

Blueberry in the improvement of metabolic syndrome: A literature review

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Abstract

Metabolic syndrome represents a growing public health challenge, associated with factors such as obesity, insulin resistance, hypertension, dyslipidemias, and low-grade chronic inflammation. This condition substantially increases the risk of cardiovascular diseases, type 2 diabetes, and stroke. In this scenario, dietary strategies based on foods with functional properties, such as those rich in bioactive compounds, have shown promise as preventive and complementary measures. Among these foods, blueberries (*Vaccinium* spp.) stand out for their unique nutritional profile, characterized by a high concentration of polyphenols, particularly anthocyanins, as well as vitamins, fiber, and minerals. Consistent clinical evidence indicates that their consumption is associated with improvements in cardiometabolic markers, including endothelial function, insulin sensitivity, lipid profile, and oxidative stress parameters, as well as with cognitive and psychophysiological benefits. These effects are primarily attributed to the antioxidant and anti-inflammatory properties of blueberries' bioactive compounds, which act synergistically to prevent and manage metabolic syndrome. This review compiles and discusses the most recent evidence regarding the chemical composition and biological effects of blueberries in mitigating metabolic syndrome and its associated risk factors.

Keywords: metabolic syndrome; blueberry; *Vaccinium*.

Practical Application: Blueberry as a functional strategy for modulating metabolic syndrome.

1 INTRODUCTION

Driven by modern lifestyle trends toward a more balanced and adequate diet, the functional food sector has experienced significant growth. Functional foods, whether natural or processed, contain biologically active compounds that provide numerous health benefits beyond basic nutrition (Mondal et al., 2021).

In this context, metabolic syndrome (MetS) stands as a growing and serious global public health challenge. Characterized by a cluster of factors such as obesity, insulin resistance, hypertension, dyslipidemias, and low-grade chronic inflammation, MetS substantially increases the risk of cardiovascular diseases, type 2 diabetes, and other severe comorbidities, impacting both quality and life expectancy (C. V. F. Silva et al., 2024; D. Zhang et al., 2025). Dietary strategies based on functional foods rich in bioactive compounds have shown promise as preventive and complementary measures for managing MetS.

Blueberries (*Vaccinium* spp.) are notable for their distinctive nutritional profile and characteristic flavor. They are rich in bioactive compounds, including organic acids, phenolics, minerals, and vitamins, which confer multiple therapeutic properties, including antioxidant, anti-inflammatory, anticancer, neuroprotective, and vision-improving effects (Duan et al., 2022). The high content of bioactive compounds, such as anthocyanins and

vitamin C, underscores their potential to promote nutritional health (Kim et al., 2021). Although fresh blueberries have a limited shelf life (Zia & Alibas, 2021), various preservation techniques are employed to ensure their availability and efficacy (Sun et al., 2019).

Given the above, the objective of this review is to compile and discuss the most recent evidence regarding the chemical composition and biological effects of blueberries in mitigating metabolic syndrome and its associated risk factors.

1.1 Relevance of the work

This review proposes a way to modulate metabolic syndrome, a pressing global health challenge. By consolidating current evidence on blueberries' chemical composition and biological effects, the work highlights their significant potential as a functional food strategy. It underscores how blueberries' antioxidant and anti-inflammatory properties can effectively modulate key cardiometabolic risk factors, offering a valuable, natural, and accessible dietary intervention. This synthesis is crucial for guiding future research, informing public health recommendations, and fostering innovative approaches for metabolic syndrome prevention and management, ultimately enhancing quality of life.

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2 MATERIAL AND METHODS

The literature search was conducted in December 2024 using the search terms “Vaccinium,” “Blueberry,” “biological activities of blueberry,” and “blueberry clinical trials” using platforms such as PubMed, ScienceDirect, and ResearchGate to select studies published in the last 5 years (2019–2024) in high-impact journals.

As a selection criterion, only clinical studies that investigated the effects of blueberry consumption in humans, using the fruit or freeze-dried pulp in standardized doses, were included. Studies that exclusively used isolated extracts, encapsulated supplements, or formulations combined with other fruits were excluded to ensure a specific analysis of the effects of blueberries and their bioactive compounds. Thus, we sought to ensure greater comparability among the selected studies with respect to the administration method and the assessment of biological outcomes.

3 RESULTS AND DISCUSSION

The results of this review are presented and discussed in an integrated manner, considering recent evidence on blueberries and their relationship with metabolic syndrome and associated risk factors. Initially, botanical, agronomic, and compositional characteristics of the fruit are addressed, with emphasis on its bioactive compounds. Next, the chemical composition of blueberries, especially in their freeze-dried form, is discussed, highlighting nutrients and phytochemicals relevant to metabolic health. Finally, clinical studies in humans investigating the biological effects of blueberry consumption on cardiometabolic, inflammatory, oxidative, gastrointestinal, and cognitive parameters are analyzed, enabling a critical discussion of the mechanisms involved and the potential of blueberries as a complementary functional strategy in the management of MetS.

3.1 Blueberry (*Vaccinium spp.*)

Blueberries belong to the genus *Vaccinium* and the subgenus *Cyanococcus*. Generally, highbush blueberries (*V. corymbosum* L.) and rabbiteye blueberries (*V. ashei* R.) are considered commercially essential blueberry types. Blueberries originated in Canada and North America and subsequently became widely distributed worldwide, primarily in North America, Asia, Europe, and South America. Global blueberry cultivation zones increased from 58 regions in 2016 to 71 in 2020, with cultivated area and yield increasing from 132,560 ha and 622,900 t to 205,670 ha and 850,900 t, respectively (Zia & Alibas, 2021).

In Brazil, propagation methods for blueberries have been studied for at least a decade to improve cultivation practices (Schuch & Tomaz, 2019). Blueberries of the “Biloxi” cultivar have been disappointing in cold climates and have been favored in milder regions, where the shrub can be grown as an evergreen, thereby promoting cultivation in tropical countries (Lobos & Hancock, 2015). In the Cerrado, this cultivar has a production cycle of 137 days, from pruning to the beginning of harvest, maintained for 19 consecutive weeks (Lima, 2021).

In addition to Biloxi, the cultivars Emerald and Jewel were developed for tropical climates (S. H. G. Silva et al., 2024). In

Brazil, the American varieties Snowchaser and Primadonna are also cultivated, although Biloxi remains the most widely planted (Antunes & Baccan, 2023). Successful cultivation of these blueberry varieties has been seen in the regions of Piracicaba (SP), the São Francisco Valley, Petrolina (PE), Senador Amaral (MG), Chapada Diamantina, Nova Soure (BA), and Ceará. Although interest in the crop is growing, Brazil is estimated to import approximately 80% of its consumption, mainly from the United States, Canada, and Peru (Schuch & Tomaz, 2019).

These fruits are rich in bioactive compounds, primarily flavonoids and other polyphenolics, resulting in high antioxidant activity. Because of their higher antioxidant activity than other berries, blueberries have attracted significant interest in the phytogetic prebiotics market (Duan et al., 2022). Phytogetic prebiotics are plant-based substrates selectively utilized by beneficial microorganisms to promote host health benefits (Souza et al., 2019). They are distinguished by their diverse content of health-promoting bioactive compounds (Sater et al., 2021). For this, blueberries are among the five foods considered healthy for humans, as certified by the Food and Agriculture Organization of the United Nations (FAO) (Cheng et al., 2020).

3.2 Chemical composition of freeze-dried blueberry fruits

Fresh blueberries are highly perishable due to their high moisture content (Meng et al., 2012). Freeze-drying, in turn, can reduce blueberry moisture to an average of 2.41 g/100 g (Díaz-Álvarez et al., 2024; Hui et al., 2021). When seeking to preserve the potentially functional components of heat-sensitive blueberries, freeze-drying is considered the most efficient dehydrating method compared with conventional drying (Sun et al., 2019; Waghmare et al., 2023).

The freeze-drying process consequently concentrates nutrients. Protein composition values have been reported in freeze-dried blueberries, ranging from 2.1 to 7.0 g/100 g (Díaz-Álvarez et al., 2024; Hui et al., 2021; Rousseau et al., 2021; Y. Wang et al., 2022; Wood et al., 2023). Furthermore, 19 types of amino acids have already been identified (Feng et al., 2019) some of which have already been quantified by H. Zhang et al. (2014) such as aspartate (2.41 mg/g), threonine (9.33 mg/g), serine (6.49 mg/g), glutamic acid (14.35 mg/g), alanine (2.21), cysteine (78.20 mg/g), vanilla (13.01 mg/g), methionine (35.74 mg/g), tyrosine (11.16 mg/g), gamma-aminobutyric acid (89.27 µg/g), lysine (4.51 mg/g), and arginine (9.19 mg/g).

In freeze-dried blueberries, carbohydrate amounts between 69.5 and 96 g/100 g have been reported (Díaz-Álvarez et al., 2024; Rousseau et al., 2021; Y. Wang et al., 2022; Wood et al., 2023); and lipids between 0.9 and 6.5 g/100 g (Díaz-Álvarez et al., 2024; Hui et al., 2021; Y. Wang et al., 2022; Wood et al., 2023). Regarding fiber in freeze-dried blueberries, results between 6.43 and 26 g/100 g of total fiber (Díaz-Álvarez et al., 2024; Hui et al., 2021; Rousseau et al., 2021; Sagbasan et al., 2024; Wood et al., 2023) with an average of 6.37 g/100 g of soluble fiber and 11.21 g/100 g of insoluble fiber (Hui et al., 2021; Wood et al., 2023) have already been reported.

Blueberries can contain a variety of organic acids with high biological activities, including phenolic acid, ursolic acid,

chlorogenic acid, and ellagic acid (Duan et al., 2022). Regarding the amount of total phenolic compounds, freeze-dried blueberries demonstrate between 122 and 451 mg of gallic acid equivalent/100 g (Antal, 2024; Hellström et al., 2024; Liović et al., 2021).

Phenolic acids are mainly derived from hydroxybenzoic and p-hydroxycinnamic acids, which are widely used in functional foods, cosmetics, and medicines (Duan et al., 2022). Hui et al. (2021) demonstrated in freeze-dried blueberries (μg phenolic acid/100 g): gallic acid (2702.76), caffeic acid (59.59), quercetin (13.56), ferulic acid (10.57), syringic acid (390.56), rutin (6.73), protocatechuic acid (22.58), hydrobenzoic acid (21.92), p-coumaric acid (19.80), catechin (100.45), epicatechin (22.99), and caftaric acid (16.59).

Thirty-six types of polyphenols have been identified in blueberries, including anthocyanins (Mustafa et al., 2022), with an average of 1597 mg/100 g in freeze-dried blueberries (Hellström et al., 2024; Sagbasan et al., 2024; Wood et al., 2023). It is important to note that current extraction methods for blueberry anthocyanins primarily employ organic solvents, ultrasonic assistance, ultrahigh-pressure treatment, supercritical fluids, and enzymatic or microwave-assisted extraction protocols (Fu et al., 2021), which can alter their content during extraction. Furthermore, anthocyanin content varies with cultivar, genetics, environment, and fruit processing conditions (Duan et al., 2022).

Hellström et al. (2024) analyzed anthocyanins in freeze-dried blueberries and reported the following results (mg/100 g): delphinidin-3-galactoside (240 ± 130), delphinidin-3-glucoside (97 ± 91), delphinidin-3-arabinoside (170 ± 70), cyanidin-3-galactoside (50 ± 35), cyanidin-3-glucoside (27 ± 26), cyanidin-3-arabinoside (19 ± 16), petunidin-3-galactoside (150 ± 80), petunidin-3-glucoside (78 ± 71), petunidin-3-arabinoside (80 ± 31), peonidin-3-galactoside (17 ± 11), peonidin-3-glucoside (23 ± 21), peonidin-3-arabinoside (13 ± 8.7), malvidin-3-galactoside (290 ± 150), malvidin-3-glucoside (190 ± 70), and malvidin-3-arabinoside (141 ± 250). However, blueberry anthocyanins are highly susceptible to environmental factors, including pH, temperature, light, oxygen, metal ions, and additives (Kim et al., 2021). Blueberry anthocyanins have been reported to have antioxidant, anti-obesity, anticancer, and anti-inflammatory properties, and to aid in the treatment of cardiovascular diseases and type 2 diabetes. They also exhibit neuroprotective effects, reinforcing their therapeutic potential (Wu et al., 2023).

3.3 Biological activities in individuals with metabolic syndrome or its risk conditions

Metabolic syndrome (MetS) does not constitute a single disease but rather a set of risk factors for cardiovascular disease, stroke, and type 2 diabetes (D. Zhang et al., 2025). According to the Brazilian Society of Endocrinology and Metabolism and the American Heart Association, MetS is characterized by clinical conditions associated with metabolic disorders (C. V. F. Silva et al., 2024), including obesity, insulin resistance, low levels of high-density lipoprotein cholesterol (HDL-c), hypertension, hypertriglyceridemia, hyperglycemia, and increased waist circumference (H. H. Wang et al., 2020).

The growing prevalence of MetS globally poses a significant challenge to public health and the economy (Lin et al., 2021). MetS is considered a global pandemic, representing one of the leading causes of reduced life expectancy and disability. In the United States, its prevalence peaked at the beginning of the 21st century. Currently, more than a fifth of the population in the United States and Europe has the disorder. In Latin America, MetS affects approximately four in ten adults, with the highest rates observed in Mexico (61%) and Ecuador (50%) (Aballay et al., 2013).

The groups most affected by MetS are women, older adults, and individuals living in urban areas. Its prevalence increases progressively with age, reaching almost 40% in the sixth decade of life. Early and accurate diagnosis is essential for urgent, integrated, and comprehensive actions to reduce the risk of associated diseases (Parra-Gómez et al., 2025). All MetS factors are closely associated with lifestyle; therefore, adopting healthy habits, particularly a balanced diet, is an effective strategy for mitigating risk (Manoharan et al., 2022). In this context, blueberries stand out for their rich content of bioactive compounds, such as flavonoids and phenolic acids, which have the potential to control MS. Among the effects attributed to the consumption of this fruit are modulation of intestinal microbiota composition and metabolic activity, with benefits for intestinal health, body weight control, attenuation of inflammatory processes, increased antioxidant capacity, and an improved overall metabolic profile (Liu & Chen, 2025).

Blueberries are widely recognized as one of the main functional fruits due to their rich composition of flavonoids, anthocyanins, and other phytochemicals with proven antioxidant properties (Wu et al., 2023). Table 1 presents the studies in which blueberries in their various preservation forms (fresh, dehydrated, and frozen) were administered to humans, and their biological effects on health were evaluated.

Eight studies were reviewed and summarized in Table 1, which describes the potential effects of blueberry consumption on MetS. The studies included male and female participants, aged 18 to 70, who presented with factors such as hypertension, gastrointestinal disorders, type 2 diabetes, overweight, obesity, insulin resistance, and a history of acute myocardial infarction.

In the cardiometabolic context, the benefits of blueberries, as reported by (Curtis et al., 2019, 2022) are strongly associated with their antioxidant activity and the consequent reduction in oxidative stress. The improvement in vascular function observed in the studies was attributed to increased bioactivity of nitric oxide (NO), a key vasodilator. This effect may have been mediated by anthocyanins, which enhance the activity of antioxidant enzymes such as superoxide dismutase, thereby protecting NO from oxidative degradation and promoting its bioavailability. Furthermore, anthocyanins can positively influence cellular redox status, thereby attenuating transient oxidative stress induced by high-energy-density meals. Thus, blueberries' ability to preserve the NO pathway and modulate cellular redox balance constitutes a plausible mechanism to explain the reported improvements in vascular function and cardiometabolic profile (Burton-Freeman et al., 2019; Kuntz et al., 2014).

Studies report reduced oxidative stress (Woolf et al., 2023) and improved insulin sensitivity (Krikorian et al., 2022), suggesting that blueberries modulate chronic inflammatory and oxidative processes. This modulation is primarily attributed to their polyphenols, which exert a synergistic action (Onuh et al., 2023). In combating oxidative stress, these compounds act both by directly neutralizing free radicals and by activating the body's own antioxidant defense pathways. This potent antioxidant

activity, combined with its ability to suppress inflammatory mediators, contributes to improved insulin sensitivity, as chronic inflammation is a key factor in insulin resistance (Johnson et al., 2017; Kalt et al., 2020; Onuh et al., 2023).

Studies indicate that blueberry consumption may provide psychophysiological benefits, such as improved mood and reduced brain fog in men with type 2 diabetes (Kalt et al., 2020; Onuh et al., 2023; Stote et al., 2017, 2021), suggesting that their

Table 1. Studies found in the literature that evaluated the biological activities of supplementing fresh, dehydrated, and frozen blueberry fruit and/or pulp in humans with metabolic syndromes and their conditions (2019–2024).

Population	Aim	Dosage/duration	Main results	References
Estrogen-deficient postmenopausal women aged 45–65 years with elevated blood pressure or stage 1 hypertension (n = 48)	To examine the effectiveness of blueberries in improving endothelial function and blood pressure in postmenopausal women with higher-than-normal blood pressure.	22 g freeze-dried blueberry powder per day/12 weeks	↑ Endothelial function; ↓ Vascular oxidative stress.	Woolf et al., 2023
Men and women, aged 18–60 years and with a body mass index of 18.5–32.9 kg/m ² and with functional gastrointestinal disorders (n = 43)	To evaluate the effects of blueberries on clinical symptoms related to functional gastrointestinal disorders	30 g of freeze-dried blueberry powder, taken in two doses of 15 g per day/6 weeks.	↓ Abdominal symptoms, with pain, bloating, diarrhea, flatulence, and nausea; ↑ Well-being, quality of life, and functioning in patients.	Wilder-Smith et al., 2023
Men with type 2 diabetes, aged 51–74 years (n = 37)	To investigate the effects of blueberry consumption on the mood of men with type 2 diabetes.	22 g freeze-dried blueberries per day/8 weeks	↓ Total mood disturbance and confusion-perplexity	Stote et al., 2021
Sedentary elderly men or women, aged 60 years or older, overweight or obese (BMI ≥ 25 to 32 kg/m ²) (n = 55)	Sedentary elderly men or women, aged 60 years or older, overweight or obese (BMI ≥ 25 to 32 kg/m ²) (n = 55)	Freeze-dried blueberry powder, equivalent to ¼ cup blueberries per day/12 weeks	↑ <i>Coriobacteriales Incertae Sedis</i>	Starr et al., 2024
Men and women with metabolic syndrome, aged 50–75 years and BMI ≥ 25 kg/m ² (n = 45)	To determine whether the consumption of blueberries, rich in anthocyanins, can mitigate the negative effects of a high-calorie meal rich in fat and sugar on cardiometabolic markers in individuals with metabolic syndrome.	26 g freeze-dried blueberries/24 h	↓ Glucose and insulin levels; ↑ Levels of HDL cholesterol and large HDL particles (L-HDL and XL-HDL) and Apo-A1; ↓ Total cholesterol; ↑ Concentration of anthocyanin-derived metabolites in blood and urine.	Curtis et al., 2022
Men and women with cognitive decline, aged 50–65 years, overweight and insulin resistant (n = 27)	To investigate the effects of daily blueberry supplementation in middle-aged individuals with insulin resistance and high risk of dementia.	14 g freeze-dried blueberries per day/12 weeks.	↑ Executive function, especially in working memory tasks; ↓ Fasting glucose levels and improved insulin sensitivity; ↑ Peripheral mitochondrial function.	Krikorian et al., 2022
Men who suffered an AMI and a mean age of 68 years (n = 50)	To evaluate the effects of dietary consumption of freeze-dried blueberries in patients after acute myocardial infarction.	40 g of freeze-dried blueberries per day/8 weeks.	↑ 6MWT (6-minute walk test).	Arevström et al., 2019
Men and women with metabolic syndrome and a mean age of 63 years (n = 115)	To evaluate the effects of blueberry consumption on insulin resistance, vascular function, and cardiometabolic biomarkers	To evaluate the effects of blueberry consumption on insulin resistance, vascular function, and cardiometabolic biomarkers	↑ Endothelial function (1.45% in flow-mediated dilation) ↓ Arterial stiffness (–2.24%) ↑ HDL cholesterol (+0.08 mmol/L) and HDL particle density in non-statin users; ↑ Anthocyanin-derived metabolites in serum and urine.	Curtis et al., 2019

AMI: acute myocardial infarction; HDL: high density lipoprotein; MWT: minute walk test.

effects extend beyond cardiometabolic parameters. These results are attributed to the potent anti-inflammatory action of polyphenols, as systemic inflammation is associated with depressed mood and the intensification of negative bodily sensations through the gut-brain axis (Benson et al., 2023). Thus, by reducing the inflammatory burden, blueberries may mitigate this process and directly contribute to mental well-being.

The neuroprotective effects of blueberries are also being investigated. (Krikorian et al., 2022) demonstrated that supplementation with freeze-dried blueberries for 12 weeks improved executive function and peripheral mitochondrial function, in addition to reducing glucose levels and increasing insulin sensitivity in middle-aged individuals with insulin resistance and a high risk of dementia, reinforcing the hypothesis that their antioxidant compounds exert benefits on both the central nervous system and metabolic parameters. Preclinical studies elucidate the mechanisms underlying these effects, showing that blueberry anthocyanins optimize mitochondrial health by promoting biogenesis and maintaining mitochondrial dynamics through activation of the sirtuina-1/peroxisome proliferator-activated receptor gamma coactivator-1 alpha pathway (Ma et al., 2025), in addition to combating oxidative stress, reducing neuronal apoptosis, and protecting deoxyribonucleic acid against genotoxic damage. This protection extends to maintaining adequate levels of essential neurotransmitters, providing a consistent molecular basis for the improvement in executive function observed in humans (Ma et al., 2025; Shao et al., 2019).

Regarding physical recovery, Arevström et al. (2019) observed improved functional capacity, as measured by the 6-minute walk test, in patients with post-acute myocardial infarction after 8 weeks of freeze-dried blueberry supplementation, without significant changes in key inflammatory biomarkers. This effect may be associated with the vasodilatory action of blueberry polyphenols, which increase NO availability, promoting vascular smooth muscle relaxation and blood flow. The metabolites formed after ingestion also correlate with flow-mediated dilation, suggesting additive and synergistic effects on vascular modulation. Together, these mechanisms contribute to reducing endothelial dysfunction and improving cardiovascular health, including in individuals with metabolic syndrome (Onuh et al., 2023).

Finally, Wilder-Smith et al. (2023) demonstrated gastrointestinal benefits, observing significant improvements in individuals with functional gastrointestinal disorders after 6 weeks of freeze-dried blueberry supplementation. The treatment reduced a range of abdominal symptoms, notably abdominal pain, diarrhea, and constipation, and improved overall quality of life. These effects are associated with blueberry polyphenols and fiber, which act differently from the fruit's sugars. In patients with Gastrointestinal Fistula Disease (GIFD), whose pathogenesis involves immune activation and nervous system sensitization, polyphenols exert anti-inflammatory, antioxidant, and neuroprotective actions, modulating gut-brain interaction and contributing to the relief of discomfort.

The results of clinical trials across diverse population groups support the applicability of blueberries as a functional ingredient. Their incorporation into technological matrices, such

as bioactive edible films, represents a promising strategy for delivering bioactive compounds, adding nutritional and functional value to foods, in addition to enhancing their therapeutic action in various physiological contexts (Ashique et al., 2024; Bambace et al., 2021).

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