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MINIREVIEW

ANTHOCYANINS IN MEDICINE

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Anthocyanins belong to water-soluble plant pigments. They are derivatives of 2-phenylbenzopyrylium. Due to the commonness of occurrence (among others in fruit) they are components of human diet. Owing to scientific research they have become not only food products but also therapeutic agents. They exhibit, among others, antioxidative and anti-inflammatory activity, they also show favorable effect in the treatment of some types of neoplasms.

Key words: *anthocyanins, apoptosis, free radicals, inflammation, neoplasms*

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Anthocyanins are representatives of a wide group of plant pigments, flavonoids (Fig. 1). They are derivatives of 2-phenylbenzopyrylium [22]. In nature, there are over 200 compounds belonging to this group, usually bound to saccharide residues: glucose, galactose, rhamnose, arabinose as 3-glycosides or 3,5-diglycosides. They rarely occur as aglucones. Proanthocyanidins are a group of condensed tannins (dimers, trimers etc.) metobolized to anthocyanidins.

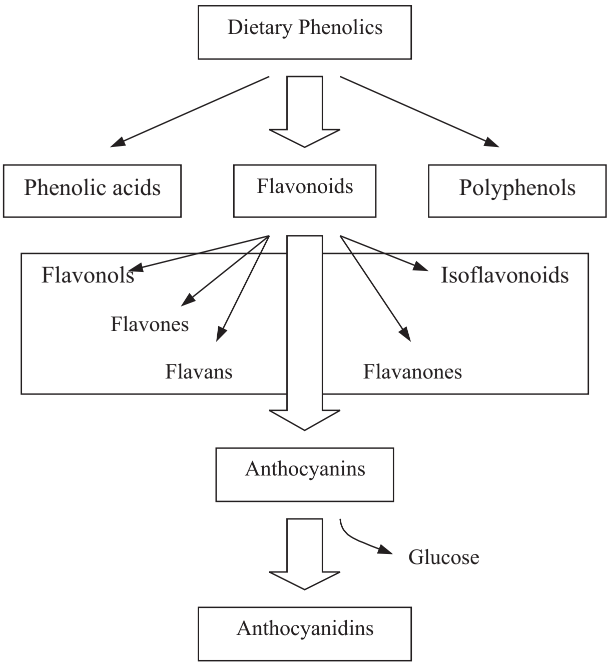
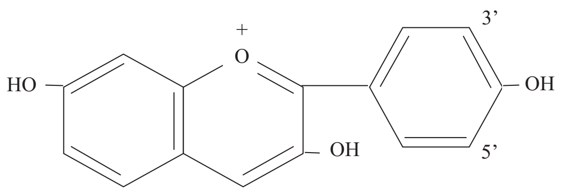


Fig. 1. Dietary phenolics



Anthocyanidins:

Compound	Carbon ring B substitution 3'	Carbon ring B substitution 5'
Pelargonidin	-H	-H
Cyanidin	-OH	-H
Delphinidin	-OH	-OH
Peonidin	-OCH3	-H
Petunidin	-OCH3	-OH
Malvinidin	-OCH3	-OCH3

Fig. 2. Diagram of anthocyanidin skeleton

Differences in their structure include: 1) number and position of hydroxyl and methoxyl substituents in aglucone skeleton; 2) number and position of saccharide residues bound to anthocyanidin skeleton; 3) acylation of these groups. Owing to the ability of these molecules to associate into complexes characterized by higher absorbance of light waves, copigmentation and formation of complexes with metals, they are responsible in vegetable tissues for their color: blue, violet, purple and even black [13].

They are common components of human diet (studies of the USA population estimate daily consumption at about 180–215 mg [24]). Various products of vegetable origin may be a source of these compounds, particularly fruits of aronia, black currant, raspberry, grapes, apples and also tomatoes, onion, garlic, hawthorn. They are absorbed in alimentary tract to inconsiderable degree. About 0.01% of the orally administered dose is excreted with urine [9]. Metabolism of anthocyanins in animals is not fully understood.

Due to their chemical structure, these dyes are able to react with many active substances in human body. Studies confirmed antioxidative properties of anthocyanins. They result from the chemical structure of these compounds, particularly from the presence of hydroxyl groups in position 3 of ring C and also in 3' and 4' positions in ring B. The presence of hydroxyl group at ring C enables chelation of metal ions, e.g. Fe, Cu. Antioxidative activity is also increased by acylation of sugar residues with aromatic hydroxy acids [21]. Comparison of antioxidative properties of anthocyanins with widely known antioxidants (expressed as IC_{50}, i.e. an amount of the investigated antioxidant necessary to decrease LDL oxidation rate by half), showed that these compounds had higher antioxidative activity than vitamin E (α-tocopherol), ascorbic acid and β-carotene. Our experiments [11] in animals demonstrated anthocyanins-induced decrease in the contents of thiobarbituric acid reactive substances (TBARS), increase in total level of antioxidants and increase in glutathione peroxidase activity (GPX).

Antioxidative properties of anthocyanins are used, among others, in the therapy of cardiovascular diseases. Anthocyanins decrease the amount of oxidized LDL, show antiaggregative and vasodilating activities [20] and, by inhibition of free radical formation in the process of reperfusion [19], they protect cardiomyocytes after ischemic episodes. Tsuda et al. [23] have reported that anthocyanins are able to decrease the activity of nitric oxide synthase and the level of nitric oxide.

Anthocyanin dyes affect the course of inflammatory process, as they are inhibitors of cyclooxygenase. Apart from antioxidative activity, they inhibit adhesion and reaction of leucocytes with endothelial cells by inhibiting VCAM molecule expression. They inhibit degranulation of mast cells [16] and decrease the level of IL-2, INF-γ, TNF-α [14]. Anthocyanins and proanthocyanins have antibacterial properties as well, for instance they inhibit, among others, adhesion of bacteria to mucous membrane of urinary tract [7]. The ability to regulate permeability of capillary vessels became the basis to define them as "vitamin P". They show protective properties towards hepatocytes in hepatitis A and B [10] and also in paracetamol-induced hepatotoxicity [1]. In inflammatory states of joints and connective tissue, they act as COX-2 inhibitors, causing a decrease in prostaglandin levels (particularly PGE 2). Contrary to commonly used anti-inflammatory drugs, they activate the synthesis of type II collagen [5]. Microscopic examinations demonstrated also a positive effect of proanthocyanins in patients with pancreatitis, they slowed down pathologic changes of the organ and alleviated clinical symptoms (abdominal pain, nausea, vomiting) [3]. Investigation of the effect of these compounds on systemic sugar balance demonstrated their hypoglycemic activity through inhibiting α-glucosidase in intestinal lumen [15] and sensitization of cells to insulin A.

Anthocyanin dyes affect cell growth cycle. It has been demonstrated that they are able to induce the expression of antiapoptotic gene Bcl-2 and to inhibit the activity of proapoptotic genes e-myc and p53 [2]. Investigations on laboratory animals proved that they also inhibited the activity of enzymes inducing apoptosis, increasing survival rate of cells subjected to the action of stressors. It has been demonstrated that proanthocyanins protect cardiomyocytes against apoptosis in the course of ischemic injury [9]. Oral administration of these dyes prevents also the programmed death of oral cavity keratinocytes in cigarette smokers [2].

Studies on antineoplastic activity of anthocyanins are also in progress. Anthocyanins from white grapefruits and apples aid the treatment of pulmonary carcinomas, particularly in cigarette smokers, whereas those originating from lemon are a supplement of pharmacological treatment of lymphoma induced by Epstein-Barr virus [8]. The effectiveness of anthocyanins has also been proved in the treatment of ovarian carcinoma [17] and gastric adenocarcinoma [2]. *In vitro* investigations demonstrated their ability to inhibit mutagenesis in cells of pancreatic neoplasms (proanthocyanins) [25], smooth muscles, liver [12] and cells of colonic carcinoma – HT 29 clone 19A [4]. We observed an inhibition of angiogenesis in LIA test (lymphocyte-induced angiogenesis) after the application of flavonoids from *Baicaline* thyroid and anthocyanins from *Aronia melanocarpa* (study prepared for publication).

Due to antioxidative properties and ability to inhibit metalloproteases: MMP-1, MMP-9, anthocyanins applied with other antioxidants act photoprotectively upon exposure of experimental animals' skin to UV radiation [6].

Scientific research greatly contributed to the fact that anthocyanins have become not only food products but also therapeutic agents. The presented selected literature data on anthocyanins raise high hopes for using them extensively in prophylaxis or therapy of many diseases.

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