



## CHEMICAL AND POTENTIAL ASPECTS OF ANTHOCYANINS – A WATER-SOLUBLE VACUOLAR FLAVONOID PIGMENTS: A REVIEW

**Raghvendra<sup>\*1</sup>, Vipin Sharma<sup>1</sup>, Ambika Shakya<sup>1</sup>, MD. Hedaytullah<sup>2</sup>, Ganesh Shankar Arya<sup>2</sup>, Amlan Mishra<sup>3</sup>, Anshu Deo Gupta<sup>4</sup>, Amol P. Pachpute<sup>5</sup>, Dharmendra Patel<sup>6</sup>**

<sup>1</sup>Aligarh College of Pharmacy, Aligarh (dt), U.P, India-202001.

<sup>2</sup>Shivdan Singh Institute of Technology & Management, Aligarh (dt), Uttar Pradesh, India-202001.

<sup>3</sup>K.M. College of Pharmacy, Madurai (dt), Tamil Nadu, India-625107.

<sup>4</sup>Goel Institute of Pharmacy and Sciences, Faizabad road, Lucknow (dt), Uttar Pradesh, India- 227105.

<sup>5</sup>Senior Clinical Research Associate, Clinical Department, Macleods Pharmaceuticals Limited, Mumbai, Maharashtra, India-400093.

<sup>6</sup>K.L.E. University's College of Pharmacy, Belgaum (dt), Karnataka, India-590010.

**\*Corresponding author's E-mail: [raghvendra\\_mpharm@rediffmail.com](mailto:raghvendra_mpharm@rediffmail.com)**

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### ABSTRACT

Anthocyanins are water-soluble vacuolar flavonoid pigments ranging from red to blue to purple shades that provide the colour in certain flowers and fruits (red, blue and purple tints in apples, berries, red grapes, eggplant, red cabbage and radishes). They are synthesized by organisms of the plant kingdom and bacteria, and have been observed to occur in all tissues of higher plants, providing colour in leaves, stems, roots, flowers, and fruits. Anthocyanins consist of sugar molecules bound to a benzopyrylium salt (called anthocyanidin). Anthocyanins are synthesized by organisms in the plant kingdom, and have been observed to occur in all tissues of higher plants, including leaves and stems. Anthocyanins exist only in plants with bright colours in everything from flower petals to autumn leaves and edible fruits or vegetables. Chemical identification studies reveal that there are as many as 600 unique anthocyanins in nature. It has been found that anthocyanins have shown potential health effects against various disorders like cancer, aging, neurological diseases, inflammation, diabetes as well as bacterial infections. Anthocyanin pigments and other flavonoids that are uniformly, predictably produced in rigorously controlled plant cell culture systems can be a great advantage for health and nutrition research because they are quickly, easily isolated, lack interferences found in whole fruits, can be elicited to provoke rapid and prolific accumulation, and are amenable to biolabeling so that metabolic fate can be investigated after ingestion. This article presents a brief review of Anthocyanins with an emphasis on their chemical and potential aspects.

**Keywords:** Anthocyanin, cyanin, anthocyan, anthocyan.

### INTRODUCTION

Anthocyanins are water-soluble vacuolar pigments that may appear red, purple, or blue according to pH. They belong to a parent class of molecules called flavonoids synthesized via the phenylpropanoid pathway; they are odourless and nearly flavourless, contributing to taste as a moderately astringent sensation. Anthocyanins occur in all tissues of higher plants, including leaves, stems, roots, flowers, and fruits. Anthoxanthins are their clear, white to yellow counterparts occurring in plants. Anthocyanins are derivatives of anthocyanidins which include pendant sugars. In flowers, bright reds and purples are adaptive for attracting pollinators. In fruits, the colourful skins also attract the attention of animals, which may eat the fruits and disperse the seeds. In photosynthetic tissues (such as leaves and sometimes stems), anthocyanins have been shown to act as a "sunscreen", protecting cells from high-light damage by absorbing blue-green and UV light, thereby protecting the tissues from photoinhibition, or high-light stress. This has been shown to occur in red juvenile leaves, autumn leaves, and broad-leaved evergreen leaves that turn red during the winter. It has also been proposed that red coloration of leaves may camouflage leaves from herbivores blind to red wavelengths, or signal unpalatability, since anthocyanin synthesis often

coincides with synthesis of unpalatable phenolic compounds. In addition to their role as light-attenuators, anthocyanins also act as powerful antioxidants. However, it is not clear whether anthocyanins can significantly contribute to scavenging of free-radicals produced through metabolic processes in leaves, since they are located in the vacuole, and thus, spatially separated from metabolic reactive oxygen species. Some studies have shown that hydrogen peroxide produced in other organelles can be neutralized by vacuolar anthocyanin.

Anthocyanins are members of the flavonoid group of phytochemicals, a group predominant in teas, honey, wines, fruits, vegetables, nuts, olive oil, cocoa, and cereals. The flavonoids, perhaps the most important single group of phenolics in foods, comprise a group of over 4000 C<sub>15</sub> aromatic plant compounds with multiple substitution patterns. The primary players in this group include the anthocyanins (e.g., cyanidin, pelargonidin, petunidin), the flavonols (quercetin, kaempferol), flavones (luteolin, apigenin), flavanones (myricetin, naringin, hesperetin, naringenin), flavan-3-ols (catechin, epicatechin, gallic acid, gallocatechin), and, although sometimes classified separately, the isoflavones (genistein, daidzein). Phytochemicals in this class are frequently referred to as bioflavonoids due to their multifaceted roles in human health maintenance, and anthocyanins in food are



typically ingested as components of complex mixtures of flavonoid components. Daily intake is estimated from 500 mg to 1 g, but can be several g/d if an individual is consuming flavonoid supplements (grape seed extract, ginkgo biloba, or pycnogenol<sup>1</sup>).

### How Anthocyanins synthesised from plant?

Anthocyanins are formed from chemical raw materials in the plant, using the amino acid phenylalanine, or another chemical called malonyl coenzyme A. These two substrates join to form the base material for anthocyanins called "chalcones" that lead to the production of anthocyanins after a series of enzyme steps.

The parent material of anthocyanins is a group of similar structures named "anthocyanidins" or "proanthocyanidins" which contain no sugar molecules. When sugars become attached, an anthocyanin glycoside is formed, taking the characteristic shape of anthocyanins. When first isolated by chemists, many anthocyanins were named after the colourful flowers from which they were extracted, such as petunidin (petunia), rosinidin (rose) and peonidin (peonies). The large class of antioxidant cyanidins is also anthocyanins – all these compounds belong to the group of compounds called flavonoids within the super-family of antioxidants named phenolics or polyphenols.

### Occurrence of Anthocyanins

Anatomically, anthocyanins are found in the cell vacuole, mostly in flowers and fruits but also in leaves, stems, and roots. In these parts they are found predominantly in outer cell layers such as the epidermis and peripheral mesophyll cells. Most frequent in nature are the glycosides of cyanidin, delphinidin, malvidin, pelargonidin, peonidin and petunidin. Roughly 2% of all hydrocarbons fixated in photosynthesis are converted into flavonoids and their derivatives such as the anthocyanins. There are no less than 10<sup>9</sup> tons of anthocyanins produced in nature per year. Not all land plants contain anthocyanin; in the Caryophyllales (including cactus, beets, and amaranth), they are replaced by betalains. Plants rich in anthocyanins are Vaccinium species, such as blueberry, cranberry and bilberry, Rubus berries including black raspberry, red raspberry and blackberry, blackcurrant, cherry, eggplant peel, black rice, Concord grape and muscadine grape, red cabbage and violet petals. Anthocyanins are less abundant in banana, asparagus, pea, fennel, pear and potato, and may be totally absent in certain cultivars of green gooseberries<sup>2</sup>. The highest recorded amount appears to be specifically in the seed coat of black soybean (*Glycine max* L. Merr.) containing some 2,000 mg per 100 g<sup>3</sup> and in skins and pulp of black chokeberry (*Aronia melanocarpa* L). However, the Amazonian palmberry, açai, having about 320 mg per 100 g<sup>4</sup> of which cyanidin-3-glucoside is the most prevalent individual anthocyanin (approximately 10 mg per 100 g)<sup>5</sup>, is also a high-content source for which only a small fraction of total anthocyanins has been determined to date. Due to critical differences in sample origin,

preparation and extraction methods determining anthocyanin content<sup>6, 7</sup>; the values presented in the adjoining table are not directly comparable.

Nature, primitive agriculture, and plant breeding have produced various uncommon crops containing anthocyanins, including blue- or red-fleshed potatoes and purple or red broccoli, cabbage, cauliflower, carrots and corn. Tomatoes have been bred conventionally for high anthocyanin content by crossing wild relatives with the common tomato to transfer a gene called the anthocyanin fruit tomato ("aft") gene into a larger and more palatable fruit<sup>8</sup>. Tomatoes have also been genetically modified with transcription factors from snapdragons to produce high levels of anthocyanins in the fruits<sup>9</sup>. Anthocyanins can also be found in naturally ripened olives, and are partly responsible for the red and purple colours of some olives<sup>10</sup>. Anthocyanins occur in nearly all plant families and thus in many edible plants. In food, the main sources of anthocyanins are berries, such as blackberries, grapes, blueberries etc, and some vegetables, such as egg-plants (aubergine) and avocado.

Other sources include oranges, elderberry, olives, red onion, fig, sweet potato, mango and purple corn. The natural production of anthocyanins in nature is estimated to be 10<sup>9</sup> tonnes/year. Table 1 highlights the Anthocyanin content in some edible plants.

**Table 1:** Anthocyanin content in some edible plants.

foodstuff	Anthocyanin in mg per 100 g food
aubergine (egg plant)	750
black currant	130-400
blackberry	83-326
blueberry	25-497
cherry	350-400
chokeberry	200-1000
cranberry	60-200
elderberry	450
orange	~200
radish	11-60
raspberry	10-60
red currant	80-420
red grape	30-750
red onions	7-21
red wine	24-35
strawberry	15-35

### Chemistry and Structural features

The anthocyanins, anthocyanidins with sugar group(s), are mostly 3-glucosides of the anthocyanidins. The anthocyanins are subdivided into the sugar-free anthocyanidin aglycones and the anthocyanin glycosides. As of 2003 more than 400 anthocyanins had been reported<sup>11</sup>, while more recent literature (early



2006), put the number at more than 550 different anthocyanins. The difference in chemical structure that occurs in response to changes in pH is the reason why anthocyanins are often used as pH indicator, as they change from red in acids to blue in bases.

Anthocyanin pigments are assembled from two different streams of chemical raw materials in the cell: both starting from the C2 unit acetate (or acetic acid) derived from photosynthesis, one stream involves the shikimic acid pathway to produce the amino acid phenylalanine. The other stream (the acetic acid pathway) produces 3 molecules of malonyl-Coenzyme A, a C3 unit. These streams meet and are coupled together by the enzyme chalcone synthase (CHS), which forms an intermediate chalcone via a polyketide folding mechanism that is commonly found in plants. The chalcone is subsequently isomerized by the enzyme chalcone isomerase (CHI) to the prototype pigment naringenin, which is subsequently oxidized by enzymes like flavonoid hydroxylase and coupled to sugar molecules by enzymes like UDP-O-glucosyl transferase to yield the final anthocyanins. More than five enzymes are thus required to synthesize these pigments, each working in concert. Any even minor disruption in any of the mechanism of these enzymes by

either genetic or environmental factors would halt anthocyanin production. Over 500 different anthocyanins have been isolated from plants. They are all based on a single basic core structure, the flavyllium ion (figure 1).

**Figure 1:** The flavyllium ion, the basic structure of anthocyanins.



As shown in figure 1 there are 7 different side groups on the flavyllium ion. These side groups can be a hydrogen atom, a hydroxide or a methoxy-group. The most frequent combination of side groups and their names<sup>11</sup> are shown in Table 2.

**Table 2:** Selected anthocyanidins and their substitutions. R1-R7 are the side groups as shown in figure 1.

Anthocyanidin	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>	R <sub>6</sub>	R <sub>7</sub>	main colour	E-number
Apigeninidin	-H	-OH	-H	-H	-OH	-H	-OH	orange	
Aurantidin	-H	-OH	-H	-OH	-OH	-OH	-OH	orange	
Capensinidin	-OCH <sub>3</sub>	-OH	-OCH <sub>3</sub>	-OH	-OCH <sub>3</sub>	-H	-OH	bluish-red	
Cyanidin	-OH	-OH	-H	-OH	-OH	-H	-OH	magenta	E163a
Delphinidin	-OH	-OH	-OH	-OH	-OH	-H	-OH	purple, blue	E163b
Europinidin	-OCH <sub>3</sub>	-OH	-OH	-OH	-OCH <sub>3</sub>	-H	-OH	bluish red	
Hirsutidin	-OCH <sub>3</sub>	-OH	-OCH <sub>3</sub>	-OH	-OH	-H	-OCH <sub>3</sub>	bluish-red	
Luteolinidin	-OH	-OH	-H	-H	-OH	-H	-OH	orange	
Pelargonidin	-H	-OH	-H	-OH	-OH	-H	-OH	orange, salmon	E163d
Malvidin	-OCH <sub>3</sub>	-OH	-OCH <sub>3</sub>	-OH	-OH	-H	-OH	purple	E163c
Peonidin	-OCH <sub>3</sub>	-OH	-H	-OH	-OH	-H	-OH	magenta	E163e
Petunidin	-OH	-OH	-OCH <sub>3</sub>	-OH	-OH	-H	-OH	purple	E163f
Pulchellidin	-OH	-OH	-OH	-OH	-OCH <sub>3</sub>	-H	-OH	bluish-red	
Rosinidin	-OCH <sub>3</sub>	-OH	-H	-OH	-OH	-H	-OCH <sub>3</sub>	red	
Triacetidin	-OH	-OH	-OH	-H	-OH	-H	-OH	red	

#### Some concerned important aspects associated with anthocyanins:

Anthocyanins are members of a class of nearly universal, water-soluble, terrestrial plant pigments that can be classified chemically as both flavonoid and phenolic. They are found in most land plants, with the exception of the cacti and the group containing the beet. They contribute colours to flowers and other plant parts ranging from shades of red through crimson and blue to purple, including yellow and colourless. (Every colour but green has been recorded). Anthocyanin pigments can be produced by growing plant cells in tissue culture. Plants having no pigmentation themselves in cultivation were

subsequently demonstrated to produce anthocyanin in tissue culture. Environmental factors affecting anthocyanin production included light (intensity and wavelength, with blue and UV being most effective), temperature, water and carbohydrate levels, and the concentrations of the elements nitrogen, phosphorous and boron in the growth medium. Anthocyanin production can be induced by light, blue being the most effective colour. Low light levels also induce the formation of different flavonoid pigments, which is another interesting adaptive response on the part of plants. (Tillandsias, for example, develop a bright red coloration due to induced anthocyanin production if

grown in strong light). Anthocyanin-type pigments are found only in terrestrial plants. They are not found in animals, marine plants or in microorganisms.

It is theorized that anthocyanin production is an evolutionary response to plants first venturing onto the stark primordial landscape under intense UV radiation. (Significant screening of the earth's surface from the effects of UV radiation didn't occur until after the advent of terrestrial plants. Oxygen in large amounts first had to be generated by the photosynthesis of land plants before the UV-screening ozone layer was formed). The evolution of insect vision to respond to the unique wavelengths of light presented by flowering plants is an interesting scenario, as is the evolution of these plants to take advantage of the insect's attraction to the sight of anthocyanins. Obviously, the plants came first and developed anthocyanins as a defence mechanism long before the first insect evolved. Flowering plants subsequently found in anthocyanin a handy way to attract pollinators. Carnivorous plants took advantage of the pollination attraction mechanism to serve as an effective visual lure for their prey.

#### Potential benefits, uses and role of anthocyanins

Anthocyanins are considered secondary metabolites as a food additive with E number 163. Although anthocyanins are powerful antioxidants in vitro<sup>12</sup>, it is unlikely this antioxidant property is conserved after the plant which produced the anthocyanins is consumed. As interpreted by the Linus Pauling Institute and European Food Safety Authority, dietary anthocyanins and other flavonoids have little or no direct antioxidant food value following digestion<sup>13, 14</sup>. Unlike controlled test tube conditions, the fate of anthocyanins in vivo shows they are poorly conserved (less than 5%), with most of what is absorbed existing as chemically-modified metabolites which become rapidly excreted. The increase in antioxidant capacity of blood seen after the consumption of anthocyanin-rich foods may not be caused directly by the anthocyanins, but instead may result from increased uric acid levels derived from metabolism of flavonoids. Anthocyanins are being used in organic solar cells because of their ability to absorb light and convert it into electrons<sup>15</sup>. There are many benefits to using cells instead of the traditional silicon cells, such as abundance of anthocyanins, the projected 90% efficiency, and the ability to bend or print inks used in newer manufacturing processes<sup>16</sup>.

#### Research being done on Anthocyanins

Richly concentrated as pigments in berries, anthocyanins were the topics of research presented at a 2007 symposium on health benefits that may result from berry consumption. Laboratory-based evidence was provided for potential health effects against:

- cancer
- aging and neurological diseases

- inflammation
- diabetes
- bacterial infections

Cancer research on anthocyanins is the most advanced, where black raspberry (*Rubus occidentalis* L.) preparations were first used to inhibit chemically induced cancer of the rat esophagus by 30-60% and of the colon by up to 80%.

Effective at both the initiation and promotion/progression stages of tumour development, black raspberries are a practical research tool and a promising therapeutic source, as they contain the richest contents of anthocyanins among native North American *Rubus* berries<sup>17</sup>.

1. stalling growth of pre-malignant cells
2. accelerating the rate of cell turnover, called apoptosis, effectively making the cancer cells die faster
3. reducing inflammatory mediators that initiate tumour onset
4. inhibiting growth of new blood vessels that nourish tumours, a process called angiogenesis
5. Minimizing cancer-induced DNA damage.

On a molecular level, berry anthocyanins were shown to turn off genes involved with proliferation, inflammation and angiogenesis<sup>18-20</sup>, while switching on apoptosis<sup>21, 22</sup>. In 2007, black raspberry studies entered the next pivotal level of research – the human clinical trial – for which several approved studies are underway to examine anti-cancer effects of black raspberries and cranberries on tumours in the esophagus, prostate and colon<sup>23</sup>. Anthocyanins also fluoresce; combined with their antioxidant properties, this can be a powerful tool for plant cell research, allowing live cell imaging for extended periods of time without a requirement for other fluorophores<sup>24</sup>.

#### Miscellaneous uses of anthocyanins

Not only do anthocyanins reflect red and blue light, they also absorb dangerous UV-B, making them an excellent natural sunscreen. In particular they are used by young leaves for this purpose before they are capable of producing more permanent (and costly) protective waxes on their cortex. Apparently, there is some evidence that these antioxidants can be used to treat a number of health problems as well, including boosting insulin production, and fighting leukaemia and lymphoma. Reportedly, the concentrated black raspberry extracts used in one study gave 200 times the anti-inflammatory benefits of aspirin, but without the side effects. However, other research has shown that the health benefits from consuming flavonoids of any sort (including presumably anthocyanins) is due to increased uric acid levels that



result from the body trying to flush them out of the system as fast as possible.

## DISCUSSION AND CONCLUSION

It may be concluded that anthocyanins are versatile and plentiful flavonoid pigments found in red/purplish fruits and vegetables, including purple cabbage, beets, blueberries, cherries, raspberries and purple grapes. Within the plant they serve as key antioxidants and pigments contributing to the coloration of flowers. Anthocyanins are flavonoids. A major function of anthocyanins is to provide colour to most flowers and fruits. The colours can help attract pollinating animals to flowers and animals that will help disperse seeds. Anthocyanins are also thought help protect leaves from ultraviolet radiation but some botanists think that may not be true for all plant species. Anthocyanins are also thought to deter herbivores in some species. Anthocyanins are a very large group of red-blue plant pigments. Anthocyanins occur in all higher plants, mostly in flowers and fruits but also in leaves, stems, and roots. In these parts they are found predominantly in outer cell layers.

Chemically anthocyanins are subdivided into the sugar-free anthocyanidine aglycons and the anthocyanin glycosides.

They are used as food additive with E number E163. Medical research has been examining potential health or anti-disease benefits of having anthocyanin-enriched plant foods like berries included in the regular human diet. Although the work must be considered preliminary until thorough clinical trials are completed, the lists of potential benefits are many and include positive effects against:

- Cancer
- Diabetes
- Inflammation
- Heart and vascular disease
- Alzheimer's disease
- Other types of neurodegeneration
- High blood cholesterol
- Stroke
- Bacterial infections
- Urinary tract infections
- Age-related eyesight deterioration
- Premature aging

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**About Corresponding Author: Mr. Raghvendra**

Mr. Raghvendra graduated at Uttar Pradesh Technical University, Lucknow, U.P, India and at post graduation level, had taken specialization in Pharmaceutics from Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India. Now working as a Senior Lecturer in Aligarh College of Pharmacy, Aligarh, U.P, India.