AFMN BIOMEDICINE

REVIEW ARTICLE

ANTI-INFLAMMATORY EFFECT OF BILBERRY (VACCINIUM MYRTILLUS L.) PREPARATION: A SYSTEMATIC REVIEW

Andjela V. Dragićević[1] **Nikola M. Stojanović**[2] **Dragana R. Pavlović**[1]

[1]Department of Pharmacy, University of Niš Faculty of Medicine, Niš, Serbia [2]Department of Physiology, University of Niš Faculty of Medicine, Niš, Serbia

Naturally-derived anti-inflammatories, such as bilberry (*Vaccinium myrtillus*), are particularly interesting due to their health benefits. Bilberries are a rich source of primary metabolites, such as sugars and organic acids, which give the fruit its taste. They also contain anthocyanins, the most abundant group of secondary metabolites, possessing various biological properties, including anti-inflammatory effects. This paper reviews current knowledge on the bioactive compounds found in *V. myrtillus* (bilberry) berries and summarizes clinical studies investigating the anti-inflammatory effects of various bilberry preparations.

The literature review was conducted using the databases PubMed, Scopus, Web of Science, Science Direct, NCBI, Google Scholar, and ClinicalTrials.gov.

V. myrtillus was found to be a significant source of bioactive molecules since components of bilberry fruits, such as polyphenols, anthocyanins, and flavonoids, are well known for their ability to modify cellular pathways implicated in the pathophysiology of many diseases. A brief review of the clinical study data related to the bilberry application highlighted its health-promoting effects, specifically its anti-inflammatory effect.

Bilberry fruit is a rich source of phenolic compounds with high biological potential. These compounds can be used commercially in pharmaceutical, cosmetic, and natural products industries. However, due to the wide variety of constituents in the fruit, their potential interactions, and the complexity of their metabolism, further in-depth studies are needed to better define and characterize the contribution of each active component and possible synergies between different compounds. Numerous clinical studies have highlighted the anti-inflammatory properties of *V. myrtillus* fruits, which could help prevent various diseases.

Keywords: berry, cyanidin 3-O-glucoside chloride, inflammation, Myrtilli fructus

Submitted: January 8, 2025 **Accepted:** February 27, 2025
Published online: December 17, 2025

Correspondence to:
Andjela V. Dragićević
Department of Pharmacy
University of Niš Faculty of Medicine
Bulevar dr Zorana Đinđića 81, Niš, Serbia
E-mail: dragicevic.andjela@gmail.com

INTRODUCTION

According to the Food and Agriculture Organization of the United Nations, fruit production has risen continuously in recent decades (1). However, given the growing world population and current consumer preferences for organic, high-quality food and tendency towards healthy lifestyles, current fruit production may not be sufficient to meet global demand (2). As fruit production continues to increase, a significant number of by-products will inevitably be generated (3). To address this issue and improve the nutritional value of various foods, it is important to investigate the use of these by-products in functional foods as a sustainable approach to reducing waste production (3-5).

The Vaccinium species, a genus with great morphological diversity, belonging to the Ericaceae family, are widespread in Europe, Asia, North and Central America as well as in Southeast and Central Africa (3, 6-8). Due to their numerous health benefits, the use of Vaccinium species is steadily increasing. They have been shown to be effective in various diseases such as diabetes (9, 10), obesity (10), rheumatoid arthritis (11), cardiovascular and neurological disorders (12-14), atherosclerosis (8), and cancer (15). Humans consume the fruits of different species including cranberries, blueberries, bilberries, and lingonberries, some of which are of commercial importance. These species, including their flowers, leaves and fruits, are also widely used in traditional medicine in many countries (16).

The European blueberry, also known as the bilberry (*Vaccinium myrtillus L., Ericaceae*), is a small, dark blue fruit that grows on shrubs of the genus *Vaccinium* (6-8). The berries usually ripen between July and September, and this process is influenced by factors such as site conditions, altitude, and habitat type (6). Due to their limited shelf life, the fruits are best eaten fresh, but can also be preserved by freezing, drying or processing into products such as jams, juices, wines or liqueurs (17). In the past, bilberries were used in traditional medicine and today they are mainly cultivated in Northern and Eastern Europe and North Africa (18). The appearance and taste of the fruits of the cultivated bilberry (*Vaccinium sp.*) are very similar, but as there are numerous varieties of the species, no commercial bilberry cultivars have yet been introduced to the market. Bilberry cultivation areas are spread globally, and their market share is growing rapidly. The economic importance of blueberries is evident from the expansion of global production, which in 2021 for example, amounted to 163,741 hectares and 1,113,260.6 tonnes – nearly three times the acreage and double the yield compared to 2010 (19), this trend continues today.

Bilberries are considered a rich source of carotenoids and phenolic compounds, and they also contain modest amounts of various minerals and vitamins (7). Anthocyanins, the primary class of flavonoids found in berries, are responsible for giving bilberries their distinctive blue color (7,8). Research has linked anthocyanins to various beneficial health outcomes, including potential treatment or prevention of cancer, cardiovascular disease, diabetes, obesity, aging-related illnesses, urinary tract infections, and periodontal disease (3-15). Moreover, bilberries' high flavonoid content has garnered attention as a source of coloring compounds for use in food and medicine. The growing consumer preference for meals perceived as healthier and more natural has spurred increased interest in these fruits (20). Currently, many products on the market incorporate bilberries, highlighting their beneficial effects, particularly their antioxidant potential (7). In the European Union, according to the Cosmetic Ingredients and Substances Database (CosIng), extracts from *V. myrtillus* fruit, fruit water (an aqueous solution of steam distillates from the fruit), and fruit juice are used for skin conditioning (21). Additionally, extracts of the fruit and leaves are employed as astringents, refreshers, skin conditioners, and tonics (21).

Inflammation is a natural defense mechanism of the human body, triggered by potential threats such as allergens and tissue damage (22). While it serves a protective role, uncontrolled inflammation can lead to various disorders, including cancer, autoimmune diseases, cardiovascular issues, allergies, and metabolic syndrome. These conditions not only affect individuals but also have significant societal impacts. Drugs such as steroids, non-steroidal anti-inflammatory drugs (NSAIDs), and immunosuppressants are commonly used to treat and suppress inflammation. However, it is important to recognize that these medications can have side effects. Therefore, administering the lowest effective dose while achieving optimal efficacy and minimizing side effects is crucial (22,23). To enhance pharmaceutical efficacy and reduce side effects, incorporating natural anti-inflammatory agents into therapy is essential. There is a growing need to explore herbal medicines, as they play a vital role in modern healthcare. Guidelines for herbal medicines largely stem from complementary, alternative, and traditional practices. However, these guidelines must

be scientifically validated before being integrated into modern medicine.
The present review is designed to report the current knowledge on the bioactive compounds of berries from the V. myrtillus and to summarize the clinical study of the anti-inflammatory effects of different bilberry preparations published from 2007 to 2024.

METHODS

The literature search was conducted using several electronic databases, including PubMed, Scopus, Web of Science, ScienceDirect, NCBI, Google Scholar, and ClinicalTrials.gov. The search strategy used the keywords 'anti-inflammatory', 'bilberry', and '*Vaccinium myrtillus*'. Only studies published in English were included. The search covered the period from 2007 to the present and initially identified 40 records. After screening for relevance and applying the predefined inclusion and exclusion criteria, 13 studies were excluded, resulting in a final selection of 27 studies for analysis.

Bioactive compounds

Phenolic compounds represent the primary group of phytochemicals found in *V. myrtillus* berries (3, 24-25). The concentration of these compounds can be affected by various factors, including the stage of ripeness, storage conditions, and environmental factors during growth. Research has demonstrated that berry bushes grown in cold climates with short growing seasons produce fruits with higher levels of phenolic compounds compared to those cultivated in moderate climates (26). The berries from *V. myrtillus* represent an exceptionally rich natural source of anthocyanins, containing the highest levels found in any fruit (300–700 mg/100 g of fresh fruit) (3).
Anthocyanins are present in the outer layer of fruits, along with phenolic compounds, and smaller amounts can also be found in the pulp and seeds. The *V. myrtillus* is characterized by the presence of delphinidin and cyanidin, petunidin, peonidin, and malvidin (3, 24-27). The vibrant color of *V. myrtillus* berries is attributed to the high concentration of anthocyanidins, which can constitute up to 2% of the fresh mass in the peels and pulp. Approximately 90% of the phenolic compounds in bilberry fruits are anthocyanins. In bilberries, common derivatives of delphinidin, cyanidin, peonidin, petunidin, and malvidin include mono-, di-, and trisaccharides. The principal sugars found are glucose, galactose, xylose, rhamnose, and arabinose (3,8). The cyanidin 3-O-galactoside, cyanidin 3-O-glucoside, cyanidin 3-O-arabinoside, delphinidin 3-O-galactoside, delphinidin 3-O-arabinoside, delphinidin 3-O-glucoside, malvidin 3-O-galactoside, malvidin 3-O-arabinoside, malvidin 3-O-glucoside, petunidin 3-O-galactoside, petunidin 3-O-arabinoside, petunidin 3-O-acetylglucoside, peonidin 3-O-galactoside, and peonidin 3-O-arabinoside were identified in the fruits of *V. myrtillus* (8,28). According to the 10th edition of the European Pharmacopoeia, the anthocyanins in bilberry extracts are significantly abundant, with recommended level between 32% and 40% of anthocyanidins (the aglycone form of anthocyanins) (29). The fresh bilberry fruits (*Myrtilli fructus recens*) should contain at least 0.3% anthocyanins (expressed as cyanidin 3-O-glucoside chloride) and the dried fruits (*Myrtilli fructus siccus*) should have at least 1.0% of tannins (expressed as pyrogallol), according to the European Pharmacopoeia monographs (30,31).
In bilberry fruits, the predominant flavonol is quercetin, constituting over half of the total flavonoid content (3,8). The second most abundant flavonoid is myricetin, while other flavonols such as isorhamnetin, syringetin, and laricitrin are present in lower concentrations (3,8). The two primary glycosides found in bilberry fruits are rhamnosides and glucuronides (32-34). Apigenin, chrysoeriol, myricetin, myricetin-3-xyloside, quercetin 3-O-glucuronide, quercetin 3-O-xyloside, isorhamnetin 3-O-glucoside, luteolin (35) as well as kaempferol, isorhamnetin, laricitrin, syringetin, isorhamnetin 3-O-galactoside, myricetin 3-O-glucuronide, laricitrin 3-O-glucoside, syringetin 3-O-glucoside, kaempferol 3-O-glucoside, myricetin 3-O-galactoside are also described in *V. myrtillus* (36).
The fruits of the *V. myrtillus* are also a valuable source of organic acids and their byproducts. Bilberry fruits contain citric, malic, quinic, and shikimic acids. Additionally, they are rich in phenolic and hydroxycinnamic acids such as gallic, ellagic, and syringic, as well as p-coumaric, caffeic, and ferulic acids. There is also a smaller amount of dihydroxybenzoic acid, salicylic acid, and vanillic acid in the fruits. These organic acids can exist in free, etherified, or esterified forms. During the etherification process, various saccharide fractions are typically involved, forming esters with each other or with distinct phenolic compounds (32-34).

Clinical studies of different bilberry preparations

In the traditional medicine, bilberries have been used to treat various conditions, including skin ulcers, hemorrhoids, nausea, vomiting, diarrhea, mucosal inflammation, and to improve eyesight (37). Their anti-inflammatory effects are attributed to the downregulation of pro-inflammatory molecules s, such as tumor necrosis factor alpha (TNF-*α*), interleukin-1 beta (IL-1*β*), and interleukin-6 (IL-6) and enzymes inducible nitric oxide synthase (iNOS), and cyclooxygenase-2 (COX-2). These effects involve alterations in signaling pathways, including nuclear factor-kappa beta (NF-*kβ*) and Janus kinase-signal transducer and activator of transcription (JAK-STAT), as well as a reduction in reactive oxygen species (ROS) levels in both cell cultures and experimental animals (38,39). The anti-inflammatory action of different formulations of bilberries has been confirmed in several clinical studies (40-45). In these studies, bilberries were administered in the form of juices, fresh/frozen berries, freeze-dried preparations, or anthocyanin rich extract (Medox®). The anti-inflammatory effects of bilberry extracts and anthocyanins were clearly documented, and notably, none of these formulations reported any side effects (Table 1). Daily intake of anthocyanins, which are the main group of phenolic compounds in bilberries, was administered at doses of up to 640 mg/day without adverse effects reported (46).

Medox® capsules contained purified anthocyanins isolated from bilberries (*V. myrtillus*) and blackcurrant (*Ribes nigrum*), with cyanidin and delphinidin-3-O-*β*-glucosides accounting for at least 40–50% of the total anthocyanins. In a study involving 120 participants over three weeks, these capsules were shown to reduce levels of the pro-inflammatory mediators interleukin-4 (IL-4), interleukin-8 (IL-8), interleukin-13 (IL-13), and interferon alpha (IFN*α*) (40). Supplementation with bilberry juice also reduced levels of circulating high-sensitivity C-reactive protein (hs CRP), IL-6 and interferon-gama (INF-*γ*)-induced monokine (MIG). Interestingly, this study observed an unexpected increase in plasma levels of TNF-*α*; however, there were no significant effects on clinical factors, antioxidant status, or free radical levels (41). Lehtonen and co-workers (47) reported that consumption of 100 g whole frozen bilberries for 33–35 days reduces plasma levels of TNF-*α*, circulating vascular cell adhesion molecule-1 (sVCAM-1) and adiponectin in overweight and obese women. Circulating adiponectin levels positively correlate with insulin sensitivity and inversely with body fat and inflammation. The lower adiponectin levels observed after whole frozen bilberry consumption may not have been directly caused by the bilberries, but rather due to an insufficient interval between ingestion and the measurement of circulating adiponectin levels. Widén and co-workers (42) documented that consumption of 500 g of bilberries per day decreases inflammatory cytokine levels (IL-1*β*, IL-6, and vascular endothelial growth factor (VEGF)), resulting in a reduction of gingival inflammation. Additionally, the anti-inflammatory properties of bilberry anthocyanins may expedite the healing process after physical activity. A study by Lynn and co-authors (43) showed how bilberry juice consumption affects inflammation and exercise-induced muscle injury in recreational runners training for a half-marathon.

An inflammatory reaction promotes the generation of reactive oxygen species, creating a pro-inflammatory environment. In a double-blind, placebo-controlled intervention study, the ingestion of 660 mL of bilberry/red grape juice per day for nine weeks was found to reduce biomarkers of inflammation and oxidative stress in 60 men with subjective memory impairment (48). The intervention resulted in decreased levels of macrophage inflammatory protein (Mip)1*β*, VEGF, IL-6, TNF-*α*, and other biomarkers of inflammation and tissue damage (lactate dehydrogenase, LDH). Even though these markers were decreased, the memory scores of the participants remained unchanged (48).

Reactive oxygen species are produced in the inflamed colon as a result of an excess of neutrophils and macrophages associated with ulcerative colitis. In an open pilot trial involving 13 patients with mild to moderate ulcerative colitis, the consumption of 160 g of bilberry preparation, providing 210 mg of anthocyanins per day for six weeks, significantly reduced mucosal inflammation (49). This intervention also decreased the level of calprotectin in feces and modulated inflammatory changes. Specifically, it reduced the expression of IFN-*γ*, TNF-*α*, and interferon gamma receptor 2 (IFN-*γ*R2), increased serum levels of monocyte chemoattractant protein-1 (MCP-1), and altered the expression of IL-10 (44).

Metabolic syndrome (MetS) is a global health concern associated with inflammation, dyslipidemia, obesity, and hyperglycemia. In a study, the serum levels of hsCRP, IL-6, IL-12, and lipopolysaccharides (LPS) were significantly decreased in men and women with MetS when 400 g of fresh bilberries (equivalent to 200 g of berry puree and 40 g of dried berries) were incorporated into their diets (45). Interestingly, the levels of leptin and adiponectin were

Table 1. *Summary of clinical studies on anti-inflammatory effects of different bilberry extracts published from 2007 to 2024*

Intervention (reference)	Chemical profile	Study design	Outcome measure	Results
Billberry powder 3 times daily (7)	NA	Double blinded, randomized, clinical trial, 50 patients suffering from STEMI (ST-segment elevation myocardial infarction) or non-STEMI (non-ST-segment elevation myocardial infarction) 3 months	6-minute walk test, CRP, IL-6, TNF-*α*, INF-*γ*, markers of oxidative stress: (oxidized LDL, carbonylated proteins, H_2O_2, hexanoyl L lysine, NOS), markers of myocardial damage and heart failure: BNP and troponin I, markers of endothelial function: VEGF, 8-isoprostane, E-selectin, plasma lipids; total cholesterol, LDL-cholesterol, TGA	Study results have not been submitted. This may be because the study hasn't been done, the deadline for submitting results has not passed, or this study does not require the results to be submitted.
275-mg *Medox*® capsules 2 times/day, providing a total of 300 mg anthocyanins/day (40)	*Medox*® capsules contained purified anthocyanins isolated from bilberries (*V. myrtillus*) and blackcurrant (*Ribes nigrum*); cyanidin and delphinidin 3-O-*β*-glucosides constituted at least 40–50% of the total anthocyanins	Parallel-designed, placebo controlled clinical study, 120 participants, 3 weeks	Cytokines (IL-1*β*, IL-1Ra, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-13, IL-17, TNF*α*, IFN*α*, IFN*δ*), GM-CSF, Mip-1*α*, MIP-1*β*, IP-10, MCP-1, eotaxin, RANTES, CRP	↓IL-4, ↓IL-8, ↓IL-13, ↓IFN*α*, ↓RANTES
330 ml bilberry juice/day (diluted to 1 L using tap water) (41)	NA	Parallel-designed randomized clinical study, 62 participants, 4 weeks	CRP, IL-1*β*, IL-1*α*, IL-1 IL-1Rα IL-2, IL-2R IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, IL-15, IL-17, TNF-*α*, IFN-*α*, IFN-*γ*, GM-CSF, MIP-1*α*, MIP-1*β*, IP-10, MCP-1, MIG, eotaxin, RANTES, WBC, fibrinogen, uric acid, γ-GT, total proteins, cholesterol, TGA, biomarkers of oxidative stress status (DHAA, D-ROM, oxidized glutathione, plasma GSH redox potential)	↓CRP, ↓IL-6, ↓IL-15, ↓MIG, ↑TNF-*α*, ↑plasma quercetin, ↑ *p*-coumaric acid, no differences were observed for clinical parameters, oxidative stress or antioxidant status
250 or 500 g bilberries daily over seven days (42)	NA	24 adult with gingivitis, 7 days	BOP, cytokines (IL-1*β*, IL-1Rα, IL-6, IL-12, IP-10, PDGF-BB, MIP-1*α*, and VEGF	↓ BOP, significant differences between baseline and study endpoint after intake of 500 g of bilberries/day for three of the cytokines studied: IL-1*β* IL-6 and VEGF
200 mL bilberry juice twice per day, each 200 ml bottle also contained 80.04 ± 3.51 mg of total anthocyanins (43)	NA	Single blind, randomized, placebo-controlled, parallel study, 8 days, 21 recreational runners	DOMS, muscle damage (CK), CRP	↑moderate CRP 24 h post-race
160 g of bilberry preparation (44)	NA	Open pilot trial, 13 patients with mild to moderate ulcerative colitis, 6 weeks	TNF-*α*, MCP-1, IL-10, IL-13, IL-17*α*, IFN-γ	↓IFN-*γ*, ↓TNF-*α*, ↓p65, ↓NF-*κβ*,↑IL-22, ↑IL-10
400 g fresh bilberries 200 g of bilberry puree and 40 g of dried bilberries (eq. 200 g of fresh bilberries) (45)	NA	Randomized controlled study, 27 participants with MetS features 4-week run-in, 8-week dietary intervention, and 4-week recovery periods	Body weight, body composition, blood pressure, inflammation score, glucose and lipid metabolism, transcriptomic gene expression analyses	No differences in body weight, glucose or lipid metabolism, ↓hsCRP, IL-6, IL-12, LPS, transcriptomic gene expression analyses
100 g frozen, whole berries (47)	NA	Randomized, cross-over study, 110 female overweight and obese women, intervention (33–35 days) and wash-out (30–39 days) periods	Body composition, plasma glucose, serum total cholesterol, HDL, LDL, triacylglycerols, *γ*-GT , glycated hemoglobin, hsCRP, insulin, sICAM-1, sVCAM-1, TNF-*α*, IL-6, adipokine, HbA1c	↓TNF-*α*, ↓sVCAM-1, ↓adiponectin
330 mL of bilberry/red grape preparation, 2 times a day (48)	NA	Double blind, placebo-controlled study, 60 men with subjective memory, 9 weeks	Neuropsychological test scores and whole blood gene regulation	↓IL6, ↓TNF-*α*, ↓EGF, ↓Mip1*β*, ↓VEGF
160 g of bilberry preparation, 210 mg anthocyanins per tray (49)	NA	Open pilot trial, 13 patients with mild to moderate ulcerative colitis, 6 weeks	Sigmoidoscopy, fecal calprotectin, CAI assessment, SIBDQ	↓Fecal calprotectin levels, ↓endoscopic Mayo score
2 x 80-mg *Medox*® capsules two times per day (morning and evening) (50)	NA	Randomized, placebo controlled trial, 55 MetS or normal, 28 days	Serum levels of lipid concentration, uric acid, hsCRP, FBG, expression of P-selectin/CD62P	↓FBG, ↓TG, ↓LDL-C, ↓hsCRP, ↓ADP-induced platelet
2x 80 mg anthocyanin capsules twice daily (30 min after breakfast and supper) for a total intake of 320 mg anthocyanins/d (51)	bilberries and blackcurrants	Randomized, double-blind, placebo controlled study, 150 hypercholesterolemic participants, 24 weeks	hsCRP, sVCAM-1, TNF-*α*, IL-1*β*, lipids and glucose	↓hsCRP, ↓sVCAM-1, ↓IL-1*β*, ↓LDL-cholesterol ↑HDL-cholesterol, no significant differences in the levels of glucose and insulin
Medox® capsules - anthocyanin capsule contained 80 mg (52)	Anthocyanins that were extracted from bilberry (blueberry) (*V. myrtillus*) and black currant (*R. nigrum*)	Double-blind, randomized placebo-controlled crossover study, 31 healthy men, 4-week with a 4-week washout	Sitting systolic BP, CVD-related parameters; total cholesterol, HDL-C, total cholesterol/HDL-C ratio, LDL-C, triglycerides, lipoprotein a, fasting glucose, HbA1c, albumin/creatinine ratio, insulin, HOMA-IR, homocysteine, hematological and liver- and kidney markers, markers of inflammation and oxidative stress and plasma polyphenols	↑HDL, ↑blood glucosevon Willebrand factor No effects were observed on inflammation or oxidative stress

Medox® capsules (53)	Anthocyanins that were extracted from bilberry (blueberry) (*V. myrtillus*) and black currant (*R. nigrum*)	Randomized, double-blinded placebo-controlled study, 169 participations, 12-weeks	Anthropometric measurement, plasma ceramide, fasting blood TC, HDL-C, TG, ApoA-I, ApoB, glucose, insulin, plasma cholesterol efflux	↓ Cer 16:0, ↓ Cer 18:0, ↓ Cer 20:0, ↓ Cer 22:0, ↓ Cer 24:0, ↓ Cer 24:1, ↑enhanced cholesterol efflux capacity
Mirtoselect® (54)	Standardised bilberry extract (36 % (w/w) anthocyanins)) which equates to about 50 g of fresh bilberries formulated in gelatin capsules	Randomised, double-blinded cross-over study, 8 males with type 2 diabetes	Oral glucose tolerance testing, glucagon-like peptide-1c, antioxidant assays	↓glucose ↓insulin no change in the gut (glucagon-like peptide-1, gastric inhibitory polypeptide), pancreatic (glucagon, amylin) or anti-inflammatory (monocyte chemotactic protein-1) peptides, antioxidant (Trolox equivalent antioxidant capacity, ferric-reducing ability of plasma)
Bilberry-blackcurrant purée, 139 g Lingonberry purée, 122 g Bilberry soup, 250 ml (55)	NA	Randomized, single-blinded crossover study, 26 participations	Postprandial glucose, insulin, free fatty acids, satiety scores assessed by using visual analogy scales, heart rate variability	↓glucose ↓ insulin, ↓ non-esterified fatty acids (NEFA)
650 mg per tablet with 150mg *V. myrtillus* L. extracts, twice a day (56)	NA	Randomized double-blind study, 80 participations, 3 months	Plasma AGEs, sRAGE levels, urinary AGEs levels, transcription levels of RAGE and AGER1, gut microbiota, skin AGEs levels, body weight, body composition (body fat mass and lean mass), plasma total cholesterol, LDL, HDL and triglycerides, CRP, IL-6 and TNF-α, SCFA	Study results have not been submitted. This may be because the study hasn't been done, the deadline for submitting results has not passed, or this study does not require the results to be submitted.
Billberry powder 3 times daily (57)	NA	Double blinded, randomized, clinical trial, 50 patients suffering from STEMI (ST-segment elevation myocardial infarction) or non-STEMI (non-ST-segment elevation myocardial infarction) 3 months	6 minutes walk test, C-reactive protein, IL-6, TNF-α, INF-γ, markers of oxidative stress (oxidized LDL, carbonylated proteins, 2-OHDG, H_2O_2, hexanoyl L lysine, nitrogen oxide synthase), markers of myocardial damage and heart failure (BNP and troponin I), markers of endothelial function (VEGF, 8-isoprostane, E-selectin, LDL, TGA)	Study results have not been submitted. This may be because the study isn't done, the deadline for submitting results has not passed, or this study isn't required to submit results.
Bilberry shakes 2 times daily (containing in total 40g of dried bilberry powder equalling 480 g of fresh berries per day) (58)	NA	Randomized, double-blind, placebo-controlled study, 900 participations, 3 months	Lipid profile (HDL, TGA, total cholesterol, LDL, apo A, apo B, Lp(a) and oxidized LDL), symptom-limited bicycle ergometer test, dynamic unilateral heel-lft and unilateral shoulder flexion tests, self-reported physical activity level, troponin, NT-proBNP, hsCRP, IL-6 and HbA1c, insulin, creatinine, Cystatin C, glucose and C-peptide, fecal samples of gut microbiota composition, left ventricular systolic function, resting heart rate, systolic and diastolic blood pressure	Study results have not been submitted. This may be because the study hasn't been done, the deadline for submitting results has not passed, or this study does not require the results to be submitted.
Bilberry capsule (59)	containing bilberry dried extracts at 23.2 mg and bilberry powder at 3.2 mg,	Randomized, double-blind placebo-controlled study, 80 participations with confirmed diagnosis of dry eye, 30days and washout period for 20 days.	Schirmer's Test, Tear Film Breakup Time, Ocular Surface Index, Intraocular Pressure	Study results have not been submitted. This may be because the study hasn't been done, the deadline for submitting results has not passed, or this study does not require the results to be submitted.
Bilberry-based probiotic beverage (60)	NA	Randomized, parallel study, 32 participations	Postprandial levels of serum insulin	Study results have not been submitted. This may be because the study hasn't been done, the deadline for submitting results has not passed, or this study does not require the results to be submitted.
Capsules containing 320 mg anthocyanins derived from bilberry fruit (delphinidin type), 320 mg anthocyanins derived from black rice (cyanidin type) and a placebo control (61)	NA	Randomized, double blind,placebo contoled cross-over study, 55 participations, eaach treatment will be ingested for 28 days with a wash-out period of 4 weeks in-between.	Total/HDL cholesterol, TGA, cholesterol efflux capacity, PON-1 activity, bile acids and derivatives, glucose, fructosamine and insulin, MicroRNA expression	Study results have not been submitted. This may be because the study hasn't been done, the deadline for submitting results has not passed, or this study does not require the results to be submitted.
Bilberry extract capsules, 160 mg (25% anthocyanosides) (62)	NA	Double-blind, randomized, placebo controlled, cross-over trial 2 x 28 days	Change of the dark adaption of the pupil using the method of the dark adaption Goggles (DAG), Changes of the dark adaption using dark flashes, Changes of the weakest, correctly recognised contrast	Study results have not been submitted. This may be because the study hasn't been done, the deadline for submitting

			level, Assessment of subjective efficacy based on a visual analogue scale (VAS) rating questionnaire, assessment of clinical global impression on a 5-point rating scale	results has not passed, or this study does not require the results to be submitted.
A powder product (4 g) that will be mixed into a drink and consumed immediately prior to eating a high-fat meal consists of 3 g of a mix a maltodextrins, and 1 g of anthocyanin-rich plant polyphenol blend (100 mg bilberry extract, 300 mg black currant extract, and 600 mg black rice extract). The placebo (4 g) consists of a mix of maltodextrins (3.85 g) and Red Dye No. 40 (0.125 g) and Blue Dye No. 1 (0.025 g) (63)	NA	Randomized, placebo-controlled cross-over study, 27 participations	Plasma endotoxin, IL-6, insulin, GLP-1, GLP-2, GIP, plasma adiponectin, leptin, ghrelin, TGA, plasma total cholesterol, HDL, LDL, zonulin, plasma total polyphenols, anthocyanidins, catechins, glucose, PBMC (IL-8, IL-10, IL -1β, IL -12$_P$70, TNFα, NF-kβ)	Study results have not been submitted. This may be because the study hasn't been done, the deadline for submitting results has not passed, or this study does not require the results to be submitted.
Several different berry powders including rose hip, bilberry, blackcurrant, sea buckthorn, and lingonberry, start with 6.25 g berry powder and double the dosage each week until we reach a maximum dosage of 50 g according to the Swedish National Food Agencies recommendations, placebo comparator potato starch (64)	NA	Randomized, placebo-controlled study, 18 participations, 5 weeks	Changes in the extent of gingivitis, as determined by severity of gingival bleeding, VSEGF, saliva and gingival fluid	Study results have not been submitted. This may be because the study hasn't been done, the deadline for submitting results has not passed, or this study does not require the results to be submitted. .
ACRB - softgels consisting of anthocyanin-rich blend.. Product consumed once daily, preferably with breakfast (65)	Softgel contain: 49 mg bilberry extract; 101 mg black currant extract; and 303 mg black rice extract. The product also contain olive oil, sunflower lecithin, yellow beeswax, bovine gelatin, and water	Randomized placebo controlled study, 30 participants, 8 weeks	Plasma TGA, free fatty acids, HDL, LDL, glucose, insulin, LPS, LPS binding protein, PBMC gene expression, plasma total polyphenols, plasma total anthocyanidins, Irisin, total blood gene expression, fecal microbiota, fecal short chain fatty acids, skin carotenoids	Study results have not been submitted. This may be because the study hasn't been done, the deadline for submitting results has not passed, or this study does not require the results to be submitted.
320-mg anthoycanins twice daily (66)	Total of 17 different purified anthocyanins (mostly cyanidin 3-O-β-glucosides and delphinidin 3-O-β-glucosides were extracted from bilberry (*V. myrtillus*) and black currant (*R. nigrum*)	Double-blind randomized placebo-controlled crossover study, 31 healthy men, 4-week with a 4-week washout	Sitting systolic, diastolic blood pressure (BP) and heart rate (HR), supine BP and HR, 24-h ambulatory BP and HR, Finometer BP and HR, cardiovascular and catecholamine stress reactivity, renin, aldosterone, angiotensin-converting enzyme and catecholamines in platelets	Not significantly changed sitting BP or 24-h ambulatory BP, differences in components of the rennin–angiotensin–aldosterone system, platelet catecholamines or
				differences in CV or catecholamine responses between treatment periods were not found. Resting supine BP measured by Finometer tended to be lower in the anthocyanin period.
Standardized bilberry extract (67)	Cyanidin 3-glucoside as the anthocyanin reference 35.82%	Randomized, double-blind, placebo-controlled, parallel study, 109 healthy adult men and women, 12 weeks	Ocular tests, Ocular fatigue test	Post-load HFC-1 values were significantly improved

apolipoprotein A-I–ApoA-I; apolipoprotein B—ApoB; bleeding on probing—BOP; brain natriuretic peptide—BNP; C-reactive protein—CRP; creatine kinase— CK; delayed onset muscle soreness—DOMS; granulocyte-macrophage colony-stimulating factor—factor GM-CSF; fasting blood glucose—FBG; fecal short chain fatty acids—SCFA; glycated haemoglobin—HbA1c; γ-glutamyltransferase—γ -GT; γ glutamyl transpeptidase GGT—γ-GT; granolyte/macrophage colony-stimulating lipopolysaccharides—LPS; high sensitivity C-reactive protein—hsCRP; high-density lipoprotein cholesterol—HDL; homeostasis model assessment of insulin resistance—HOMA-IR; interferon gamma-induced protein 10—IP-10; immunoprotein—IP-10; monocyte chemoattractant protein—MCP; IL-1 receptor antagonist—IL-1Ra; low-density lipoprotein cholesterol—LDL; macrophage inflammatory protein—MIP; monokine induced by IFN-γ—MIG; nitrogen oxide synthase—NOS; platelet-derived growth factor —PDGF; platelet surface marker—P-selectin/CD62P; plasma advanced glycation end products AGEs; regulated upon activation, normal T cell expressed and secreted—RANTES; soluble intercellular adhesion molecule—sICAM-1; soluble vascular cell adhesion molecule—sVCAM-1; soluble receptor for advanced glycation end products—sRAGE; triacylglycerides—TGA;vascular cell adhesion molecule-1—VCAM-1; vascular endothelial growth factor—VEGF; white blood cells—WBC.

unaffected by bilberry administration. This suggests that bilberries may help alleviate MetS through their mild anti-inflammatory potential. In another study, Aboonabi and co-workers (50) found that subjects with MetS who consumed Medox® capsules twice a day for four weeks, experienced significant reductions in inflammation and improvements in their lipid profiles. This was evidenced by the decreased levels of inflammatory biomarkers, fasting blood glucose, low-density lipoprotein (LDL) cholesterol, triglycerides, and total serum cholesterol levels.

Supplements containing anthocyanins enhance the lipid profile by increasing high-density lipoprotein cholesterol (HDL) and lowering LDL cholesterol. In a study involving 150 hypercholesterolemic participants, Zhu and co-workers (51) found that 24 weeks of supplementation with a processed anthocyanin mixture (320 mg/day bilberry and blackcurrant) decreased serum levels of hsCRP, sVCAM-1, IL-1β, and LDL cholesterol, but increased HDL cholesterol. A similar effect was observed in a study with 31 healthy men conducted by Hassellund and associates (52). Furthermore, among the 169 participants, 12 weeks of supplementation with 40, 80, or 320 mg/day of anthocyanins resulted in a dose-dependent decrease in plasma ceramide levels accompanied by an increase in cholesterol efflux capacity (53). Hoggard and co-workers (54) conducted a randomized, double-blind, crossover study involving males with type 2 diabetes. They found that treatment with a standardized bilberry extract containing 36% (w/w) anthocyanins, equivalent to about 50 g of fresh bilberries in gelatin capsules, resulted in reduced levels of glucose and insulin. Similarly, another study also reported decreased glucose and insulin levels following bilberry supplementation (55).

Some clinical studies involving subjects treated with bilberry powder, extracts, or bilberry-based shakes and probiotic drinks have not yet produced results. This may be due to various reasons, such as the studies still being ongoing, the submission deadlines for results not yet passing, or the studies not being required to submit results at all. While research on humans has indicated that bilberries possess anti-inflammatory properties, these findings come with certain limitations. Considerable variation has been observed across these studies, which can be attributed to differences in regimens, doses, durations, sites, and populations involved.

CONCLUSION

Bilberry is well-regarded for its potential health benefits and as a functional food, supported by numerous studies that have identified and quantified various bioactive phytochemicals known to benefit human health. Research findings have demonstrated the anti-inflammatory effects of different *V. myrtillus* fruit preparations, which could contribute to the prevention of several diseases. Upon ingestion, anthocyanins are metabolized into various conjugates, which further break down into phenolic acid degradation products. Accumulating evidence suggests that the combined effects of these metabolites may explain their health-promoting properties. Additionally, there is significant inter-individual and intra-individual variability in the absorption, metabolism, distribution, and excretion of anthocyanins. Current research indicates that bilberries are among the fruits with the most significant positive impact on human health.

Acknowledgements

This research was supported by the Ministry of Science, Technological Development and Innovation of the Republic of Serbia (Grant No. 451-03-65/2024-03/200113 and 451-03-66/2024-03/200113).

Competing Interest

The authors declare no relevant conflicts of interest.

REFERENCES

1. FAO. Data Food and Agriculture Data (Datenbank). Available online: https://www.fao.org/faostat/en/#data

2. Precup G, Pocol CB, Teleky BE, Vodnar DC. Awareness, Knowledge, and Interest about Prebiotics-A Study among Romanian Consumers. Int J Environ Res Public Health 2022; 19:1208. [CrossRef]

3. Martău GA, Bernadette-Emőke T, Odocheanu R et al. Vaccinium species (Ericaceae): Phytochemistry and biological properties of medicinal plants. Molecules 2023; 28:1533. [CrossRef]

4. Szabo K, Mitrea L, Călinoiu LF et al. Natural polyphenol recovery from apple-, cereal-, and tomato-processing by-products and related health-promoting properties. Molecules 2022; 27:7977. [CrossRef]

5. Teleky BE, Martău GA, Ranga F et al. Biofunctional soy-based sourdough for improved rheological properties during storage. Sci Rep 2022; 12:17535. [CrossRef]

6. Ștefănescu BE, Călinoiu LF, Ranga F et al. Chemical composition and biological activities of the nord-west romanian wild bilberry (Vaccinium myrtillus L.) and lingonberry (Vaccinium vitis-idaea L.) leaves. Antioxidants 2020; 9:495. [CrossRef]

7. Pires TC, Caleja C, Santos-Buelga C et al. Vaccinium myrtillus L. fruits as a novel source of phenolic compounds with health benefits and industrial applications-a review. Curr Pharm Des 2020; 26:1917-28. [CrossRef]

8. Tundis R, Tenuta MC, Loizzo MR et al. Vaccinium species (Ericaceae): From chemical composition to bio-functional activities. Applied Sciences 2021; 11:5655. [CrossRef]

9. Chehri A, Yarani R, Yousefi Z et al. Phytochemical and pharmacological anti-diabetic properties of bilberries (Vaccinium myrtillus), recommendations for future studies. Prim Care Diabetes 2022; 16:27-33. [CrossRef]

10. Shi M, Loftus H, McAinch AJ, Su XQ. Blueberry as a source of bioactive compounds for the treatment of obesity, type 2 diabetes and chronic inflammation. J Func Foods 2017; 30:16-29. [CrossRef]

11. South S, Lucero J, Vijayagopal P, Juma S. Anti-Inflammatory Action of Blueberry Polyphenols in HIG-82 Rabbit Synoviocytes. J Med Food 2019; 22:1032-40. [CrossRef]

12. Onuh JO, Dawkins NL, Aluko RE. Cardiovascular disease protective properties of blueberry polyphenols (Vaccinium corymbosum): a concise review. Food Prod Process and Nutr 2023; 5:27. [CrossRef]

13. Kopystecka A, Kozioł I, Radomska D et al. Vaccinium uliginosum and Vaccinium myrtillus-two species-one used as a functional food. Nutrients 2023; 15:4119. [CrossRef]

14. Shamilov AA, Olennikov DN, Pozdnyakov DI et al. Caucasian blueberry: comparative study of phenolic compounds and neuroprotective and antioxidant potential of Vaccinium myrtillus and Vaccinium arctostaphylos leaves. Life (Basel) 2022; 12:2079. [CrossRef]

15. Alsharairi NA. Experimental studies on the therapeutic potential of Vaccinium berries in breast cancer-A Review. Plants (Basel) 2024;5 :13(2):153. [CrossRef]

16. Ştefănescu Braic R, Vari C, Imre S et al. Vaccinium extracts as modulators in experimental type 1 diabetes. J Med Food 2018; 21:1106-12. [CrossRef]

17. Zorenc Z, Veberic R, Mikulic-Petkovsek M. Are processed bilberry products a good source of phenolics? J Food Sci 2018; 83:1856-61. [CrossRef]

18. Zoratti L, Klemettilä H, Jaakola L. Bilberry (Vaccinium myrtillus L.). Ecotypes Nutr Compos Fruit Cultiv; 2016. pp. 83-99. [CrossRef]

19. Hellström J, Karhu S, Karhu J et al. Phenolic profiles differentiate wild bilberry and cultivated blueberry fruit. LWT 2024; 199:116080. [CrossRef]

20. Murley T, Chambers E. The influence of colorants, flavorants and product identity on perceptions of naturalness. Foods 2019; 8:317. [CrossRef]

21. European Commission. Cosmetic ingredient database https://single-market-economy.ec.europa.eu/sectors/cosmetics/cosmetic-ingredient-database_en, accessed 26 September 2024).

22. Bagad AS, Joseph JA, Bhaskaran N, Agarwal A. Comparative evaluation of anti-inflammatory activity of curcuminoids, turmerones, and aqueous extract of Curcuma longa. Adv Pharmacol Pharm Sci 2013; 2013:7. [CrossRef]

23. López Zúñiga MÁ, Moreno-Moral A, Ocaña-Granados A et al. High-dose corticosteroid pulse therapy increases the survival rate in COVID-19 patients at risk of hyper-inflammatory response. PLoS One 2021; 16: e0243964. [CrossRef]

24. Zorenc Z, Veberic R, Mikulic-Petkovsek M. Are processed bilberry products a good source of phenolics. J Food Sci 2018; 83:1856-61. [CrossRef]

25. Može Š, Polak T, Gašperlin L et al. Phenolics in slovenian bilberries (Vaccinium myrtillus L.) and blueberries (Vaccinium corymbosum L.). J Agric Food Chem 2011; 59: 6998-7004. [CrossRef]

26. Değirmencioğlu N, Gürbüz O, Karatepe GE, Irkin R. Influence of hot air drying on phenolic compounds and antioxidant capacity of blueberry (Vaccinium myrtillus) fruit and leaf. J App Bot Food Qual 2017; 90: 115-25.

27. Ancillotti C, Ciofi L, Pucci D et al. Polyphenolic profiles and antioxidant and antiradical activity of Italian berries from Vaccinium myrtillus L. and Vaccinium uliginosum L. subsp. Gaultherioides (Bigelow) S.B. Young Food Chem 2016; 204: 176-84. [CrossRef]

28. Su, Z. Anthocyanins and flavonoids of Vaccinium, L. Pharm. Crops 2012; 3:7-37. [CrossRef]

29. European Pharmacopoeia (Ph. Eur.) 10.0 edition. Strasbourg, France: European Directorate for the quality of medicines and healthcare. Council of Europe, 2021.

30. Committee on Herbal Medicinal Products (HMPC), European Union herbal monograph on Vaccinium myrtillus L., fructus recens (EMA/HMPC/375808/2014) https://www.ema.europa.eu/en/documents/herbal-monograph/final-european-union-herbal-monograph-vaccinium-myrtillus-l-fructus-recens_en.pdf accessed 26 September 2024).

31. Committee on Herbal Medicinal Products (HMPC), Assessment report on Vaccinium myrtillus L., fructus recens and Vaccinium myrtillus L., fructus siccus (EMA/HMPC/555161/2013) https://www.ema.europa.eu/en/documents/herbal-report/final-assessment-report-vaccinium-myrtillus-l-fructus-recens-and-vaccinium-myrtillus-l-fructus-siccus_en.pdf accessed 26 September 2024).

32. Urbonaviciene D, Bobinaite R, Viskelis P et al. Geographic variability of biologically active compounds, antioxidant activity and physico-chemical properties in wild bilberries (Vaccinium myrtillus L.). Antioxidants (Basel) 2022; 11:588. [CrossRef]

33. Cho MJ, Howard LR, Prior RL, Clark JR. Flavonoid glycosides and antioxidant capacity of various blackberry, blueberry, and red grape genotypes determined by high-performance liquid chromatography/mass spectrometry. J Sci Food Agric 2004: 84: 1771-1782. [CrossRef]

34. Vaneková Z, Rollinger JM. Bilberries: curative and miraculous - A review on bioactive constituents and clinical research. Front Pharmacol 2022; 13:909914. [CrossRef]

35. Ferlemi AV, Lamari FN. Berry leaves: An alternative source of bioactive natural products of nutritional and medicinal value. Antioxidants (Basel) 2016; 5:17. [CrossRef]

36. Tian Y, Liimatainen J, Alanne A-L et al. Phenolic compounds extracted by acidic aqueous ethanol from berries and leaves of different berry plants. Food Chem 2017; 220: 266-81. [CrossRef]

37. Sharma S, Pandita G, Bhosale YK. Anthocyanin: potential tool for diabetes management and different delivery aspects. Trends Food Sci Technol 2023; 140;104170. [CrossRef]

38. Luo H, Lv XD, Wang GE et al. Anti-inflammatory effects of anthocyanins-rich extract from bilberry (Vaccinium myrtillus L.) on croton oil-induced ear edema and Propionibacterium acnes plus LPS-induced liver damage in mice. Int J Food Sci Nutr 2014; 65:594-601. [CrossRef]

39. Roth S, Spalinger MR, Müller I et al. Bilberry-derived anthocyanins prevent IFN-γ-induced pro-inflammatory signalling and cytokine secretion in human THP-1 monocytic cells. Digestion 2014; 90:179-89. [CrossRef]

40. Karlsen A, Retterstol L, Laake P et al. Anthocyanins inhibit nuclear factor-kappa β activation in monocytes and reduce plasma concentrations of pro-inflammatory mediators in healthy adults. J Nutr 2007; 137:1951-4. [CrossRef]

41. Karlsen A, Paur I, Bøhn SK et al. Bilberry juice modulates plasma concentration of NF-κβ related inflammatory markers in subjects at increased risk of CVD. Eur J Nutr 2010; 49:345-55. [CrossRef]

42. Widén C, Coleman M, Critén S et al. Consumption of bilberries controls gingival inflammation. Int J Mol Sci 2015; 16:10665-73. [CrossRef]

43. Lynn A, Garner S, Nelson N et al. Effect of bilberry juice on indices of muscle damage and inflammation in runners completing a half-marathon: a randomised, placebo-controlled trial. J Int Soc Sports Nutr 2018;15:22. [CrossRef]

44. Roth S, Spalinger MR, Gottier C et al. Bilberry-derived anthocyanins modulate cytokine expression in the intestine of patients with ulcerative colitis. PLoS One 2016; 11:e0154817. [CrossRef]

45. Kolehmainen M, Mykkanen O, Kirjavainen PV et al. Bilberries reduce low-grade inflammation in individuals with features of metabolic syndrome. Mol Nutr Food Res 2012; 56:1501-10. [CrossRef]

46. Prior RL, Wilkes SE, Rogers TR et al. Purified blueberry anthocyanins and blueberry juice alter development of obesity in mice fed an obesogenic high-fat diet. J Agric Food Chem 2010; 58:3970-3976. [CrossRef]

47. 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. [CrossRef]

48. Bøhn SK, Myhrstad MCW, Thoresen M et al. Bilberry/red grape juice decreases plasma biomarkers of inflammation and tissue damage in aged men with subjective memory impairment -a randomized clinical trial. BMC Nutr 2021; 7: 75. [CrossRef]

49. Biedermann L, Mwinyi J, Scharl M et al. Bilberry ingestion improves disease activity in mild to moderate ulcerative colitis-An open pilot study. J Crohns Colitis 2013; 7: 271-9. [CrossRef]

50. Aboonabi A, Meyer RR, Gaiz A, Singh I. Anthocyanins in berries exhibited anti-atherogenicity and antiplatelet activities in a metabolic syndrome population. Nutr Res 2020; 76: 82-93. [CrossRef]

51. Zhu Y, Ling W, Guo H et al. Anti-inflammatory effect of purified dietary anthocyanin in adults with hypercholesterolemia: a randomized controlled trial. Nutr Metab Cardiovasc Dis 2013; 23: 843-9. [CrossRef]

52. 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. [CrossRef]

53. Zhao Y, Xu H, Tian Z et al. Dose-dependent reductions in plasma ceramides after anthocyanin supplementation are associated with improvements in plasma lipids and cholesterol efflux capacity in dyslipidemia: A randomized controlled trial. Clin Nutr 2021; 40:1871-8. [CrossRef]

54. Hoggard N, Cruickshank M, Moar KM et al. A single supplement of a

standardised bilberry (Vaccinium myrtillus L.) extract (36 % wet weight anthocyanins) modifies glycaemic response in individuals with type 2 diabetes controlled by diet and lifestyle. J Nutr Sci 2013; 2: e22. [CrossRef]

55. Törrönen R, Järvinen S, Kolehmainen, M. Postprandial glycemic responses to a high-protein dairy snack and energy-enriched berry snacks in older adults. Clin Nutr ESPEN 2022; 51: 231-8. [CrossRef]

56. ClinicalTrials.gov ID NCT03316612, The effect of Vaccinium Myrtillus L. extract intake on human metabolism: A randomized double-blind trial. [ClinicalTrialsNCT03316612]

57. ClinicalTrials.gov ID NCT01958034, Bilberry as a dietary supplement after myocardial infarction (The BEAR SMART Trial). [ClinicalTrialsNCT01958034]

58. ClinicalTrials.gov ID NCT03620266, Effects of bilberry and oat intake after AMI (BIOAMI). [ClinicalTrialsNCT03620266]

59. ClinicalTrials.gov ID NCT05737108, Bilberry-containing capsules for dry eye mitigation. [ClinicalTrialsNCT05737108]

60. ClinicalTrials.gov ID NCT03185676, The long term efficacy of a bilberry-based probiotic product on glucose tolerance and insulin resistance as compared to a control. [ClinicalTrialsNCT03185676]

61. ClinicalTrials.gov ID NCT03213288, Bilberry fruit and black rice derived anthocyanins on lipid status. [ClinicalTrialsNCT03213288]

62. ClinicalTrials.gov ID NCT02194361, Efficacy of a standardised bilberry extract in improving the night vision of healthy volunteers. [ClinicalTrialsNCT02194361]

63. ClinicalTrials.gov ID NCT03309982, A randomized placebo-controlled cross-over design study investigating the effects of a plant polyphenol blend on the intestinal inflammatory and metabolic responses to a high fat meal in healthy subjects. [ClinicalTrialsNCT03309982]

64. ClinicalTrials.gov ID NCT02370966, Berry intake - effects on systemic and oral inflammation. [ClinicalTrialsNCT02370966]

65. ClinicalTrials.gov ID NCT04637945, A randomized placebo-controlled study investigating the effects of a long-term dietary supplementation with an anthocyanin-rich blend on the metabolic and inflammatory responses to a high-fat meal in healthy subjects. [ClinicalTrialsNCT04637945]

66. Hassellund SS, Flaa A, Sandvik L et al. Effects of anthocyanins on blood pressure and stress reactivity: a double-blind randomized placebo-controlled crossover study. J Hum Hypertens 2012; 26:396-404. [CrossRef]

67. Kosehira M, Machida N, Kitaichi N. A 12-week-long intake of bilberry extract (Vaccinium myrtillus L.) improved objective findings of ciliary muscle contraction of the eye: A randomized, double-blind, placebo-controlled, parallel-group comparison trial. Nutrients 2020; 25: 600. [CrossRef]