery period, compared with subjects who received the placebo.[36] Another study provided 30 mL aronia extract for 12 weeks to handball players and measured SOD, glutathione, and CAT activity pre- and post-exercise.[61] After 6 weeks, the levels of glutathione decreased, and the levels of SOD were lower, specifically, after exercise. At 12 weeks, catalase levels had increased, while reduced glutathione levels decreased pre- and post-exercise.

Moreover, a growing amount of research is investigating the relationship between inflammatory markers and aronia supplementation. A study on rowers subsequently assessed 24-hour post-exercise inflammation markers during 8 weeks of 150 mL/day aronia juice consumption. The findings from the research indicated that TNF-α levels were lower in rowers with aronia supplementation compared with those administered a placebo.[56] Supporting the previous evidence, Stankiewicz et al (2023)[54] found that IL-6 levels decreased, whereas IL-10 levels increased, following supplementation in football players. On the other hand, other research from Stankiewicz et al (2021)[55] reported no change in IL-6 levels in adolescent football players after 7 weeks of 200 mL/day aronia juice consumption.[55] Thus far, these findings suggest that aronia may have anti-inflammatory potential, which could be particularly valuable in exercise recovery, by mitigating inflammation-related damage to skeletal muscle.

Similar studies have investigated the effects of other types of berries on inflammatory status. In 3 studies evaluating the anti-inflammatory effects of blueberries on athletes, no changes were observed in IL-6 levels.[43,100,101] Comparable with the study by Stankiewicz et al (2023)[54] with aronia supplementation, one of those studies showed an increase in IL-10 levels[100]; however, another study showed no change in IL-10 levels after blueberry supplementation: the IL-6, IL-8, and IL-10 inflammation markers were not altered in trained athletes who consumed 250 g/day of whole blueberries for 6 weeks.[43] In a randomized controlled study, the subjects showed no differences in their IL-8 or IL-6 levels, but their IL-10 levels increased after consuming 375 g of blueberries 1 hour before running on a treadmill for 2.5 hours at the end of a 6-week experimental period.[100] Additionally, in study participants who consumed a blueberry smoothie after a 60-hour exercise session, there were no reductions in IL-6 levels, compared with those who consumed a placebo smoothie without blueberries.[101] In contrast, college students who drank 450 mL of black currant nectar twice a day for 8 consecutive days showed a decrease in IL-6 levels 24 hours post-exercise, compared with those in a placebo group.[102] Overall, the evidence for a beneficial

relationship between other types of berries and inflammatory status is currently inconclusive.

Findings varied across studies, with some reporting reductions in oxidative stress and inflammation markers, while others showed an increase in antioxidant capacity. These results highlight the complexity of the effects of aronia on these biological markers and underscore the need for further research.[47,54,64] In summary, although the current studies have offered some insight into the potential benefits of aronia supplementation for exercise performance and recovery, more extensive and well-controlled investigations are necessary to determine the practical applications and benefits of incorporating aronia into athletes' dietary regimens. Further studies are needed to help establish a clearer understanding of its effects on the biological responses of athletes.

Studies of Healthy Individuals

Aronia studies on healthy individuals have demonstrated a significant increase in activity of the antioxidant defense system. The findings of the studies in this section on oxidative stress and inflammatory markers were as follows: IL-6 exhibited no change; CAT demonstrated no change; GPx showed both increases and no change; and SOD displayed decreases, no change, and increases.

The literature has evaluated the impact of aronia not only on inflammation in diseases but also on healthy individuals.[51,52,64] In a study of healthy women who consumed 100 mL of organic aronia juice daily for 3 months, Kardum et al (2014)[52] observed that GPx activity tended to rise from the beginning of the study until its end, and that SOD activity showed an increase only after the mid-point of the study.

Moreover, a study by Chung et al (2023)[64] with a non-athletic healthy adult population, revealed that aronia may modulate the glutathione defense system by increasing glutathione availability and GPx activity, immediately as well as 30 minutes post-exercise. In a 4-week aronia extract intervention study involving 50 mL doses administered to healthy male volunteers, Bakuradze et al (2019)[51] reported a decrease in SOD activity, while the GPx and CAT activities remained unaffected. Contrarily, in a randomized crossover study involving 30 healthy adults, consumption of 200 mL/day of either açaí or juçara juice for 4 weeks was associated with significant increases in CAT activity (275.1% for açaí) and GPx activity (15.3% for açaí), with juçara juice showing a notable increase in CAT activity (∼15.0%) compared with the baseline.[103]

Additionally, in studies involving other berries (eg, black currant, bilberry, and sea buckthorn berry) conducted in healthy populations, significant outcomes have been observed for inflammation parameters.[104–106] Although these parameters are not directly comparable with those examined in the aronia studies in our review, notable results have been documented. In one study, supplementation with 240 mg of black currant extract taken, both before and after exercise in healthy men and women, resulted in early suppression of TNF-α and IL-6 secretion 24 hours post-exercise.[104] Similarly, a study with 110 overweight and obese women reported decreased plasma TNF-α concentrations following a 33–35 day intervention with 100 g of frozen whole bilberries daily.[105] In another study involving a healthy population, consumption of 28 g/day of frozen sea buckthorn berries for 90 days was associated with a reduction in hs-CRP levels.[106]

STRENGTH AND LIMITATIONS

The systematic review undertaken has several strengths that enhance its credibility and significance. The adherence to PRISMA guidelines ensured a comprehensive and systematic analysis of clinical studies, mainly focusing on aronia's anti-inflammatory properties. Additionally, exclusively including randomized controlled trials supported the review's reliability, ensuring a higher quality of evidence. However, the review encountered limitations that were primarily caused by considerable heterogeneity among the included studies. Variability in intervention types, dosages, participant demographics, and participant health conditions hindered the synthesis of the evidence and the formulation of evidence-based recommendations. Furthermore, the lack of consistent reporting and analysis of the anthocyanin content in certain aronia supplements limited the precision of the outcome assessments and the determination of optimal dosages. It should be underlined that the level of antioxidant activity and the quantities of the polyphenolic compounds in chokeberries can vary depending on the environmental factors affecting the plant, such as climate conditions and crop growth.[22] Importantly, aronia supplementation appears to pose little risk of interaction with existing interventions, compared with other herbal supplements that have demonstrable adverse effects.[107,108] Although there are no known reports of aronia supplementation having adverse or injurious side effects, clinicians should still exercise caution when administering it to patients. Including mixed-quality evidence from nonrandomized or single-blinded studies underscores the need for cautious interpretation and highlights the necessity for further well-controlled investigations in this field. Despite these limitations, the systematic review is a valuable platform for future research, offering a basis for more

robust investigations into the efficacy and potential applications of aronia supplements in reducing inflammation.

CONCLUSION

The present systematic review highlighted the potential of *Aronia melanocarpa* to exert positive effects on inflammatory markers, including in patients with various diseases, healthy participants, and athletes. The variation in the observed outcomes for aronia supplementation, in terms of exercise-related markers exhibited diverse and complex responses, reflect the intricate system of interactions involved in oxidative stress, inflammation, and antioxidant capacity. Consequently, more rigorous, controlled investigations are imperative in order to comprehensively elucidate aronia's potential health benefits and applications in athletes' dietary regimens. These findings should be confirmed in a long-term study, with the integration of a greater number of randomized controlled studies, to determine the effect of aronia on the indicated oxidative markers.

Acknowledgments

We thank the authors of all of the studies included in this research.

Author Contributions

B.S.: designed the research, undertook screening of the studies, performed quality assessment of the studies, extracted and analyzed data, and contributed to the writing of the paper; E.K.: supervised the systematic review process, contributed to quality assessment of the studies, undertook screening of the studies, edited and revised the manuscript, and contributed to the writing of the paper; M.G.C.: undertook screening of the studies, extracted and analyzed data, and contributed to the writing of the paper; A.Y.Z.: undertook screening of the studies, extracted and analyzed data, and contributed to the writing of the paper; and Ş.A.: contributed to data interpretation, and final editing and revising of the manuscript. All of the authors reviewed the manuscript, offered comments, and approved the final version.

Supplementary Material

Supplementary Material Table S1: Phenolic content of Aronia, Figure S1: Research Strategy for Databases is available at *Nutrition Reviews* online.

Funding

None declared.

Conflict of interest

None declared.

REFERENCES

1. Ekiert H, Kubica P, Szopa A. Successful cultivation and utilization of *Aronia melanocarpa* (Michx.) Elliott (Black Chokeberry), a species of North-American origin, in Poland and the biosynthetic potential of cells from in vitro cultures. In: Ekiert HM, Ramawat KG, Arora J, eds. *Medicinal Plants: Sustainable Development and Biodiversity*. Springer; 2021:69–111. https://doi.org/10.1007/978-3-030-74779-4_4
2. Kasprzak-Drozd K, Oniszczuk T, Soja J, et al. The efficacy of black chokeberry fruits against cardiovascular diseases. *Int J Mol Sci*. 2021;22:6541. https://doi.org/10.3390/ijms22126541
3. Jakobek L, Šeruga M, Medvidović-Kosanović M, Novak I. Antioxidant activity and polyphenols of *Aronia* in comparison to other berry species. *Agric Conspec Sci*. 2007;72:301–306.
4. Sidor A, Gramza-Michałowska A. Black chokeberry *Aronia melanocarpa* L.—a qualitative composition, phenolic profile and antioxidant potential. *Molecules*. 2019;24:3710. https://doi.org/10.3390/molecules24203710
5. Kaloudi T, Tsimogiannis D, Oreopoulou V. *Aronia melanocarpa*: identification and exploitation of its phenolic components. *Molecules*. 2022;27:4375. https://doi.org/10.3390/molecules27144375
6. Ćujić N, Kardum N, Šavikin K, Zdunić G, Janković T, Menković N. Potential of chokeberry (*Aronia melanocarpa* L.) as a therapeutic food. In: Grumezescu A, Holban AM, eds. *Therapeutic Foods*. Academic Press; 2018:209–237. https://doi.org/10.1016/B978-0-12-811517-6.00007-6
7. Liu ZQ. Bridging free radical chemistry with drug discovery: a promising way for finding novel drugs efficiently. *Eur J Med Chem*. 2020;189:112020. https://doi.org/10.1016/j.ejmech.2019.112020
8. Pisoschi AM, Pop A. The role of antioxidants in the chemistry of oxidative stress: a review. *Eur J Med Chem*. 2015;97:55–74. https://doi.org/10.1016/j.ejmech.2015.04.040
9. Poljsak B, Šuput D, Milisav I. Achieving the balance between ROS and antioxidants: when to use the synthetic antioxidants. *Oxid Med Cell Longev*. 2013;2013:956792. https://doi.org/10.1155/2013/956792
10. Liguori I, Russo G, Curcio F, et al. Oxidative stress, aging, and diseases. *Clin Interv Aging*. 2018;13:757–772. https://doi.org/10.2147/CIA.S158513
11. Kany S, Vollrath JT, Relja B. Cytokines in inflammatory disease. *Int J Mol Sci*. 2019;20:6008. https://doi.org/10.3390/ijms20236008
12. Koelman L, Pivovarova-Ramich O, Pfeiffer AFH, Grune T, Aleksandrova K. Cytokines for evaluation of chronic inflammatory status in ageing research: reliability and phenotypic characterisation. *Immun Ageing*. 2019;16:11. https://doi.org/10.1186/s12979-019-0151-1
13. Süntar I. Importance of ethnopharmacological studies in drug discovery: role of medicinal plants. *Phytochem Rev*. 2020;19:1199–1209. https://doi.org/10.1007/s11101-019-09629-9
14. Moussa Z, Judeh ZM, Ahmed SA. Nonenzymatic exogenous and endogenous antioxidants. In: Das K, Das S, Biradar MS, Bobbarala V, Tata SS, eds. *Free Radical Medicine and Biology*. IntechOpen; 2019:11–22.
15. Joseph SV, Edirisinghe I, Burton-Freeman BM. Berries: anti-inflammatory effects in humans. *J Agric Food Chem*. 2014;62:3886–3903. https://doi.org/10.1021/jf4044056
16. Martin DA, Taheri R, Brand MH, Draghi IIA, Sylvester FA, Bolling BW. Anti-inflammatory activity of aronia berry extracts in murine splenocytes. *J Funct Foods*. 2014;8:68–75. https://doi.org/10.1016/j.jff.2014.03.004
17. Oszmiański J, Lachowicz S. Effect of the production of dried fruits and juice from chokeberry (*Aronia melanocarpa* L.) on the content and antioxidative activity of bioactive compounds. *Molecules*. 2016;21:1098. https://doi.org/10.3390/molecules21081098
18. Putta S, Yarla NS, Kumar K E, et al. Preventive and therapeutic potentials of anthocyanins in diabetes and associated complications. *Curr Med Chem*. 2018;25:5347–5371. https://doi.org/10.2174/0929867325666171206101945
19. Zielińska A, Bryk D, Paradowska K, Wawer I. *Aronia melanocarpa* leaves as a source of chlorogenic acids, anthocyanins, and sorbitol, and their anti-inflammatory activity. *Pol J Food Nutr Sci*. 2020;70:409–418. https://doi.org/10.31883/pjfns/130255

20. King ES, Bolling BW. Composition, polyphenol bioavailability, and health benefits of aronia berry: a review. *J Food Bioact*. 2020;11:13–30. https://doi.org/10.31665/JFB.2020.11235
21. Trenka M, Nawirska-Olszańska A, Oziembłowski M. Analysis of selected properties of fruits of black chokeberry (*Aronia melanocarpa* L.) from organic and conventional cultivation. *Appl Sci*. 2020;10:9096. https://doi.org/10.3390/app10249096
22. Jurendić T, Ščetar M. *Aronia melanocarpa* products and by-products for health and nutrition: a review. *Antioxidants (Basel)*. 2021;10:1052. https://doi.org/10.3390/antiox10071052
23. Skupien K, Oszmianski J. The effect of mineral fertilization on nutritive value and biological activity of chokeberry fruit. *AFSci*. 2008;16:46–55. https://doi.org/10.2137/145960607781635822
24. Jung H, Kwak H-K, Hwang KT. Antioxidant and antiinflammatory activities of cyanidin-3-glucoside and cyanidin-3-rutinoside in hydrogen peroxide and lipopolysaccharide-treated RAW264.7 cells. *Food Sci Biotechnol*. 2014;23:2053–2062. https://doi.org/10.1007/s10068-014-0279-x
25. Amin HP, Czank C, Raheem S, et al. Anthocyanins and their physiologically relevant metabolites alter the expression of IL-6 and VCAM-1 in CD40L and oxidized LDL challenged vascular endothelial cells. *Mol Nutr Food Res*. 2015;59:1095–1106. https://doi.org/10.1002/mnfr.201400803
26. Olechno E, Puścion-Jakubik A, Zujko ME. Chokeberry (*A. melanocarpa* (Michx.) Elliott)—a natural product for metabolic disorders? *Nutrients*. 2022;14:2688. https://doi.org/10.3390/nu14132688
27. Jurikova T, Mlcek J, Skrovankova S, et al. Fruits of black chokeberry *Aronia melanocarpa* in the prevention of chronic diseases. *Molecules*. 2017;22:944. https://doi.org/10.3390/molecules22060944
28. Hawkins J, Hires C, Baker C, Keenan L, Bush M. Daily supplementation with *Aronia melanocarpa* (chokeberry) reduces blood pressure and cholesterol: a meta analysis of controlled clinical trials. *J Diet Suppl*. 2021;18:517–530. https://doi.org/10.1080/19390211.2020.1800887
29. Appel K, Meiser P, Millán E, et al. Chokeberry (*Aronia melanocarpa* (Michx.) Elliot) concentrate inhibits NF-κB and synergizes with selenium to inhibit the release of pro-inflammatory mediators in macrophages. *Fitoterapia*. 2015;105:73–82. https://doi.org/10.1016/j.fitote.2015.06.009
30. Jang BK, Lee JW, Choi H, Yim SV. *Aronia melanocarpa* fruit bioactive fraction attenuates LPS-induced inflammatory response in human bronchial epithelial cells. *Antioxidants (Basel)*. 2020;9:816. https://doi.org/10.3390/antiox9090816
31. Ohgami K, Ilieva I, Shiratori K, et al. Anti-inflammatory effects of aronia extract on rat endotoxin-induced uveitis. *Invest Ophthalmol Vis Sci*. 2005;46:275–281. https://doi.org/10.1167/iovs.04-0715
32. Zapolska-Downar D, Bryk D, Małecki M, Hajdukiewicz K, Sitkiewicz D. *Aronia melanocarpa* fruit extract exhibits anti-inflammatory activity in human aortic endothelial cells. *Eur J Nutr*. 2012;51:563–572. https://doi.org/10.1007/s00394-011-0240-1
33. Handeland M, Grude N, Torp T, Slimestad R. Black chokeberry juice (*Aronia melanocarpa*) reduces incidences of urinary tract infection among nursing home residents in the long term—a pilot study. *Nutr Res*. 2014;34:518–525. https://doi.org/10.1016/j.nutres.2014.05.005
34. Loo BM, Erlund I, Koli R, et al. Consumption of chokeberry (*Aronia mitschurinii*) products modestly lowered blood pressure and reduced low-grade inflammation in patients with mildly elevated blood pressure. *Nutr Res*. 2016;36:1222–1230. https://doi.org/10.1016/j.nutres.2016.09.005
35. Naruszewicz M, Laniewska I, Millo B, Dłuzniewski M. Combination therapy of statin with flavonoids rich extract from chokeberry fruits enhanced reduction in cardiovascular risk markers in patients after myocardial infraction (MI). *Atherosclerosis*. 2007;194:e179–e184. https://doi.org/10.1016/j.atherosclerosis.2006.12.032
36. Pilaczynska-Szczesniak L, Skarpanska-Steinborn A, Deskur E, Basta P, Horoszkiewicz-Hassan M. The influence of chokeberry juice supplementation on the reduction of oxidative stress resulting from an incremental rowing ergometer exercise. *Int J Sport Nutr Exerc Metab*. 2005;15:48–58. https://doi.org/10.1123/ijsnem.15.1.48
37. Nunes-Silva R, Freitas-Lima LC. The association between physical exercise and reactive oxygen species (ROS) production. *J Sports Med Doping Stud*. 2015;5:1–7. https://doi.org/10.4172/2161-0673.1000152
38. Taherkhani S, Suzuki K, Castell L. A short overview of changes in inflammatory cytokines and oxidative stress in response to physical activity and antioxidant supplementation. *Antioxidants (Basel)*. 2020;9:886. https://doi.org/10.3390/antiox9090886
39. Lu Y, Wiltshire HD, Baker JS, Wang Q. Effects of high intensity exercise on oxidative stress and antioxidant status in untrained humans: a systematic review. *Biology (Basel)*. 2021;10:1272. https://doi.org/10.3390/biology10121272
40. Orlando P, Silvestri S, Galeazzi R, et al. Effect of ubiquinol supplementation on biochemical and oxidative stress indexes after intense exercise in young athletes. *Redox Rep*. 2018;23:136–145. https://doi.org/10.1080/13510002.2018.1472924
41. de Oliveira DCX, Rosa FT, Simões-Ambrósio L, Jordao AA, Deminice R. Antioxidant vitamin supplementation prevents oxidative stress but does not enhance performance in young football athletes. *Nutrition*. 2019;63–64:29–35. https://doi.org/10.1016/j.nut.2019.01.007
42. Brandenburg JP, Giles LV. Blueberry supplementation reduces the blood lactate response to running in normobaric hypoxia but has no effect on performance in recreational runners. *J Int Soc Sports Nutr*. 2021;18:26. https://doi.org/10.1186/s12970-021-00423-7
43. McAnulty LS, Nieman DC, Dumke CL, et al. Effect of blueberry ingestion on natural killer cell counts, oxidative stress, and inflammation prior to and after 2.5 h of running. *Appl Physiol Nutr Metab*. 2011;36:976–984. https://doi.org/10.1139/h11-120
44. d'Unienville NMA, Blake HT, Coates AM, Hill AM, Nelson MJ, Buckley JD. Effect of food sources of nitrate, polyphenols, L-arginine and L-citrulline on endurance exercise performance: a systematic review and meta-analysis of randomised controlled trials. *J Int Soc Sports Nutr*. 2021;18:76. https://doi.org/10.1186/s12970-021-00472-y
45. Rahmani J, Clark C, Kord Varkaneh H, et al. The effect of aronia consumption on lipid profile, blood pressure, and biomarkers of inflammation: a systematic review and meta-analysis of randomized controlled trials. *Phytother Res*. 2019;33:1981–1990. https://doi.org/10.1002/ptr.6398
46. Christiansen CB, Mellbye FB, Hermansen K, Jeppesen PB, Gregersen S. Effects of *Aronia melanocarpa* on cardiometabolic diseases: a systematic review of quasi-design studies and randomized controlled trials. *Rev Diabet Stud*. 2022;18:76–92. https://doi.org/10.1900/RDS.2022.18.76
47. Zare R, Kimble R, Redha AA, Cerullo G, Clifford T. How can chokeberry (*Aronia*) (poly)phenol-rich supplementation help athletes? A systematic review of human clinical trials. *Food Funct*. 2023;14:5478–5491. https://doi.org/10.1039/d3fo00336a
48. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:L4898. https://doi.org/10.1136/bmj.l4898
49. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919. https://doi.org/10.1136/bmj.i4919
50. McGuinness LA, Higgins JP. Risk-of-bias VISualization (robvis): an R package and Shiny web app for visualizing risk-of-bias assessments. *Res Synth Methods*. 2021;12:55–61. https://doi.org/10.1002/jrsm.1411
51. Bakuradze T, Becker D, Reischmann J, et al. Protection from DNA damage by use of an aronia food supplement—results from a pilot human intervention study. *Curr Pharmacol Rep*. 2019;5:188–195. https://doi.org/10.1007/s40495-019-00178-5
52. Kardum N, Takić M, Šavikin K, et al. Effects of polyphenol-rich chokeberry juice on cellular antioxidant enzymes and membrane lipid status in healthy women. *J Funct Foods*. 2014;9:89–97. https://doi.org/10.1016/j.jff.2014.04.019
53. Milosavljevic I, Jakovljevic V, Petrovic D, et al. Standardized *Aronia melanocarpa* extract regulates redox status in patients receiving hemodialysis with anemia. *Mol Cell Biochem*. 2021;476:4167–4175. https://doi.org/10.1007/s11010-021-04225-y
54. Stankiewicz B, Cieślicka M, Mieszkowski J, et al. Effect of supplementation with black chokeberry (*Aronia melanocarpa*) extract on inflammatory status and selected markers of iron metabolism in young football players: a randomized double-blind trial. *Nutrients*. 2023;15:975. https://doi.org/10.3390/nu15040975
55. Stankiewicz B, Cieślicka M, Kujawski S, et al. Effects of antioxidant supplementation on oxidative stress balance in young footballers—a randomized double-blind trial. *J Int Soc Sports Nutr*. 2021;18:44. https://doi.org/10.1186/s12970-021-00447-z
56. Skarpańska-Stejnborn A, Basta P, Sadowska J, Pilaczyńska-Szcześniak L. Effect of supplementation with chokeberry juice on the inflammatory status and markers of iron metabolism in rowers. *J Int Soc Sports Nutr*. 2014;11:48. https://doi.org/10.1186/s12970-014-0048-5
57. Broncel M, Koziróg M, Duchnowicz P, Koter-Michalak M, Sikora J, Chojnowska-Jezierska J. *Aronia melanocarpa* extract reduces blood pressure, serum endothelin, lipid, and oxidative stress marker levels in patients with metabolic syndrome. *Med Sci Monit*. 2010;16:28–34.
58. Tasic N, Jakovljevic VLJ, Mitrovic M, et al. Black chokeberry *Aronia melanocarpa* extract reduces blood pressure, glycemia and lipid profile in patients with metabolic syndrome: a prospective controlled trial. *Mol Cell Biochem*. 2021;476:2663–2673. https://doi.org/10.1007/s11010-021-04106-4
59. Milutinovic M, Velickovic Radovanovic R, Savikin K, et al. Chokeberry juice supplementation in type 2 diabetic patients—impact on health status. *J Appl Biomed*. 2019;17:218–224. https://doi.org/10.32725/jab.2019.020
60. Kardum N, Milovanović B, Šavikin K, et al. Beneficial effects of polyphenol-rich chokeberry juice consumption on blood pressure level and lipid status in hypertensive subjects. *J Med Food*. 2015;18:1231–1238. https://doi.org/10.1089/jmf.2014.0171
61. Cikiriz N, Milosavljevic I, Jakovljevic B, et al. The influences of chokeberry extract supplementation on redox status and body composition in handball players during competition phase. *Can J Physiol Pharmacol*. 2021;99:42–47. https://doi.org/10.1139/cjpp-2020-0095

62. Gancheva S, Ivanova I, Atanassova A, et al. Effects of *Aronia melanocarpa* fruit juice on oxidative stress, energy homeostasis, and liver function in overweight and healthy-weight individuals. *SSM*. 2021;53:39–46. https://doi.org/10.14748/ssm.v0i0.7833
63. Sangild J, Faldborg A, Schousboe C, et al. Effects of chokeberries (*Aronia* spp.) on cytoprotective and cardiometabolic markers and semen quality in 109 mildly hypercholesterolemic Danish men: a prospective, double-blinded, randomized, crossover trial. *J Clin Med*. 2023;12:373. https://doi.org/10.3390/jcm12010373
64. Chung J-W, Kim J-E, Nam Y-E, et al. Eight-week supplementation of aronia berry extract promoted the glutathione defence system against acute aerobic exercise–induced oxidative load immediately and 30 min post-exercise in healthy adults: a double-blind, randomised controlled trial. *J Hum Nutr Diet*. 2023;36:1589–1599. https://doi.org/10.1111/jhn.13150
65. Xie L, Vance T, Kim B, et al. Aronia berry polyphenol consumption reduces plasma total and low-density lipoprotein cholesterol in former smokers without lowering biomarkers of inflammation and oxidative stress: a randomized controlled trial. *Nutr Res*. 2017;37:67–77. https://doi.org/10.1016/j.nutres.2016.12.007
66. Chakraborty S, Verma A, Garg R, Singh J, Verma H. Cardiometabolic risk factors associated with type 2 diabetes mellitus: a mechanistic insight. *Clin Med Insights Endocrinol Diabetes*. 2023;16:11795514231220780. https://doi.org/10.1177/11795
67. Furman D, Campisi J, Verdin E, et al. Chronic inflammation in the etiology of disease across the life span. *Nat Med*. 2019;25:1822–1832. https://doi.org/10.1038/s41591-019-0675-0
68. Costa C, Tsatsakis A, Mamoulakis C, et al. Current evidence on the effect of dietary polyphenols intake on chronic diseases. *Food Chem Toxicol*. 2017;110:286–299. https://doi.org/10.1016/j.fct.2017.10.023
69. Leri M, Scuto M, Ontario ML, et al. Healthy effects of plant polyphenols: molecular mechanisms. *Int J Mol Sci*. 2020;21:1250. https://doi.org/10.3390/ijms21041250
70. Alotaibi BS, Ijaz M, Buabeid M, Kharaba ZJ, Yaseen HS, Murtaza G. Therapeutic effects and safe uses of plant-derived polyphenolic compounds in cardiovascular diseases: a review. *Drug Des Devel Ther*. 2021;15:4713–4732. https://doi.org/10.2147/DDDT.S327238
71. Skoczyńska A, Jędrychowska I, Poręba R, et al. Influence of chokeberry juice on arterial blood pressure and lipid parameters in men with mild hypercholesterolemia. *Pharmacol Rep*. 2007;59(suppl 1):177–182.
72. .Noce A, Di Lauro M, Di Daniele F, et al. Natural bioactive compounds useful in clinical management of metabolic syndrome. *Nutrients*. 2021;13:630. https://doi.org/10.3390/nu13020630
73. Krawczyk M, Burzynska-Pedziwiatr I, Wozniak LA, Bukowiecka-Matusiak M. Impact of polyphenols on inflammatory and oxidative stress factors in diabetes mellitus: nutritional antioxidants and their application in improving antidiabetic therapy. *Biomolecules*. 2023;13:1402. https://doi.org/10.3390/biom13091402
74. Kolehmainen M, Mykkänen O, Kirjavainen PV, et al. Bilberries reduce low-grade inflammation in individuals with features of metabolic syndrome. *Mol Nutr Food Res*. 2012;56:1501–1510. https://doi.org/10.1002/mnfr.201200195
75. Kim H, Simbo SY, Fang C, et al. Açaí (*Euterpe oleracea* Mart.) beverage consumption improves biomarkers for inflammation but not glucose- or lipid-metabolism in individuals with metabolic syndrome in a randomized, double-blinded, placebo-controlled clinical trial. *Food Funct*. 2018;9:3097–3103. https://doi.org/10.1039/c8fo00595h
76. Basu A, Du M, Leyva MJ, et al. Blueberries decrease cardiovascular risk factors in obese men and women with metabolic syndrome. *J Nutr*. 2010;140:1582–1587. https://doi.org/10.3945/jn.110.124701
77. Lee I, Chan Y, Lin C, Lee W, Sheu WHH. Effect of cranberry extracts on lipid profiles in subjects with type 2 diabetes. *Diabet Med*. 2008;25:1473–1477. https://doi.org/10.1111/j.1464-5491.2008.02588.x
78. Huang L, Xiao D, Zhang X, et al. Strawberry consumption, cardiometabolic risk factors, and vascular function: a randomized controlled trial in adults with moderate hypercholesterolemia. *J Nutr*. 2021;151:1517–1526. https://doi.org/10.1093/jn/nxab034
79. Lee YJ, Ahn Y, Kwon O, et al. Dietary wolfberry extract modifies oxidative stress by controlling the expression of inflammatory mRNAs in overweight and hypercholesterolemic subjects: a randomized, double-blind, placebo-controlled trial. *J Agric Food Chem*. 2017;65:309–316. https://doi.org/10.1021/acs.jafc.6b04701
80. Rodrigo R, González J, Paoletto F. The role of oxidative stress in the pathophysiology of hypertension. *Hypertens Res*. 2011;34:431–440. https://doi.org/10.1038/hr.2010.264
81. Loperena R, Harrison DG. Oxidative stress and hypertensive diseases. *Med Clin North Am*. 2017;101:169–193. https://doi.org/10.1016/j.mcna.2016.08.004
82. Krzemińska J, Wronka M, Młynarska E, Franczyk B, Rysz J. Arterial hypertension—oxidative stress and inflammation. *Antioxidants (Basel)*. 2022;11:172. https://doi.org/10.3390/antiox11010172
83. Richter CK, Skulas-Ray AC, Gaugler TL, Meily S, Petersen KS, Kris-Etherton PM. Effects of cranberry juice supplementation on cardiovascular disease risk factors in adults with elevated blood pressure: a randomized controlled trial. *Nutrients*. 2021;13:2618. https://doi.org/10.3390/nu13082618
84. Johnson SA, Figueroa A, Navaei N, et al. Daily blueberry consumption improves blood pressure and arterial stiffness in postmenopausal women with pre- and stage 1-hypertension: a randomized, double-blind, placebo-controlled clinical trial. *J Acad Nutr Diet*. 2015;115:369–377. https://doi.org/10.1016/j.jand.2014.11.001
85. Hassellund SS, Flaa A, Kjeldsen SE, et al. Effects of anthocyanins on cardiovascular risk factors and inflammation in pre-hypertensive men: a double-blind randomized placebo-controlled crossover study. *J Hum Hypertens*. 2013;27:100–106. https://doi.org/10.1038/jhh.2012.4
86. Khor B-H, Narayanan SS, Sahathevan S, et al. Efficacy of nutritional interventions on inflammatory markers in haemodialysis patients: a systematic review and limited meta-analysis. *Nutrients*. 2018;10:397. https://doi.org/10.3390/nu10040397
87. Marx W, Kelly J, Marshall S, Nakos S, Campbell K, Itsiopoulos C. The effect of polyphenol-rich interventions on cardiovascular risk factors in haemodialysis: a systematic review and meta-analysis. *Nutrients*. 2017;9:1345. https://doi.org/10.3390/nu9121345
88. Riso P, Klimis-Zacas D, Del Bo' C, et al. Effect of a wild blueberry (*Vaccinium angustifolium*) drink intervention on markers of oxidative stress, inflammation and endothelial function in humans with cardiovascular risk factors. *Eur J Nutr*. 2013;52:949–961. https://doi.org/10.1007/s00394-012-0402-9
89. Karlsen A, Paur I, Bøhn SK, et al. Bilberry juice modulates plasma concentration of NF-κB related inflammatory markers in subjects at increased risk of CVD. *Eur J Nutr*. 2010;49:345–355. https://doi.org/10.1007/s00394-010-0092-0
90. Manna P, Jain SK. Obesity, oxidative stress, adipose tissue dysfunction, and the associated health risks: causes and therapeutic strategies. *Metab Syndr Relat Disord*. 2015;13:423–444. https://doi.org/10.1089/met.2015.0095
91. Marseglia L, Manti S, D'Angelo G, et al. Oxidative stress in obesity: a critical component in human diseases. *Int J Mol Sci*. 2014;16:378–400. https://doi.org/10.3390/ijms16010378
92. Fernández-Sánchez A, Madrigal-Santillán E, Bautista M, et al. Inflammation, oxidative stress, and obesity. *Int J Mol Sci*. 2011;12:3117–3132. https://doi.org/10.3390/ijms12053117
93. Stull AJ, Cash KC, Johnson WD, Champagne CM, Cefalu WT. Bioactives in blueberries improve insulin sensitivity in obese, insulin-resistant men and women. *J Nutr*. 2010;140:1764–1768. https://doi.org/10.3945/jn.110.125336
94. Ellis CL, Edirisinghe I, Kappagoda T, Burton-Freeman B. Attenuation of meal-induced inflammatory and thrombotic responses in overweight men and women after 6-week daily strawberry (*Fragaria*) intake—a randomized placebo-controlled trial. *J Atheroscler Thromb*. 2011;18:318–327. https://doi.org/10.5551/jat.6114
95. Schell J, Scofield RH, Barrett JR, et al. Strawberries improve pain and inflammation in obese adults with radiographic evidence of knee osteoarthritis. *Nutrients*. 2017;9:949. https://doi.org/10.3390/nu9090949
96. Hsia DS, Zhang DJ, Beyl RS, Greenway FL, Khoo C. Effect of daily consumption of cranberry beverage on insulin sensitivity and modification of cardiovascular risk factors in adults with obesity: a pilot, randomised, placebo-controlled study. *Br J Nutr*. 2020;124:577–585. https://doi.org/10.1017/S0007114520001336
97. Novotny JA, Baer DJ, Khoo C, Gebauer SK, Charron CS. Cranberry juice consumption lowers markers of cardiometabolic risk, including blood pressure and circulating C-reactive protein, triglyceride, and glucose concentrations in adults. *J Nutr*. 2015;145:1185–1193. https://doi.org/10.3945/jn.114.203190
98. Elisia I, Lam V, Cho B, et al. The effect of smoking on chronic inflammation, immune function and blood cell composition. *Sci Rep*. 2020;10:19480. https://doi.org/10.1038/s41598-020-76556-7
99. Alfaddagh A, Martin SS, Leucker TM, et al. Inflammation and cardiovascular disease: from mechanisms to therapeutics. *Am J Prev Cardiol*. 2020;4:100130. https://doi.org/10.1016/j.ajpc.2020.100130
100. Brittenden J, Heys SD, Ross J, Eremin O. Natural killer cells and cancer. *Cancer*. 1996;77:1226–1243.
101. McLeay Y, Barnes MJ, Mundel T, Hurst SM, Hurst RD, Stannard SR. Effect of New Zealand blueberry consumption on recovery from eccentric exercise-induced muscle damage. *J Int Soc Sports Nutr*. 2012;9:19. https://doi.org/10.1186/1550-2783-9-19
102. Hutchison AT, Flieller EB, Dillon KJ, Leverett BD. Black currant nectar reduces muscle damage and inflammation following a bout of high-intensity eccentric contractions. *J Diet Suppl*. 2016;13:1–15. https://doi.org/10.3109/19390211.2014.952864
103. de Liz S, Cardoso AL, Copetti CLK, et al. Açaí (*Euterpe oleracea* Mart.) and juçara (*Euterpe edulis* Mart.) juices improved HDL-c levels and antioxidant defense of healthy adults in a 4-week randomized cross-over study. *Clin Nutr*. 2020;39:3629–3636. https://doi.org/10.1016/j.clnu.2020.04.007
104. Lyall KA, Hurst SM, Cooney J, et al. Short-term blackcurrant extract consumption modulates exercise-induced oxidative stress and lipopolysaccharide-stimulated

inflammatory responses. *Am J Physiol Regul Integr Comp Physiol*. 2009;297:R70–R81. https://doi.org/10.1152/ajpregu.90740.2008
105. Lehtonen HM, Suomela J, Tahvonen R, et al. Different berries and berry fractions have various but slightly positive effects on the associated variables of metabolic diseases on overweight and obese women. *Eur J Clin Nutr*. 2011;65:394–401. https://doi.org/10.1038/ejcn.2010.268
106. Larmo P, Alin J, Salminen E, Kallio H, Tahvonen R. Effects of sea buckthorn berries on infections and inflammation: a double-blind, randomized, placebo-controlled trial. *Eur J Clin Nutr*. 2008;62:1123–1130. https://doi.org/10.1038/sj.ejcn.1602831
107. Ronis MJ, Pedersen KB, Watt J. Adverse effects of nutraceuticals and dietary supplements. *Annu Rev Pharmacol Toxicol*. 2018;58:583–601. https://doi.org/10.1146/annurev-pharmtox-010617-052844
108. Schmitz SM, Lopez HL, Mackay D, Nguyen H, Miller PE. Serious adverse events reported with dietary supplement use in the United States: a 2.5 year experience. *J Diet Suppl*. 2020;17:227–248. https://doi.org/10.1080/19390211.2018.1513109

Nutrition Reviews, 2024, 00, 1–16
https://doi.org/10.1093/nutrit/nuae143
Systematic Review