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Research Article

The Effects of Anthocyanins in the Treatment of Metabolic Syndrome: A Systematic Review

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Abstract

The present study aimed to review studies on anthocyanin consumption and its benefits in three of the parameters of the metabolic syndrome, namely total cholesterol, insulin resistance and blood pressure control. The articles were selected from the SCIELO, PubMed and Science Direct databases. The descriptors that were used in English are anthocyanin, metabolic syndrome, benefits, treatment and based on these descriptors, the following word combinations were investigated: benefits of anthocyanins in metabolic syndrime, treatment of metabolic syndrome with anthocyanins. Selected 9 studies found within the parameters sought, results were obtained in 8 articles demonstrating that anthocyanins can help reduce total cholesterol, 5 proving that beneficial actions occur in decreasing insulin resistance and 6 articles emphasized that ANTs can have effects positive regarding the decrease in blood pressure. It is common to find individuals with at least 1 of the parameters of the metabolic syndrome, the articles found show that it is possible to control and improve some of these parameters through the consumption of antioxidants such as ANTs, however there is a lack of studies relating the benefit of consumption of these antioxidants in these factors of aggravating risk for future cardiovascular problems.

Introduction

Metabolic Syndrome (MS) is characterized by a clinical situation with a grouping of factors for the development of cardiovascular diseases, among which, arterial hypertension, dyslipidemia, visceral obesity and manifestations of endothelial dysfunction stand out. The presence of insulin resistance has also been considered a relevant physiopathogenic factor, as it is present in physiological changes normally associated with the development of type 2 Diabetes Mellitus (DM2) and the increased risk of cardiovascular events in the long term [1]. The initial definition of MS is based on laboratory and clinical data, which can be easily measured, such as fasting blood glucose, Glycated Hemoglobin (Hb1Ac), glycemic curve, blood pressure, triglycerides, HDL cholesterol (High Density Lipoprotein) and microalbuminuria. These data, which were recommended in the guidelines of the World Health Organization (WHO) in 19991 and the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) in 20012 and persist to this day as the gold standard for the closing the diagnosis of the clinical condition. According to the NCEP-ATP III, MS is defined as the combination of at least three factors: abdominal obesity measured through waist circumference, with men >102 cm and women >88 cm; triglycerides in both sexes ≥ 150 mg/dL; HLD in men being < 40 mg/dL and in women < 50 mg/dL; blood pressure ≥ 130 mmHg or ≥ 85 mmHg and fasting blood glucose ≥110 mg/Dl [3]. Of the components mentioned, six of them are related to cardiovascular disease (CVD), such as abdominal obesity, dyslipidemic atherogenesis, high blood pressure, insulin resistance, glucose intolerance, pro-inflammatory state and prothrombotic state [4].

In addition to control through dietary strategies and medications, compounds are sought to assist in the treatment of MS, including anthocyanin (ANT). Recent studies indicate that ANT is considered one of the most important natural resources that promote health. They have bioactive and water-soluble plant pigments belonging to the group of flavonoids, from the class of polyphenolic phytochemicals [5] that promote, even at homeopathic doses, the angioprotection effect. ANTs are commonly found in fruits and vegetables such as cranberries, strawberries, blueberries, blackberries, elderberries, grapes, plums, red cabbage, red onions and sweet potatoes. These pigments are generally distributed in fruits and flowers, however, stems, leaves and roots of some plants may also contain different types of anthocyanins [6]. The literature indicates that the consumption of colorful fruits and vegetables, rich in anthocyanins, has been associated with numerous health benefits [7]. As they have antioxidant properties, they are able to prevent free radicals from cellular metabolism from forming lesions or from the loss of cell integrity, in addition to promoting cell repair in cases where the lesion has already occurred [8]. Still in relation to the benefits of anthocyanins, it can be seen that the consumption of fruits rich in this antioxidant, evidenced an improvement in the conditions of insulin resistance, with an evident increase in the consumption and uptake of glucose by the observed cells, suggesting that ATNs can effectively reduce the metabolic effects caused by excessive consumption of carbohydrates [9]. Given the above, the objective of this study was to analyze the effect of using anthocyanins as adjuncts in the treatment of MS, verifying their impact on blood pressure, cholesterol, and insulin resistance.

Materials and Methods

This is a systematic literature review, and the search for articles was performed in the SCIELO, PubMed and Science Direct databases. For the search, the English terms anthocyanin, metabolic syndrome, benefits, treatment were used. Based on these descriptors, the following combinations of words were investigated: benefits of anthocyanins in metabolic syndrome, treatment of metabolic syndrome with anthocyanins. As inclusion criteria, original articles published between 2005 and 2020 were considered, which addressed the treatment of metabolic syndrome using anthocyanin-source or supplemented foods, with the intervention being carried out both in animals and in humans. Among the exclusion factors, review articles published after the date defined for inclusion, and which evaluated individuals who had other diseases, in addition to MS, were not considered. After searching the databases using the descriptions and criteria, the articles found had their titles and abstracts read first, then articles that did not apply to the defined inclusion and exclusion criteria were excluded. The article search flowchart is described in (Figure1).

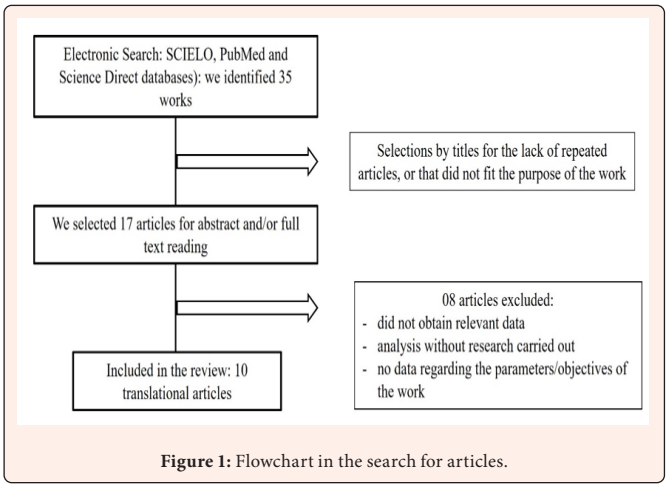

Figure 1: Flowchart in the search for articles.

Results

From the literature search [10], studies were gathered that fit the parameters sought, and of these, 8 articles evaluated the impact of anthocyanins on total cholesterol [6, 10, 11, 13-17, 19] on insulin [7, 10, 13, 14, 17-19] articles evaluated blood pressure in [10, 12-14, 16, 18, 19]. Most of them detailed benefits relating the parameters studied in them of MS and the ingestion of ANTs (Table 1), shows the methodological aspects related to the studies, as well as the parameters used for the way in which anthocyanins were consumed, the sample group and the objectives analyzed. A variation in the consumption of anthocyanins can be observed in different types of foods, being found more in red fruits because of their color. It is also observed that there was variation in the studied groups, which included from healthy individuals to individuals with at least 3 of the 5 MS parameters, such as blood pressure, total cholesterol and insulin, also counting on studies in diabetic and obese rats and mice. Most studies lasted between one and three months, and follow-ups ranged from 14 to 90 days. The sources of ANTs that were consumed varied according to the article, and in the study [10] açaí pulp containing 0.77 mg/ml of the preparation of total anthocyanins was consumed, in the study [13, 14, 16] cranberry juice was consumed with a variation of 2.80±0.19mg/l13, 12.4mg16 and 290.3 mg14 of ANT. In the study by ALVAREZ-SUAREZ et al. [11], individuals consumed strawberries with 307.59 ± 0.01 mg/day of ANT, the animals that consumed blackberry in the YAN [17] study, ingested 50 and 125 mg / kg ANT, however, the study in which the consumption of ANTs was obtained through the cherry carried out by SEYMOUR et al. [18] does not provide the total amount of anthocyanins consumed, as well as the study with black raspberries [15] and the study [12].

Where dry hibiscus extract was consumed. Only four of them [10, 13, 14, 19] analyzed the 3 parameters of MS and the other 6 [11, 12, 15-17, 19] varied from 1 to 2 parameters. (Table 2) shows the results of each of the studies. Of the 10 articles selected, eight evaluated total cholesterol, five evaluated insulin and six articles evaluated blood pressure with the consumption of anthocyanins. The studies [10, 11, 15-17], who showed a reduction in total cholesterol after consumption of anthocyanins. On the other hand, the studies [12, 16, 19] presented results of blood pressure reduction after the intervention and the articles [10, 17] showed positive results for the reduction of insulin resistance. In the studies [13, 14, 18] did not find positive results regarding the same analyzed parameters and the consumption of ANTs, however, in the first two [12, 14] improvement in vascular health, reduction of abdominal fat and disease control were observed. cardiovascular.

Table 1: Data collected and parameters to be evaluated.

Author / Year	Sample	Average Age	Duration	Intervention	Evaluated Parameters		
					Blood Pressure	Insulin	Cholesterol
UDANI, et al. [10]	10 adults (men and women) who are overweight	18-46 years	30 days	Açaí save (200g day) industrialized.	x	x	x
ALVAREZ-SUAREZ. J.M et al. [11]	Healthy volunteers	20 - 50 years	30 days	500g of strawberries in natura	-	-	x
HERRERA-ARELLANO. A, et al. [12]	Hypertensive People (I and II)	25 - 61 years	04 weeks	Hibiscus dry extract 250mg per day	x	-	-
DUTHIE, et al. [13]	Healthy women	18 - 40 years	02 weeks	cranberry juice 750ml per day	x	x	x
STULL, A.J, et al. [14]	44 pre-hypertensive and pre-diabetic volunteers	over 20 years	06 weeks	Blueberry (45g Powder in Yogurt and Smooth based on skim milk) and Placebo (Blueberry-free smoth only)	x	x	x
JEONG, S. H., et al. [15]	77 subjects (men and women) with metabolic syndrome	18 - 75 years	12 weeks	Black raspberry (powder) and placebo (cellulose, isomalto and corn powder) *750mg daily (capsules)	-	-	x
BASU. A., et al. [16]	31 women with syndrome metabolic	20 - 60 years	08 weeks	cranberry juice 480ml a day	x	-	x
BASU. A., et al. [19]	25 individuals with Metabolic Syndrome	over 21 years	08 weeks	Blueberry (50g freeze-dried, diluted in water and vanilla extract) total 960ml per day	x	x	x
YAN, F [17]	diabetic mice type 2 (in vivo)	01 week of age	08 weeks	Blackberry extract 50 and 125mg/kg body weight combined with metformin	-	x	x
SEYMOUR, et al. [18]	induced obese rats	Adults	90 days	supplemented cherry	x	x	-

Table 2: Results of each research carried out with humans and animals in vivo.

Author / Year	Results
UDANI, et al. [10]	There was a reduction in insulin levels from 8.92 ± 5.4 to 6.68 ± 3.3 and total cholesterol from 159 ± 37 mg/dl to 142 ± 28 mg/dl.
ALVAREZ-SUAREZ. J.M et al. [11]	After the use of strawberries, there was a reduction in total cholesterol from 4.58 ± 0.13 to 4.18 ± 0.12 mmol/l, LDL from 2.54 ± 2.10 to 2.19 ± 2.09 mmol/l and triglycerides from 0.85 ± 0.09 to 0.67 ± 0.06 mmol/l, reducing the risk of cardiovascular disease.
HERRERA-ARELLANO. A, et al. [12]	The group showed a significant reduction in blood pressure from 146.48/97.77 to 129.89/85.96 mmHg.
DUTHIE, et al. [13]	There was no change in blood pressure, LDL (cholesterol) and insulin.
STULL, A.J, et al. [14]	There were no significant changes in relation to blood pressure and insulin resistance in any individual, both for Blueberry and Placebo consumers. However, there was an improvement in relation to endothelial function (vascular health) in both consumers, with a greater improvement in Blueberry consumers.
JEONG, S. H., et al. [15]	There was a significant improvement in the group that consumed the Black Raspberry capsule, in relation to total cholesterol (from 198.7 ± 34.0 to 174.7 ± 30.0) and LDL (from 98.0 ± 19.4 to 88 .2 ± 20.9).
BASU. A., et al. [16]	After 8 weeks, there was a decrease in systolic blood pressure from 132.0 ± 11.6 to 125.4 ± 9.5, from diastolic pressure from 82.4 ± 9.6 to 81.4 ± 8.8, and also of total cholesterol 202.0 ± 35.0 to 196.4 ± 30.3, and LDL cholesterol 122.0 ± 28.2 to 117.0 ± 23.1.
BASU. A., et al. [19]	The final assessment resulted in an improvement in systolic and diastolic blood pressures of 26 and 24%, and also improvement in LDL cholesterol of 2.28 and 2.17%. As for insulin resistance, there was no significant change.
YAN, F. [17]	There was an improvement in both extract amounts. The intake of 50mg/day improved insulin from 4.47 ± 1.36 to 3.78 ± 0.58 µm/L and LDL cholesterol from 1.73 ± 0.31 to 1.51 ± 0.30 mM. With the 125mg day, there was a drop-in insulin by 1.13 ± 0.24 mM.
SEYMOUR, et al. [18]	There was a reduction in abdominal fat, reversal of obesity and a decrease in cardiovascular diseases.

Discussion

The clinical picture of MS, as mentioned above, is characterized by a set of factors that can lead to the development of cardiovascular diseases in the future, such as insulin resistance, high total cholesterol, high blood pressure and others. As potent antioxidants, anthocyanins, flavonoids found in foods such as vegetables and berries, are studied to fight free radicals and prevent and/or help control diseases caused by these radicals, such as heart disease. From the studies in analyzed articles, beneficial results were found when consuming ANTs, mostly contained in red fruits, in the reduction of total cholesterol, insulin resistance and hypertension. It was possible to observe that when administering anthocyanins in the diet of individuals with metabolic syndrome parameters, there is an improvement in their clinical condition. The main form of intervention was the consumption of foods rich in these antioxidants such as blueberries, açaí, among other red fruits, which contained doses of ANT that varied according to the organism chosen for the study. A study carried out with vegetables such as red lettuce, red cabbage, and some fruits such as blackberry, açaí, acerola, soursop, among others, shows that fruits, fruit pulps and vegetables that have anthocyanins in their composition showed greater antioxidant activity than the fruits. that did not present or presented in lesser amounts in systems used in the study to evaluate such antioxidant action [20].

Another review article found, analyzed the consumption of cherry and showed that there are benefits regarding the anthocyanins contained in this fruit on markers of oxidative stress, inflammation, blood pressure, diabetes, among others [21]. In yet another separate review article, it can be noted that ANTs can attenuate MetS symptoms such as insulin resistance, decreased hypertension, hyperglycemia, etc. The authors also observed that the substance reduces the plasma lipid profile in rodents with hyperlipidemia, reduces visceral adiposity, systolic blood pressure and total body fat, in addition, reduced glucose tolerance with pharmacological and biopharmaceutical studies for this confirmation [22]. More investigations to recognize and prove the metabolism, efficacy and main mechanisms of action of ANTs in MS are needed. But with such current evidence, these antioxidants can be considered for the prevention and use in the control of the metabolic syndrome and its complications.

Conclusion

From the compiled and observed studies, it can be concluded that anthocyanins contained in foods are potent antioxidants and have properties that help health, both in the prevention and control of parameters related to metabolic syndrome. More studies are needed for a more specific and detailed conclusion, with more information on consumption and evaluation, of this analysis with healthy groups and with some comorbidity for the real comparison of the results.

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