

Anthocyanins for Health

with Special Reference to Bladder Cancer Chemoprevention

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Background Note: Progress in chemical identification of food and herb active constituents, their pharmacology, and population studies of dietary and supplemental intake during the past 75 years has propelled the understanding of traditional natural health care practices and their modernization. One of the important groups of plant constituents revealed by this work are phenolic compounds classified as flavonoids. I had designed two formulas that emphasized flavonoids in the early 1990s: a product made by Health Concerns called Flavonex, featuring extracts of several flavonoid-rich Chinese herbs, and a White Tiger formula made for ITM called Quercenol, with quercetin plus grape seed and green tea extracts, each having different kinds of flavonoids. In 1997, I produced a review titled “Flavonoids and Health,” and focused on one of particular interest, quercetin, which was noted as an inhibitor of cancer development. Since then, a topic of increased investigation has been the possibility of quercetin helping treat triple-negative breast cancer, which has more limited drug interventions. Quercetin was also known for anti-allergy effects and in recent times has been noted as one of the important compounds inhibiting mast cell degranulation, a process resulting in release of histamine and other allergy symptom mediators. The current article is about a subgroup of flavonoids, anthocyanins, having the main publicized use in benefiting vision, but they are now of increasing interest in prevention and treatment of cancer, with a research focus on bladder cancer. An ITM formulation with high anthocyanin content is Lycuvin, which relies on bilberry extract.

The Source of Anthocyanins

Anthocyanins are widely distributed in fruits and vegetables; they contribute red, blue, and purple coloration. In particular, anthocyanins are common components providing some of the distinctive color of cranberries, red and black grapes, cherries, raspberries, strawberries, black berries, blue berries, elderberries, currants, choke berries (aronia), blood orange, rhubarb, purple yams, and pomegranate. Anthocyanins are comprised of a characteristic base molecule, classified as an anthocyanidin, linked to a sugar, to make a glycoside. The most commonly occurring anthocyanidin is simply called cyanidin. Blue colored flowers usually have the related compound delphinidin. About a dozen other such compounds have been identified in a variety of commonly used plants, especially those for food and herbal medicine. See Appendix 1 for primary dietary anthocyanins.

These flavonoids are considered to have multiple health benefits, including reducing cardiovascular disease risk, moderating neurodegenerative disease, and having broad anti-inflammatory and anti-cancer effects. Anthocyanins also provide pigments for the retina, and may improve vision as well as reduce risk for and severity of retinal disorders, which is a primary indication for natural products containing anthocyanin-rich extracts. One of the first reports of potential value of anthocyanins for prevention and treatment of bladder cancer was published 2014 (1), with evaluation of a blue-colored anthocyanin-rich extract from *Vaccinium myrtillus* fruit, commonly called bilberry (a relative of the common blueberry, *Vaccinium corymbosum*); the extract is a frequently recommended supplement for vision health. The particular extract employed in the bladder cancer evaluation was a product called Mirtoselect: in a bladder cancer cell line, it causes growth inhibition and apoptosis (the normal death of cells, for which cancer cells overcome the process and continue to survive and multiply, unless apoptosis can be restored). The potential value of compounds from *Vaccinium* species fruits for cancer has been extended, according to a review published in 2024 (2), to a range of reproductive system cancers (including bladder). Two Chinese publications from 2018 (3, 4) showed that anthocyanins from purple sweet potatoes also induced apoptosis in cultured bladder cancer cell lines.

The potential role of the flavonoids in human bladder cancer prevention was investigated in Italy (5) by utilizing dietary analysis of intake, indicating an inverse association between quantity of flavones and isoflavones ingested and bladder cancer occurrence. While not specific for anthocyanins, the study confirms that the anticancer potential of flavonoids could impact bladder cancer in humans, not just in the isolated cell lines. Some cancer chemoprevention compounds don't affect bladder cancer: one of the best known anticancer substances, common aspirin, is especially effective for colon cancer prevention, but not for bladder cancer (6).

A most recent publication on the subject, October 2024 (7), indicates that anthocyanins and other flavonoids from the *Clitoria termatea* flowers (a common name is bluebellvine, for its blue flowers), also show promise for prevention and treatment of bladder cancer, indicating that the botanical source is not the key element, but the presence of anthocyanins and flavonoids generally.

Effective Dosage

Most appropriate dosing of anthocyanins for human consumption, via diet and supplements, is difficult to predict for bladder cancer chemoprevention, because of the limited clinical information. Presumably, the potentially effective dosing for long-term use to prevent a first instance of bladder cancer would be lower than dosing to prevent a recurrence. Dosing information from studies of anthocyanins for other clinical applications can provide some guidance. Studies mentioned below are cited specifically for their dosing information and they are not here critically evaluated for the claimed positive results.

In a clinical evaluation of anthocyanin (derived from blueberry and blackberry) in treatment of patients with diabetes (8), dosing was 160 mg anthocyanins twice daily, for a total of 320 mg. The same anthocyanin preparation at the same dose was used in a clinical trial for patients with elevated cholesterol (9).

A recent literature review (10) indicated that consumption of anthocyanins could help raise the beneficial HDL cholesterol, reduce triglycerides, and reduce excess blood sugar. The most commonly referenced dosage, either by fruits, fruit extracts, or purified anthocyanins was at or close to 320 mg/day, sometimes about half that, and in a few cases close to or at 900 mg. In a review (11) of anthocyanin effects on cognitively impaired adults, the dose of anthocyanins was generally lower than these other studies, with three largest amounts in the range of 387-425 mg/day, but mostly below 300 mg/day.

Higher anthocyanin dosing was used in a study (12) of bilberry extract in patients with ulcerative colitis, using 800-1,000 mg/day of anthocyanins. The authors noted that lower doses had been used in other studies and that there were indications that this kind of treatment could help also with irritable bowel syndrome and in animal studies could help prevent colon cancer.

In a study (13) on effects of polyphenols, especially anthocyanins, provided as a beverage derived from choke berry, cranberry, and pomegranate, the daily dosage administered corresponded to 550 mg of anthocyanins. An elderberry juice was provided in another study (14), showing improved glucose tolerance and balanced gut flora, utilized a daily dosing corresponding to about 720 mg of anthocyanins.

Taking together, these diverse examples of application point to a daily intake of 250 – 750 mg of anthocyanins per day for potentially attaining health benefits. It is possible to consume these levels utilizing fruits and vegetables and their juices, but for those people having a limited dietary intake of the anthocyanin-rich items, supplements may be needed to attain the desired daily quantity. The content of anthocyanins from any food source can vary over a considerable range depending on the growing conditions, storage, and preparation for consumption, but reliance on the mentioned food sources, especially the fruits, should yield a significant quantity. Estimates of daily intake of anthocyanins when *not* specifically choosing foods for that purpose is about 12 mg/day, that is, at a level well below what is expected to have desired benefits.

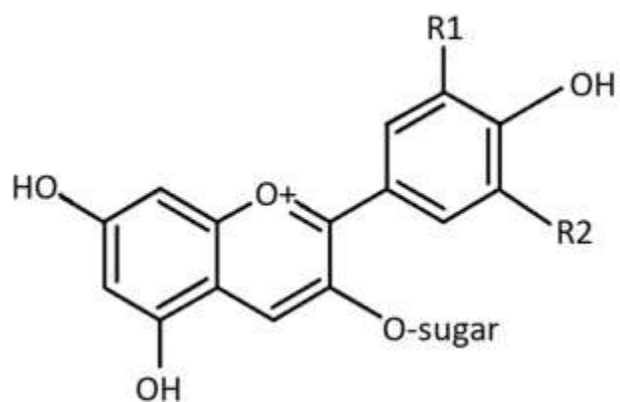
As examples of supplements that might be used, bilberry extracts at 100 mg/capsule, providing 36 mg/capsule of anthocyanins can be taken in doses of 4 capsules per day to yield 144 mg anthocyanins intake. Aronia extract capsules are available, with 250 mg extract per capsule, the anthocyanin level is not specified, but could also be taken 4 capsules per day with reasonable expectation of obtaining about 100 mg anthocyanins per capsule, or 400 mg per day.

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Appendix 1. Anthocyanin structure and variants



	R1	R2
Cyanidin	OH	H
Delphinidin	OH	OH
Malvidin	OCH ₃	OCH ₃
Pelargonidin	H	H
Peonidin	OCH ₃	H
Petunidin	OCH ₃	OH