



Review Article

A REVIEW ON ANTHOCYANINS: A PROMISING ROLE ON PHYTOCHEMISTRY AND PHARMACOLOGY

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ABSTRACT

This paper reviews the literature on occurrence of different colors of anthocyanins, different types of anthocyanins containing food materials and their pharmacological actions. These anthocyanins are naturally available colored compounds from different flowers, fruits, and vegetables. Apart from various major pharmacological actions like anti-cancer, anti-inflammatory, decrease the neuronal death, these anthocyanins are acts as natural colorants for food and beverages. There is no study reveal that toxic effect of anthocyanins on human health. However, future research is going on pharmacological actions and uses of anthocyanins.

Key Words: Anthocyanins, Transformation, Pharmacological effects

INTRODUCTION

Pigmentation is an attractive feature of various fruits, flowers and other main substances. Anthocyanins (Anthos = flower and kianos = blue) are one of the responsible for red-blue coloration, these are the most important pigments of the vascular plants, they are harmless and easy dissolve in aqueous media, so these are known as natural water-soluble colorants. These anthocyanins are most utilized vegetable colorants. In the international food and beverage industry's anthocyanins preferred natural food colors like orange, red, pink and purple to blue¹. They were used by Americans, Indians, Europeans, Japanese and the Chinese. These water-soluble anthocyanins are low stable than carotenoids. They belong to a molecule called flavonoids synthesized via the phenylpropanoid pathway they are odorless and nearly flavorless, its taste as a moderately astringent sensation. They are extracted from wide varieties of fruits, vegetables and other food materials like grapes, berries, red cabbage, apples, radishes, tulips, roses and orchids, olive oil, honey, teas, cocoa, banana, asparagus, pea, fennel, pear and potato. Recent experimental studies declared, compounds of colored fruits, berries and vegetables, which may scavenge free radicals very strongly (antioxidant effect) and prevent distinct chronic diseases like protection against liver disorders, hypertension, enhance memory, progress eyesight, anti-inflammatory and antimicrobial activities, inhibition of mutations caused by mutagens from baked food, and suppression against tumors. Other than these the consumption of anthocyanins may play a significant character in preventing lifestyle-related diseases such as cancer, hyperglycemia, and cardiovascular and neurological disorder. Anthocyanins are derived from anthocyanidins by adding sugars

BASIC STRUCTURE OF ANTHOCYANIN

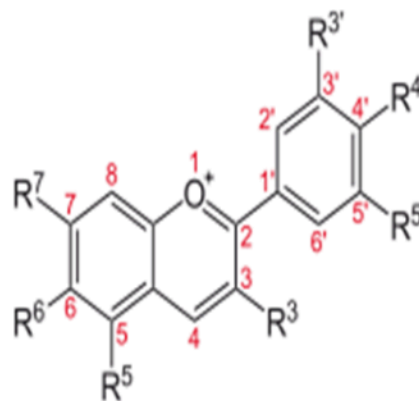


Figure 1: Basic structure of anthocyanins and its substituents²

Sugar free anthocyanins are anthocyanidins. The anthocyanins are classified into 2 types they are sugar- free anthocyanidin aglycons and the anthocyanin glycosides. Till now 500 types of anthocyanins are reported. Examples of sugar free anthocyanidin aglycons like: Delphinidin (blue-red), Pelargonidin (orange) and Cyanidin (orange-red). These sugar free anthocyanidin aglycons are the building blocks which are produce anthocyanins by reduction, dehydroxylation and glycosylation within the plant.

BIOSYNTHESIS OF ANTHOCYANINS

Anthocyanins are formed from two different parts of chemical raw materials which is present in cell: From this one part involves the production of the phenylalanine by shikimate pathway. Other part involves produce three molecules of malonyl-coA, a C3 unit

from a C2 unit (acetyl-CoA)³. These two steps are combining to form an intermediate chalcone-like compound in the presence of chalcone synthase enzyme by using polyketide folding mechanism that is commonly found in plants. The resulting product chalcone is isomerized as prototype naringenin pigment in the presence of chalcone isomerase. The formed Naringenin product is subsequently oxidized in the presence of flavanone hydroxylase, flavonoid 3' hydroxylase and flavonoid 3' 5'-hydroxylase enzymes. These resulting products are further reduced in presence of dihydroflavonol 4-reductase then forms a colorless leucoanthocyanidins⁴. Leucoanthocyanidins are precursors of the next enzyme, anthocyanidin synthase or leucoanthocyanidin dioxygenase. Flavan-3-ols, the products of leucoanthocyanidin reductase (LAR), have been recently shown to be their true substrates then unstable anthocyanidins are formed. These unstable anthocyanidin further coupled to sugar molecules by enzymes such as UDP-3-O-glucosyltransferase to yield the final relatively stable anthocyanins⁵.

FUNCTIONS OF ANTHOCYANINS

Anthocyanins used as food additive

Mainly color plays a crucial role in food industries. Acceptability of food is mostly based on appearance of food. So many industries use synthetic food colorants to improve the elegance of food. These synthetic colorants show many side effects compared to natural colorants which are synthesized from anthocyanins. They show many beneficial effects without adverse effects. Anthocyanins involve a distinct group of intensely colored pigments responsible for the orange, red, purple and blue colors. These colors extracted from many leaves fruits, vegetables, flowers, roots⁶ Cyanidin, Delphinidin and Pelargonidin are the anthocyanins which are responsible for the pigmentation. They are extracted from strawberry, radish, potato, red grapes, cranberry⁷ blueberries⁸, black chokeberries⁹, elderberries, black currents¹⁰, purple corn¹¹.

Free radical scavenging activity of anthocyanins

Free radical is any atom or molecule that contains one or more unpaired electrons. Anthocyanins scavenge free radicals shows an antioxidant activity by increased uric acid. Low-wavelength electromagnetic radiation (eg. gamma rays) can split water in the body to generate hydroxyl radical. Apart from this another radical are oxygen radical (O₂⁻) and nitric oxide. These super oxide and nitric oxide has beneficial effects in low concentration. Radicals can generate more toxic chemicals in traces amounts. These two free radicals combine to form peroxynitrite radical, which damage the proteins and react with the iron copper¹². Hydrogen peroxide radical also form during the stress condition. These are highly reactive mainly in nucleus and damaging the membrane of DNA proteins carbohydrates, lipids and target all kind of cells in body. They are produced from vital metabolic activity in body and some of the external source also responsible for the free radical formation X-rays, ozone, cigarette smoking, air pollutants, industrial chemicals, mitochondria, xanthine oxidase, peroxisome, inflammation, phagocytosis, exercise, ischemic injury, certain drug and pesticide. These free radicals may cause different diseases in body like cancer, ischemia disease. Anthocyanins rich food contains a cyanidin, delphinidin, malvidin, peonidin these all are plays a crucial role in scavenge free radicals and reduces the lipid peroxidation and DNA damage¹³. For example, eggplant shows anti-oxidant activity by scavenge the oxygen free radical¹⁴ black berries having the highest free radical scavenging capacity against super oxide radical, hydrogen peroxide radical and nitric oxide radical¹⁵ and red cabbage containing anthocyanins are protect from oxidative stress¹⁶. The anthocyanidin pelargonidin

protect the amino acid tyrosine by highly reactive peroxynitrite free radical, anthocyanidin like delphinidin called nasunin, which destroy the dangerous hydroxyl radical¹⁷. These anthocyanidin shows a four times powerful antioxidant activity than vitamin E¹⁸. Philippines Medusa, Siberian Ginseng, Arabidopsis, red onions, Chagapoli, Asargu, red cabbage broccoli tea, red orange saffron black carrot, Ceylon gooseberry, palm fennel, straw berry, black soyabean, sweet potato, Chinese bay berry, myrtle berry, orchids, black rice, sweet cherry, sour cherry, pomegranate, peach, radish, goose berry, black current, rose petals, black raspberry, tomato, elderberry, bilberry, bog berry, wheat, grapes, corn. These are the anthocyanins rich food which will discuss in below Table 2.

Antihyperglycemic activity of anthocyanins

High fat diet is the one of the risk factor of type-ii diabetes in this insulin resistance results hyperglycemia occur. Anthocyanin like cyanidin, Delphinidin, Pionidin, Pelargonidin effectively treat the hyperglycemia by decreasing the tumor necrosis factor (TNF)- α mRNA levels and decreasing oxidative stress protect pancreatic β cells¹⁹ and also it decreases the glucose production by increases the AMPK, increase the glucose absorption and transport then lower risk of diabetes²⁰. For example anthocyanin which extract from Purple corn, cornus fruits (cherry), a rich source of anthocyanins, chokeberry, litchi, cranberry shows better hypoglycemic activity. Apart from anti hyperglycemic activity these anthocyanins prevent the symptom which are associate with diabetes like diabetic retinopathy²¹. One research article proved that anthocyanins which are present in black soyabean seed upper layer acts against type-ii diabetes through regulation of glucose transporter 4 and inhibit pancreatic apoptosis²².

Effect of anthocyanin on Cardio vascular system

Oxidative stress is one of the risk factor for cardiovascular disease. Anthocyanins play a vital role in protection against oxidative stress. The anthocyanin which is extracted from elder berries acts on endothelial cells shows protective effects²³. Delphinidin, which is extracted from red wine having vasodilation activity²⁴. We already know hyperlipidemia is a dangerous risk factor for cardiovascular diseases, cyaniding rich content containing black current could be decrease the fatty acid levels²⁵. A strong evidence is there anthocyanin rich content containing grape juice have powerful antioxidant activity protect against heart attack through increase the capillary permeability and strength, and to inhibit platelet formation and increase nitric oxide (NO) production the vasodilation occurs²⁶. These anthocyanins reduce active against lipid peroxidation then protect the cell membrane finally prevent the blood vessel damage and DNA damage²⁷. The Anthocyanins are preventing the plaque formation in arteries. For example, delphinidin is an anthocyanidin, it relaxes the blood vessels and it reduces the cardiovascular mortality". During the ischemia-reperfusion free radicals are form that result in white blood cell adhesion to micro capillary walls, then capillary wall permeability increases, blood flow decreases, finally causes permanent capillary damage these anthocyanins also helped in reduces the capillary damage²⁸. Anthocyanins scavenge the free radicals then inhibit the reactive oxygen species finally inhibit the inflammation related cardiovascular diseases.

Effect of anthocyanin on nervous system

Oxidative stress is a major factor for many neurodegenerative disorders. Anthocyanins give potent relief from this oxidative damage, for example Delphinidin is an anthocyanidin which protects lipids in brain tissue from deterioration. Pelargonidin may help protect against neurological diseases by preventing

Peroxynitrite free radical. Straw berry extract contains anthocyanidins like pelargonidin and delphinidine which shows a neuroprotective activity

Anti-inflammatory activity of anthocyanins

During the inflammation condition increased production of nitric oxide free radicals and prostaglandin E₂ (PGE₂) in presence of Cyclooxygenase (COX), mainly COX-2 is a gene that is highly inducible by inflammatory stimuli. Mainly anthocyanins show anti-inflammation activity by inhibits COX pathway very effectively. For example *Punica granatum* shows anti-inflammatory activity, cyanidin glycosides containing cherries and berries also shows anti-inflammatory activity, Siberian ginseng containing anthocyanidin like cyaniding shows anti-inflammatory activity, back soybean and ipomea containing anthocyanin like Cyanidin, Delphinidin, Petunidin, and Pelargonidin, Jabuticaba containing cyanidin and delphinidin and Ceylon gooseberry containing Cyanidin, Peonidin, Malvidin, Petunidin, Delphinidin and Pelargonidin how potent anti-inflammatory effect²⁹.

Effect of anthocyanins on eye

The anthocyanins may also increase eyesight and treat eye infections. A recent study found that black currant and maqui berry containing anthocyanidins used to improve eyesight³⁰.

Effect of anthocyanins on cancer

Anthocyanins may have capability to treat the tumorigenesis and cell proliferation³¹⁻³³. It inhibits the carcinogenesis through many multiple mechanisms are antioxidant activity and potent COX enzyme inhibition³⁴. Anthocyanin act against tumors by blocking MAP kinase pathway. For example, the anthocyanins which shows anticancer activity are Siberian Ginseng, Black carrot, Palm, Ipomoea, Honey berry^{35,36}.

Effect of anthocyanins on ulcers

The anthocyanin like Bilberry, used for to treat ulcers by the increasing the production of stomach mucus and protect the stomach from injury. Elderberry extract reduced stress-induced ulcers³⁷.

Other functions of anthocyanins

Apart from above functions anthocyanins protects from microbial infections, diarrhea, anti-fungal, immunomodulatory action, analgesic, Hypertension, Dysentery³⁸. List of anthocyanins described in Table 2.

Table 1: Selected Anthocyanidins and their Substituents

Anthocyanidin	R ₃ '	R ₄ '	R ₅ '	R ₃ '	R ₅ '	R ₆ '	R ₇ '
Aurantidin	-H	-OH	-H	OH	-OH	-OH	-OH
Cyanidin	-OH	-OH	-H	OH	-OH	-H	-OH
Delphinidin	-OH	-OH	-OH	OH	-OH	-H	-OH
Europinidin	-OCH ₃	-OH	-OH	OH	-OCH ₃	-H	-OH
Pelargninidin	-H	-OH	-H	OH	-OH	-H	-OH
Malvidin	-OCH ₃	-OH	-OCH ₃	OH	-OH	-H	-OH
Peonidin	-OCH ₃	-OH	-H	OH	-OH	-H	-OH
Petunidin	-OH	-OH	-OCH ₃	OH	-OH	-H	-OH
Rosinidin	-OCH ₃	-OH	-H	-OH	-OH	-H	-OCH ₃

Table 2: List of Anthocyanin Containing Food Materials and their Pharmacological Role

Source	Anthocyanins	Function
<i>Acalypha hispida</i> ³⁹ (Philippines Medusa)	Cyanidin	Anti-fungal and Anti-oxidant activity
<i>Allium cepa</i> ⁴⁰ (Red onions)	Cyanidin and Peonidin	Anti-oxidant activity
<i>Arabidopsis thaliana</i> ⁴¹ (Arabidopsis)	Cyanidin	Antioxidative activity
<i>Ardisia compressa</i> K ⁴² (Chagalapoli)	Malvidin, petunidin and Delphinidin	Anti-oxidant activity
<i>Aristotelia chilensis</i> ⁴³ (Maqui berry)	Delphinidin	Treat eye diseases
<i>Aronia melanocarpa</i> ⁴⁴ (Choke berries)	Cyanidin	Cardio-protective, Antidiabetic and Immunoregulatory effects
<i>Asparagus densiflorus</i> ⁴⁵ (Asparagus)	Cyanidin and Peonidin	Anti-oxidant activity
<i>Begonia semperflorens</i> ⁴⁶ (Wax begonia)		Photo-protective capacity
<i>Brassica oleracea</i> ⁴⁷ (Red cabbage)	Cyanidin	Anti-oxidant activity
Broccoli ⁴⁸	Cyanidin	Antioxidant activity
<i>Camellia hongkongensis</i> ⁴⁹	Cyanidin and Delphinidin	Antioxidant activity
<i>Camellia sinensis</i> ⁵⁰ (Teas)	Delphinidin and Cyanidin	Anti-oxidant activity
<i>Citrus sineses</i> ⁵¹ (Blood orange)	Cyanidin	Antioxidant activity
<i>Crataegus laevigata</i> ⁵² (Haw thorne)	Cyanidin	Anti-oxidant, Anti-microbial and Protect against cardiovascular diseases

<i>Crocus sativus</i> ⁵³ (saffron tepals)	Cyanidin, Pelargonidin, Delphinidin and Petunidin	Anti-oxidant activity
<i>Daucus carota</i> ⁵⁴ (Black carrot)	Cyanidin	Anti- cancer and Anti-oxidant activity
<i>Dovyalis hebecarpa</i> ⁵⁵ (Ceylon gooseberry)	Delphinidin and cyaniding	Antioxidant activity
<i>Erythrina crista-galli</i> L ⁵⁶ (cockspur coral tree)	Cyanidin	Astringent, Narcotic, and Analgesic for wound healing
<i>Euterpe oleracea</i> ⁵⁷ (Palm)	Cyanidin, pelargonidin and peonidin	Anticancer and Antioxidant effects
<i>Foeniculum vulgare</i> ⁵⁸ (Fennel)	Cyanidin	Anti-oxidant and Anti-microbial activity
<i>Fragaria ananassa</i> ⁵⁹ (Strawberry)	Cyanidin and Pelargonidin	Neuroprotectant activity
<i>Fragaria chiloensis</i> ⁶⁰ (Chilean strawberry)	Cyanidin and Pelargonidin	Anti-oxidant activity
<i>Garcinia indica</i> ⁶¹ (Kokum)	Cyanidin	Treat Dysentery, Tumours, Heart complaints, Stomach acidity and Liver disorders
<i>Glycine max</i> L ⁶² (Black soybean)	Cyanidin, Delphinidin, Petunidin, and Pelargonidin	Antioxidant activity, protect from Ischemia, Reperfusion, Heart injury, Anti-inflammation and Wound healing
<i>Gynura bicolor</i> ⁶³	Cyanidin	Antioxidant and Anti-cancer activity
<i>Hemigraphis colorata</i> ⁶⁴	Cyanidin	Anti-bacterial activity
<i>Hibiscus sabdariffa</i> ⁶⁵ (Roselle calyces)	Delphinidin and Cyanidin	Used in the food, pharmaceutical and cosmetic industries
<i>Ipomoea batatas</i> ⁶⁶ (Sweet potato).	Peonidin and Cyanidin	Anti-oxidant activity
<i>Litchi chinensis</i> Sonn ⁶⁷ (litchi)	Cyanidin, Malvidin	Anti-oxidant, Anti-diabetic, Antimicrobial, Anti ulcers, Anti-obesity, having analgesic action, Antihyperglycemic, Antihyperlipidemic, Antiplatelet, Antiviral and Hepatoprotective activity
<i>Lonicera Caerulea</i> ⁶⁸ (Honey berry)	Cyanidin	Chemopreventive, antimicrobial, antiadherence and antioxidant effects
<i>Lonicera japonica</i> ⁶⁹ (Honeysuckle)	Cyanidin	Anti-oxidant activity
<i>Matthiola fruticulosa</i> ⁷⁰ (Sad stock)	Cyanidin	Antioxidant activity
<i>Matthiola tricuspidata</i> ⁷¹ (Three-horned stock)	Cyanidin	Antioxidant activity
<i>Morus australis</i> Poir ^{72,73} (Mulberry)	Cyanidin and Pelargonidin	Anti-fever diuretics, Liver protection, Anti-hypertensive, Anti-obesity And protects from Cardiovascular diseases
<i>Musa paradisiaca</i> ^{73,74} (Banana)	Cyanidin, Delphinidin, Pelargonidin, Peonidin, Petunidin and Malvidin	Anti-ulcer
<i>Myrciacauleiflora</i> ⁷⁵ (Jaboticaba)	Cyanidin and Delphinidin	Treat hemoptysis, Asthma, Diarrhea and Gargled for chronic inflammation of the tonsils
<i>Myrica rubra</i> Sieb ⁷⁶ (Chinese bayberry)	Cyanidin	Anti-oxidant activity
<i>Myrtus communis</i> ⁷⁷ (Myrtle berries)	Delphinidin, Petunidin, Malvidin, Peonidin and Cyanidin	Antioxidative activity
<i>Neomitrantes</i> ⁷⁸ <i>Obscura</i>	Cyanidin, Delphinidin, Peonidin and Pelargonidin	Antioxidant activity
<i>Ocimum basilicum</i> ⁷⁹ (Basil)	Cyanidin	Antioxidant activity and Anti- Parkinson's disease
<i>Orchis</i> ⁸⁰ (Orchids)	Cyanidin	Anti-oxidant activity
<i>Oryza sativa</i> ⁸¹ (Black rice)	Cyanidin and Peonidin	Anti-oxidant activity
<i>Paeonia suffruticosa</i> ^{82,83} (Peony)	Pelargolidin, Cyanidin and Peonidin.	Acaricidal activity
<i>Phaseolus vulgaris</i> ⁸⁴ (Black bean)	Delphinidine, Malvidine, Petunidin	Anti-cancer
<i>Pisum sativum</i> ⁸⁵ (peas)	Cyanidin	Anti-oxidant activity
<i>Plumeria rubra</i> ⁸⁶ (Red frangipani)	Cyanidin	Antioxidant and hypolipidemic activity
<i>Prunus avium</i> ⁸⁷ (Sweet cherries)	Cyanidin	Anti-oxidant activity
<i>Prunus cerasus</i> var. <i>Marasca</i> ⁸⁸ (Sour cherry Marasca)	Cyanidin	Anti-oxidant activity
<i>Prunus mahaleb</i> ⁸⁹ (Rock cherry)	Cyanidin, Peonidin and Pelargonidin	Natural pigment for food industry

<i>Prunus persica</i> ⁹⁰ (peach)	Peonidin and Cyanidin	Anti-oxidant and Anti-ulcers
<i>Punica granatum</i> ^{91,92} (Pomogante)	Delphinidin, Cyanidin and Pelargonidin	Protection against Cardiovascular diseases, Antioxidant activity and Anti- cancer
<i>Pyrus communis</i> ⁹³ (Pear)	Cyanidin and Peonidin	Anti-cancer activity
<i>Queen Garnet</i> ⁹⁴ (plum)	Cyanidin	Antithrombotic and Anti-oxidant activity
<i>Raphanus sativus</i> ⁹⁵ (Radish)	Cyanidin and pelargonidin	Anti-oxidant activity
<i>Rhodomyrtus tomentosa</i> ⁹⁶ (Ceylon hill gooseberry)	Cyanidin, Peonidin, Malvidin, Petunidin, Delphinidin and Pelargonidin	Antioxidant, Anticancer Anti-inflammatory, Anti artery- atherosclerosis, Anti-hypertensive and Antibacterial activities
<i>Ribes nigrum</i> ⁹⁷ (Blackcurrant)	Delphinidin and Cyanidin	Anti-oxidant, Anti-coagulant, Anti-hypertensive, Anti-inflammatory, Anti-microbial, Anti-thrombotic and Anti-viral activities
<i>Rosa hybrida</i> ⁹⁸ (Rose)	Cyanidin, Pelargonin and Peonidin	Anti-inflammatory and Anti-oxidant activities
<i>Rubus fruticosus</i> ^{99,100} (Black berry)	Cyanidin, Pelargonidin, and Peonidin	Anti-oxidant property, Protection against endothelial dysfunction, protect against vascular dysfunction, and Anti-cancer
<i>Solanum lycopersicum. L</i> ¹⁰¹ (Tomato)	Aurantininidin, Cyanidin, Delphinidin, Pelargolidin, Malvidin, Peonidin, Petunidin and Rosinidin	Anti-oxidant activity and protect against cardiac injury
<i>Solanum melongena</i> ¹⁰² (Eggplant)	Delphinidin	Anti-oxidant activity, anti-diabetic activity
<i>Solanum tuberosum</i> ¹⁰³ (Potato)	Pelargonidin, Petunidin, Cyanidin, and Malvidin	Protect against heart disease and Anti- cancer
<i>Syzygium cumini</i> ¹⁰⁴ (Jamun)	Malvidin	Anti-oxidant, Antifungal, Anti-diabetic and Anti-inflammatory activities
<i>Triticum aestivum</i> ¹⁰⁵ (Canada's spring wheat)	Cyanidin, Delphinidin and Peonidin	Antioxidant activity
<i>Vaccinium myrtillus</i> ¹⁰⁶ (Bil berry)	Pelargolidin, Cyanidini, Peonidin, Delphinidin and Malvidin	Antioxidant, Antihyperglycemia, Antihyperlipidemia, Anti-Cancer Improving vision, antiinflammatory, Dementia, Cardio Vascular disease, and other age-related diseases.
<i>Vaccinium uliginosum</i> ¹⁰⁷ (Bog berry)	Delphinidin, Cyanidin, Petunidin, Peonidin, and Malvidin	Antioxidant, Anti-inflammatory and Anti-cancer
<i>Vaccinium corymbosum</i> ¹⁰⁸ (Blue berry)	Cyanidin, Delphinidin, Petunidin, Peonidin and Malvidin	Anticancer, vascular diseases and Neurodegenerative diseases
<i>Vaccinium macrocarph</i> ¹⁰⁹ (Cran berry)	Cyanidin, Delphinidin and peonidin	Treat cancer, inflammation, dyslipidemia, hyperglycemia and oxidative stress, UTI, cardiac Diseases
<i>Vitis vinifera</i> ¹¹⁰ (Grapes)	Malvidin, Cyanidin and Peonidin	Anti-oxidant activity
<i>Zea mays</i> (corn)	Cyanidin	Antioxidant activity

SUMMARY

The improvement of living conditions has contributed to the increased longevity of people worldwide. As a result, population aging is no longer a phenomenon restricted to developed countries.

In recent years, studies have begun to investigate the specific properties of isolated anthocyanin pigments. However, many still study the health effects of anthocyanins from fruit extracts where anthocyanins are present in combination with other compounds. In fact, some reports suggest that anthocyanin activity is actually potentiated when delivered in mixtures, as opposed to isolate.

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