

## Review Article

# Anthocyanins and anthocyanin-rich extracts: role in diabetes and eye function

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Anthocyanins are the largest group of water-soluble pigments in the plant kingdom, known collectively as flavonoids. More than 8000 flavonoids, and 500 anthocyanin structures had been reported by the year 2000 and more are continually being isolated. Anthocyanins are believed to display an array of beneficial actions on human health and well-being. Due to our increasing understanding and awareness of the potential beneficial human health effects, research on anthocyanins has recently intensified. During the past two decades an increasing number of studies have investigated the diverse protective effects elicited by polyphenolics present in various fruits and vegetables. These effects include antioxidant, anti-allergic, anti-inflammatory, anti-viral, anti-proliferative, anti-mutagenic, anti-microbial, anti-carcinogenic, protection from cardiovascular damage and allergy, microcirculation improvement, peripheral capillary fragility prevention, diabetes prevention, and vision improvement. Other physiological effects are continually being investigated. The aim of the present article is to summarise the known anti-diabetic and eye function properties of anthocyanins to help in our understanding of their functional mechanism.

**Key Words:** anthocyanins, anthocyanin-rich extracts, disease prevention, diabetes, eye function

## Introduction

Anthocyanins (Greek *anthos*, flower and Greek *kyanose*, blue) used originally to describe the blue pigment of the cornflower *Centaurea cyanus*, are an important group of water-soluble plant pigments. They belong to the most common class of phenolic compounds, known collectively as flavonoids with more than 8000 flavonoid and 500 anthocyanin structures reported by the year 2000.<sup>1</sup> Anthocyanins are widespread in food plants, occurring in 27 families. The worldwide annual consumption has been estimated as 10 000 tonnes from black grapes alone. During the past two decades an increasing number of studies have investigated the diverse protective effects elicited by polyphenolics present in various fruits and vegetables. These effects include antioxidant, anti-allergic, anti-inflammatory, anti-viral, anti-proliferative, anti-mutagenic, anti-microbial, anti-carcinogenic, protection from cardiovascular damage and allergy, microcirculation improvement, peripheral capillary fragility prevention, diabetes prevention, and vision improvement.<sup>2-13</sup> Polyphenolic research has recently intensified because of this increasing understanding and awareness of the potential beneficial human health effects. There are some review articles on the general biochemical, cellular and medicinal properties of anthocyanins,<sup>9,14-18</sup> but no detailed review of their role in diabetes and eye function has yet been published. The aim of the present article is to summarise the known anti-diabetic and eye function properties of anthocyanins to help in our understanding of their functional mechanism.

## Chemical structure and distribution

Anthocyanins are water-soluble glycosides of polyhydroxyl and polymethoxyl derivatives of 2-phenylbenzopyrylium or flavylum salts. The six anthocyanidins commonly found in plants are classified according to the number and position of hydroxyl groups on the flavan nucleus, and are named cyanidin (cy), delphinidin (dp), malvidin (mv), peonidin (pn), pelargonidin (pg) and petunidin (pt). The differences between individual anthocyanins come from the number and the position of hydroxyl groups; the degree of methylation of these hydroxyl groups; the nature, number and location of sugars attached to the molecule; and aliphatic or aromatic acids attached to the sugars in the molecule.<sup>14</sup> Glycosylation confers increased structural stability and water solubility to the parent anthocyanidin.<sup>19</sup> Acylation of the sugar residues with cinnamic (*p*-coumaric, caffeic, ferulic) or aliphatic (acetic, malonic, succinic) acids<sup>14</sup> further improves anthocyanin stability. Generally, di-, tri-, or polyacylated anthocyanins have increased stability over simple and monoacylated anthocyanins.<sup>20</sup>

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It is generally accepted that anthocyanins are the most important group of water-soluble pigments in plants. In the plant tissues the anthocyanins produce blue, purple, red and intermediate hues and appear black in some products. Their hue and structure are dependent on pH and the presence of co-pigments.<sup>21,22</sup> At pH 1-3 the flavylium cation is red coloured, at pH 5 the resultant carbinol pseudo base is colourless, and at pH 7-8 the blue purple quinoidal base is formed. The glycosides of the three non-methylated anthocyanidins (cyanidin, delphinidin and pelargonidin) are the most widespread in nature, being present in 80% of pigmented leaves, 69% of fruits and 50% of flowers. The most abundant anthocyanins in the edible parts of plants are cyanidin, followed by pelargonidin, peonidin, delphinidin, petunidin, and malvidin.<sup>15,23,24</sup> Anthocyanins form the colours of many fruits and vegetables and are probably the most widespread food colours occurring as red colours in fruit juices, wines and jams. These pigments have been identified in edible plant materials as diverse as apple, berries (blackcurrant, boysenberry, blueberry, bilberry, strawberry, blackberry, raspberry, cranberry, elderberry, lingonberry, chokeberry etc.), black carrot, cabbage, cherry, grape, radish, red onions and sweet potato, to mention only a few of the vast array known.<sup>25</sup> The discovery of more stable bis- and polyacylated anthocyanins has attracted the attention of the food industry for use as safe and effective food additives.

#### **Anthocyanins and anti-diabetic properties**

The consumption of a diet low in fat and rich in antioxidants may reduce the risk of obesity and insulin resistance.<sup>26-28</sup> A number of recent reports indicate that consumption of fruits and vegetables, especially rich in polyphenols, decrease the incidence of type-2 diabetes, a condition associated with insulin resistance.<sup>29-31</sup> Insulin resistance is a disorder in which insulin inadequately stimulates glucose transport in skeletal muscle and fat and inadequately suppresses hepatic glucose production. The mechanisms that prevent the  $\beta$ -cell of the pancreas from secreting sufficient amounts of insulin to overcome peripheral insulin resistance are not yet fully understood. Oral hypoglycemic agents that directly stimulate insulin release from  $\beta$ -cells (e.g., sulfonylurea-based drugs), however, can elevate insulin secretion from islets of type-2 diabetic patients sufficiently to overcome peripheral insulin resistance and normalize blood glucose levels. One of the disadvantages of using sulfonylurea-based drugs is that they fail to control normal blood glucose levels.<sup>32</sup> These drugs also adversely affect the ability of  $\beta$ -cells to secrete consistent insulin level and cause weight gain.<sup>32</sup> Hence, it would be beneficial if dietary constituents could regulate blood glucose levels or induce insulin production by pancreatic  $\beta$ -cells in the type-2 diabetic condition. However, there is little clinical evidence that food factors can do this.

#### **Insulin secretion**

It is well known that dietary antioxidants, including anthocyanins, protect pancreatic  $\beta$ -cells from glucose-induced oxidative stress.<sup>10</sup> Recently Jayaprakasam *et al.*<sup>11</sup> demonstrated glucose-induced insulin release from pancreatic  $\beta$ -cells by anthocyanins and anthocyanidins. Simi-

larly the dimethoxy ether and the glycoside of leucopelargonidin isolated from the bark of the Indian banyan tree *Ficus bengalensis* showed significant hypoglycaemic, hypolipidemic and serum insulin-raising effects in moderately diabetic rats with close similarities to the effects of glibenclamide (an oral hypoglycaemic sulfonylurea-based drug).<sup>33-35</sup> Previously *Cornus* fruits (cherry), a rich source of anthocyanins, have been reported anecdotally as having anti-diabetic activity.<sup>36,37</sup> Results indicated that pelargonidin-3-galactoside and its aglycone, pelargonidin, caused a 1.4-fold increase in insulin secretion. Zhang *et al.*<sup>38</sup> also reported that several compounds present in grape skin or whole grapes are capable of enhancing insulin secretion as well as selectively inhibiting COX-2 enzymes. They suggested that cherries, grapes, and berries containing anthocyanins might be useful for the prevention of type-2 diabetes. In few *in vitro* and animal studies,<sup>39,40</sup> anthocyanin extracts were found to have potent alpha-glucosidase inhibitory activity, suppressing the increase in postprandial glucose level. However, no further extensive *in vivo* studies and clinical evaluation of these compounds have yet been carried out to validate the *in vitro* observations.

#### **Diabetic cataracts**

Continuous hyperglycemia is well known to cause toxic reactions in organ tissues. Loss of lens opacity control is linked with high levels of reducing sugars in *in vitro* and *in vivo* studies, i.e. experimental diabetic cataract formation. Diabetic cataract, a complication of diabetes, occurs in about 10% of diabetic patients. In the U.S.A. about 20,000 patients are reported to develop retinopathy/ataract and loss of sight annually. In Japan, about a quarter of total blindness cases annually are caused by diabetes, including diabetic retinopathy and diabetic cataract. It is said that caloric and food intake influence the progress of diabetes and diabetic complications.<sup>8</sup> Flavonoids are well known for their possible role in the prevention of diabetic cataracts.<sup>41</sup> Over forty flavone derivatives were tested and found to be potent inhibitors of aldose reductase, the enzyme that initiates cataract formation in diabetes.<sup>41</sup> Five anthocyanin monomers isolated from the extract of grape skin showed inhibitory activities for lens opacity.<sup>8</sup> Flavonoids can also prevent or delay the occurrence of cataracts in rat lenses perfused in a high-glucose solution<sup>42</sup> or in diabetic rabbits.<sup>41</sup> Several naturally extracted or synthetic anthocyanins combinations with novel anti-cataract/anti-glucoma activity have been reported in patents.<sup>43,44</sup> Therefore, it is important to discover whether diabetic complications can be restrained with food constituents in humans.

#### **Capillary permeability and vasorelaxation**

Various microcirculatory disorders have been described in diabetes. Several of them may occur before the onset of microangiopathic lesion (thickening of capillaries in many areas including the eye in diabetics) and are assumed crucial in the pathogenesis of microcirculatory complications in diabetes. In the diabetic microangiopathic condition, microvascular permeability and the number of leucocytes sticking to the venular endothelium are increased.<sup>45,46</sup> Delphinidin chloride elicited increased microvascular permeability and a reduction of leucocytes adhering to the

venular vessels in diabetic hamsters.<sup>47</sup> Anthocyanosides from berries are currently used in ophthalmology for their capacity to improve vision and prevent diabetic retinopathy.<sup>48,49</sup> Various flavonoids including anthocyanosides have been shown to be effective against experimentally induced capillary hyperfiltration.<sup>50,51</sup> In one animal study, Cohen-Boulakia *et al.*<sup>7</sup> showed that anthocyanosides can improve and even normalise capillary filtration of albumin. It was reported that blueberry extracts act as inhibitors of cyclic adenosine monophosphate and cyclic guanosine monophosphate phosphodiesterase,<sup>52</sup> as scavengers of superoxide anions and as antioxidants on human low-density lipoproteins.<sup>53</sup> Considering all these effects, together with the lack of significant adverse effects,<sup>52,51</sup> the clinical interest in anthocyanins and anthocyanin-rich extracts is increasing.

In several pathological conditions including diabetes, endothelium-dependent vasorelaxation by different vasodilator agonists is reduced.<sup>54</sup> One of the mechanisms accounting for the dysfunction of the endothelium is a decreased release of nitric oxide (NO).<sup>55</sup> It was shown that extracts from red wines, other grape products, and various plants that contain polyphenols (mainly anthocyanins), can induce endothelium-dependent vasorelaxation, probably via NO release or enhanced biological activity of NO.<sup>56-59</sup> A mixture of anthocyanins extracted from bilberry (*V. myrtillus* L.) was reported to have biological and pharmacological properties, including vasorelaxation (60) and ophthalmic activity.<sup>61</sup> Nakamura *et al.*<sup>62</sup> investigated the effect of blackcurrant (BC) concentrate on smooth muscle in rat thoracic aorta. They reported that BC concentrate dose-dependently relaxed the norepinephrine-precontracted aorta, and the response was abolished after endothelium removal. Therefore, they hypothesized that the prevention of eye and lower back fatigue probably resulted from increased blood supply to these areas caused by vasorelaxation induced by BC concentrate via the histamine H<sub>1</sub>-receptors on the endothelium. The exact identification of the anthocyanins having this vasorelaxation activity was lacking in this study. It could be a synergistic relaxant effect of a number of polyphenols.

### **Lipid lowering properties**

Increased level of triglyceride (hypertriglyceridemia) is a major feature of the insulin resistance syndrome. As obesity is strongly associated with insulin resistance, a reduction in this resistance is important in preventing the development of type-2 diabetes. A high fat diet tended to induce hyperglycemia, hyperinsulinemia and hyperleptinemia. Tsuda *et al.*<sup>63</sup> demonstrated that cyanidin 3-glucoside-rich purple corn colour may ameliorate high fat diet-induced insulin resistance in mice. Insulin resistance and oxidative stress act synergistically in the development of several metabolic syndromes including cardiovascular complications.<sup>64</sup> Postprandial hyperglycaemic episodes in diabetic patients are closely associated with increased oxidative and nitrosative stress, and are a most important factor in the onset and progress of vascular complications, both in type-1 and -2 diabetes mellitus.<sup>65-67</sup> Giving antioxidant molecules decreased insulin resistance-related oxidative stress and subsequent hypertension in fructose-fed rats.<sup>68</sup> In a short-term human dietary supplementation

study with red orange complex (anthocyanins, flavanones and hydroxycinnamic acids) significant improvement of thiol groups on proteins (an indirect measurement of glutathione activity in serum) was shown.<sup>69</sup> Furthermore, a marked decrease in serum free radical levels was also demonstrated. Pomegranate juice (PJ) consumption by diabetic patients resulted in antioxidative effects in their serum, and the oxidative state of in their monocytes/macrophages levels.<sup>70</sup> These effects were attributed specifically to anthocyanins.<sup>71</sup> The significant finding was that the PJ sugar fraction, unlike the sugar fraction of white grape juice, decreased the macrophage oxidative state under normal and diabetic conditions. These antioxidant/anti-atherogenic effects could be due to the presence of unique sugars and/or phenolic sugars in PJ.<sup>72</sup> Anthocyanin extracts and procyanidins have been shown to decrease triglycerides and increase HDL-cholesterol levels in rats<sup>10</sup>. In another short-term animal study, anthocyanin glycosides (leucopelargonin derivatives) from the bark of *F. bengalensis* have shown hypocholesterolemic and antioxidant activities.<sup>33,35,73</sup> Interestingly, decoctions and infusions of blueberry leaves are used in folk medicine as hyperglycaemic agents,<sup>74-76</sup> but very little information about the active ingredients has been documented.

### **Adipocyte dysfunction**

Adipocytes are the primary site of energy storage and accumulate triacylglycerol during nutritional excess. In recent years, it has been well publicised that adipocyte dysfunction plays an important role in the development of obesity and insulin resistance. Adipocytes synthesise and secrete biologically active molecules called adipocytokines.<sup>77</sup> Adiponectin is one of the most important adipocytokines, and is specifically and highly expressed in adipocytes. The plasma adiponectin concentration and mRNA expression level were decreased in the obese and insulin resistant state.<sup>78,79</sup> The administration of adiponectin improved insulin action, accompanied by increases in fatty acid oxidation and a decreased triacylglycerol level in muscle.<sup>80,81</sup> There are some drugs, for example the thiazolidinediones (TZD), which target the regulation of adipocyte function via peroxisome proliferator-activated receptor (PPAR) $\gamma$  regulation, to improve insulin sensitivity or glucose homeostasis. Recently, much attention has been focused on food factors that may be beneficial for the prevention of body fat accumulation and may possibly reduce the risk of diabetes and heart disease. Although a few drugs are used for the therapy of obese-related metabolic diseases or suggested for preventing body fat accumulation, there has been little evidence that food factors themselves directly improve dysfunction of the adipocytes responsible for adipocytokine secretion and lipid metabolism. However, it has been demonstrated that anthocyanins can regulate obesity and insulin sensitivity associated with adipocytokine secretion and PPAR $\gamma$  activation in adipocytes.<sup>63</sup> Recently Tsuda *et al.*<sup>82</sup> clearly demonstrated for the first time that anthocyanins enhance adipocytokine (adiponectin and leptin) secretion, the expression of PPAR $\gamma$  and adipocyte specific genes (lipoprotein lipase, adipocyte fatty acid binding protein, and uncoupling protein 2) in isolated rat adipocytes. These findings will provide a biochemical basis for the use of anthocyanins,

which also in turn will have important implications for preventing obesity and diabetes. An overview of gene expression in human adipocytes treated with anthocyanins has been published recently.<sup>83,84</sup> Significant changes in adipocytokine gene expression were found (up-regulation of adiponectin and down-regulation of plasminogen activator inhibitor-1 and interleukin-6). Some lipid metabolism related genes (uncoupling protein 2, acetylCoA oxidase 1 and perilipin) were also significantly induced in both common cyanidin and cyanidin 3-glucoside treatments. In conclusion, these studies demonstrated that anthocyanins modulated the gene expression of the adipocytokines in human and may have a unique therapeutic advantage for the regulation of adipocyte function.

### Anthocyanins and vision improvement

Of all the beneficial bio-medicinal functions of anthocyanins, the effect on vision was one of the first reported properties. British Royal Air Force aviators in World War II ate bilberry jam to improve their night vision. Since impaired visual function such as asthenopia, an ophthalmological condition that manifests itself through nonspecific symptoms such as fatigue, red eyes, eye strain, pain in or around the eyes, blurred vision, headache and occasional double vision, is a techno-stress syndrome caused by concentrated work on video display terminals in today's computerised society, the preventive or curative effects of anthocyanins on impaired vision are becoming an important field of study.

### Early studies

Early clinical trial studies<sup>85-89</sup> carried out in France and Italy suggested a positive effect of anthocyanins on vision improvement. For example, Sole *et al.*<sup>89</sup> carried out a controlled clinical trial of cyanin chloride and Heleniene (Adaptinol, xanthophyll dipalmitate) with 31 patients suffering from functional disturbances of vision in the dark, and reported that both agents significantly improved photopic visual acuity. Only cyanin chloride treatment improved mesopic and scotopic vision. A similar clinical trial using Difrel<sup>®</sup>E (anthocyanosides and vitamin E) was carried out in Germany by Politzer<sup>90</sup>. Thirty six patients with progressive myopia were treated with Difrel<sup>®</sup>E for 14.5 months and in about half of them, an increase in myopia was suppressed by approximately 50%, with 29 patients showed stabilisation of fundus-alterations, as well as a stable, or an improved visual acuity.

### Recent studies

More recent studies<sup>3,12,91,92</sup> have reported conflicting effects of anthocyanins on vision. These recent trials were carried out under stricter and more rigorous experimental conditions, including randomized, double blind, placebo-controlled and cross-over trials. Levy and Glovinsky<sup>3</sup> studied the effect of a single oral dose of 12, 24, or 36 mg anthocyanins (given as tablet containing 12 mg anthocyanins as blueberry extract and 2 mg beta-carotene) on night vision improvement in 16 young normal volunteers. Full-field scotopic retinal threshold, dark adaptation rate and mesopic contrast sensitivity were evaluated, but no significant positive effects were obtained in any tests during the first 24 h following oral administration. Zadok *et*

*al.*<sup>91</sup> also examined the effects by multiple oral administration of 12 and 24 mg of anthocyanosides (as tablet), twice a day for 4 days in 18 young normal volunteers. They concluded that multiple oral administrations of 12 and 24 mg anthocyanosides twice a day appeared not to have any significant effect on night vision.

Muth *et al.*<sup>92</sup> investigated the effect of bilberry on night visual acuity and night contrast sensitivity. Young healthy male subjects ingested either an active capsule containing 160 mg of bilberry extract (25% anthocyanosides), or a placebo, three times a day for 21 days. There was no difference between the active and placebo treatments, and thus they concluded that there was no improvement effect of bilberry anthocyanins in either night vision function.

Anthocyanins from blackcurrant (as a concentrated extract powder) were also examined for their effects on asthenopia symptoms<sup>93</sup> in 12 healthy human subjects. Blackcurrants contain only 4 anthocyanins, delphinidin-3-*O*-glucuronide, delphinidin-3-*O*-rutinoside, cyanidin-3-glucuronide and cyanidin-3-*O*-rutinoside, in contrast to the 15 anthocyanins in bilberry. Oral intake of blackcurrant anthocyanins at doses of 12.5, 20 or 50 mg was found to decrease the dark adaptation threshold in a dose-dependent manner. The decrease of refraction values for the dominant eye observed in the placebo group after the visual task was also significantly prevented in the group with anthocyanin intake. In another *in vitro* experiment nine anthocyanins from bilberry extracts were shown to suppress the photooxidation of pyridinium disretinoid A2E by quenching singlet oxygen<sup>94</sup>. The A2E, an auto-fluorescence pigment that accumulates in retinal pigment epithelial cells with age and in some retinal disorders, can mediate a detergent-like perturbation of cell membranes and light-induced damage to the cell. Cells that had taken up anthocyanins also exhibited a resistance to the membrane permeabilisation that occurs as a result of the detergent-like action of A2E. This *in vitro* study should be correlated with *in vivo* studies aiming anthocyanin uptake into ocular tissues. Very recently, Matsumoto *et al.*<sup>95</sup> has demonstrated the ocular distribution of blackcurrant anthocyanins (BCAs) in rats and rabbits after oral, intravenous and intraperitoneal administration. This study demonstrated for the first time that BCAs were absorbed and distributed in ocular tissues as intact forms and pass through the blood-aqueous barriers and blood-retinal barriers in both rats and rabbits.<sup>95</sup> These studies demonstrated that oral intake of anthocyanins or anthocyanin-rich extracts may have potential as a drug for treating ophthalmological diseases such as myopia and glaucoma. However, robust animal and human intervention trials are necessary in order to substantiate claims of human health benefits.

Recently, Lee *et al.*<sup>12</sup> looked at the effect of purified high-dose anthocyanin oligomers on nocturnal visual function and clinical symptoms using 60 patients with asthenopia and refractive errors in both eyes, and reported 73.3% of patients with improved symptoms, but only one placebo subject who showed an improvement. The authors emphasised the difference of their experimental design from that of most previous studies in terms of dose, duration and type of subjects. The anthocyanin sample they used contained purified anthocyanin oligomers pre-

pared by fermentation of anthocyanin monomers from grape pulp and skin. It comprised more than 85% anthocyanin oligomers, whereas the bilberry preparations used in previous studies contained only 5-30% anthocyanoside oligomers. Moreover, subjects were treated for 4 weeks, longer than treatments reported in other studies.

Canter and Ernst<sup>96</sup> reviewed 30 published trials of *V. myrtillus*-extracted anthocyanins on reduced light and night vision. Of these, 12 were placebo-controlled. The 4 most recent trials were all randomized controlled trials and the results did not suggest any improvement of night vision. On the other hand, positive effects were reported in 5 randomized controlled and 7 non-randomized controlled trials. Negative outcomes were associated with more rigorous methodology, but also with lower dose levels and geographically distinct anthocyanin samples. It was noted that almost all trials involved healthy volunteers with normal and above average eyesight, but no rigorous research on subjects suffering impaired night vision has been done. The authors suggested that trials of synthetic anthocyanins may warrant further comparisons with *V. myrtillus* in subjects with impaired night vision.

#### **Effect on visual transduction process**

Since bilberry anthocyanins have been reported to improve night vision, the effects of interactions of these with rhodopsin<sup>97</sup> or phosphodiesterase (PDE)<sup>98,99</sup> on phototransduction have been studied. Since blackcurrant anthocyanins showed acceleration of dark adaptation in humans, Matsumoto *et al.*<sup>100</sup> further examined the effect of purified blackcurrant anthocyanins on the regeneration of rhodopsin in frog rod outer segment membrane. They found that cyanidin, both glucoside and rutinoside, stimulated the generation but delphinidin did not. They also showed that neither cyanidin nor delphinidin affected cGMP-phosphodiesterase activity in the rod outer membrane although conflicting results have been reported previously on the effect of anthocyanins on this enzyme<sup>98,99</sup>

#### **Conclusions and future considerations**

The Diabetes Control and Complications Trial (DCCT, 1993)<sup>101</sup> demonstrated that tight control of blood glucose is effective in reducing clinical complications of diabetes significantly, but even optimal control of blood glucose could not prevent complications completely, suggesting that alternative treatment strategies are needed. A multitude of *in vitro* and *in vivo* studies have been performed utilizing the antioxidant properties of anthocyanins in cell culture and experimental diabetic models. There are differences in response to anthocyanin-rich extracts measured through certain observable biomarkers. These studies provide a foundation for further clinical trials. Results should be interpreted cautiously since these studies involved a wide variety of experimental models of diabetes, duration and type of the treatment and markers of oxidative stress. Although several *in vitro* and animal studies with anthocyanins strongly suggest their beneficial effects in cardiovascular complications in diabetes, clinical evidence for the use of anthocyanins and anthocyanin-rich extracts in diabetes is not convincing.

The vision improving effect of anthocyanins is an interesting and important field of study, because myopia is

prevalent in today's society, with decreased contrast sensitivity, a vague eye discomfort (asthenopia) arising from over-use of the eyes. After anecdotal reports suggesting the beneficial effect of bilberry extract on night vision about 60 years ago, many studies have been carried out to demonstrate that anthocyanins have a major influence on visual function. Although a few recent studies have demonstrated positive effects of anthocyanins on visual function under rigorous conditions, these used concentrated fruit extracts or fermentation products as anthocyanin test samples. The conflicting conclusions so far obtained may be a result of the differences in the type of subject, the methods of evaluating night vision and the concentration, dose and source of anthocyanoside samples. Indeed, in some studies carried out on certain visual abnormalities such as progressive myopia,<sup>12,90</sup> positive effects of anthocyanins were reported for improving vision function. Further trials of synthetic or purified anthocyanins in subjects with impaired night vision are warranted.

Published data clearly show that anthocyanins in whole extract or pure form have antioxidant activity *in vitro*, often higher than other natural antioxidants.<sup>102-105</sup> There is evidence from epidemiological studies that high dietary intake of foods rich in flavonoids, including anthocyanins is associated with low prevalence of some diseases such as cancer and cardiovascular diseases.<sup>106</sup> However, a few recently published results from observational studies and human intervention trials have raised questions about the dietary role of these in the aetiology of certain disease processes<sup>107,108</sup>. Phytochemicals can have complementary and overlapping mechanisms of action on the human body, including antioxidant effects, alteration of biotransformation enzyme activities, anti-inflammatory effects, stimulation of the immune system, reduction of platelet aggregation, modulation of cholesterol synthesis, hormone metabolism, reduction of blood pressure, and antibacterial and antiviral effects. Numerous studies have demonstrated potentially important interactions among dietary constituents as well as even between dietary constituents and pharmaceuticals. It is important to study isolated and purified anthocyanin components, along with extracts of the food from which they are derived, to compare their activities and determine how they interact with each other, so that their role in diabetes and eye function can be assessed both at the mechanistic level and when they are part of the food matrix that forms the basis of our diet.

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## Review Article

# Anthocyanins and anthocyanin-rich extracts: role in diabetes and eye function

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## 花青素及富含花青素萃取物在糖尿病及眼睛功能的角色

花青素是一种水溶性的植物色素。从广义上看，属酚类化合物中的类黄酮类。目前已经有 8000 多种酚类化合物被分离出来，其中有 500 多种是花青素。近年来对花青素可能对健康带来的好处的研究越来越多。将来花青素的这种特性在功能食品和保健食品中有可能得到日益广范的应用。在过去的二十年间越来越多的研究表明水果和蔬菜中的种酚类化合物多种多样的保护作用。其中包括抗氧化性，抗过敏，抗炎症，抗病毒，抗细胞扩散，抗突变因素，抗微生物，抗癌，保护免受心血管损伤和过敏，改善微循环，预防周边微血管脆弱，预防糖尿病，和改善视觉等作用。为了帮助我们理解花青素的作用机制，本文总结了多年来花青素对于预防糖尿病和改善视觉方面的研究成果。

關鍵字：花青素、富含花青素萃取物、疾病預防、糖尿病、眼睛功能。