REVIEW

Current advances in anthocyanins: structure, bioactivity and human health

HE LIU – KANG ZHOU – HAIQIN JIANG – LIANKUI WEN – YANG HE – SIYAN LU – BIXIANG WANG – JIA LI

Summary

Anthocyanins are a class of water-soluble flavonoid compounds, which are widely found in plants. The structure and content of anthocyanins from fruits (137–5 702 mg·kg^{-1} fresh weight, FW), cereals (363–416 920 mg·kg^{-1} dry weight, DW) and vegetables (770–3 220 mg·kg^{-1} FW) are reviewed. The relationship between anthocyanin structure, biological activities (antioxidant, anti-inflammatory, bacteriostatic) and disease improvement (cancer, organs injury, diabetes, obesity, eye diseases, neurodegenerative diseases) is discussed. The antioxidant activities of anthocyanins were delphinidin > petunidin > cyanidin > malvidin > peonidin > pelargonidin, and the antioxidant activity of anthocyanins glycosylated only on C3 position was higher than that of anthocyanins glycosylated on both C3 and C5 positions. The anticancer effects of cyanidins and peonidins were stronger than those of malvidins, and the hepatoprotective and antidiabetic effects of cyanidins were stronger than those of peonidins.

Keywords

anthocyanins; structure; bioactivity; human health

Anthocyanins are water-soluble plant pigments with biological activity, which are called "colour cell fluid". They give plants brilliant colours. To date, more than 700 anthocyanins have been identified from natural plants such as fruits, vegetables and cereals, and the number is increasing steadily [1]. At present, the edible and medicinal value of anthocyanins has been widely concerned and recognized. Anthocyanins are important contributors to human health, as they have various effects, such as antioxidant [2], anti-inflammation [3], bacteriostatic [4], anticancer [5], organ protection [6], anti-diabetes [1], anti-obesity [7], vision protective and improvement of neurodegenerative diseases [8]. Studies showed that anthocyanins from various sources are present in different contents, they have different structure and biological activities [9].

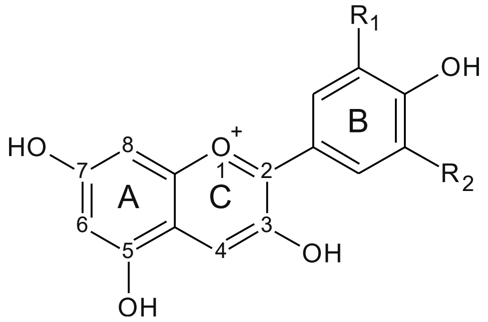
In this paper, the structure and content of anthocyanins of various sources are reviewed, together with their beneficial effects on human health. The relationship between the structure, bioactivity and disease improvement of anthocyanins is analysed to provide basis for further research of anthocyanins and for product development.

Anthocyanins sources and structure

Anthocyanins belong to flavonoid phenolic compounds, which mainly exist in plants in the form of glycosides. The basic structure unit of anthocyanins is 3,5,7-trihydroxy-2-phenylbenzopyrylium, which consists of two benzoyl rings (A and B rings) and one oxygen-containing six-membered heterocycle (C ring), constituting the basic framework of C6-C3-C6, containing 15 carbons [9]. Among them, R_1 and R_2 on B ring can be substituted by different substituents (-OH, -OCH3), resulting in six categories of anthocyanins (Fig. 1). According to their proportion in

He Liu, **Liankui Wen, Yang He, Siyan Lu, Bixiang Wang, Jia Li,** Department of Food Science and Engineering, Jilin Agricultural University, Xincheng Street 2888, 130118 Changchun, China.
Kang Zhou, Agriculture and Technology Magazine, Jilin Province Science and Technology Information Research Institute, Shenzhen Street 940, 130033 Changchun, China.
Haiqin Jiang, Food Inspection Agency, Administration for Market Regulation, Kenfeng Street 67, 063003 Tangshan, China.

Correspondence author:
Liankui Wen, tel.: +86-0431-84533104, fax: +86-0431-84533104, e-mail: wenliankui@jlau.edu.cn
Yang He, e-mail: heyang200704@jlau.edu.cn



R_1	R_2	Anthocyanin species
-OH	-H	Cyanidin
-OH	-OH	Delphinidin
-H	-H	Pelargonidin
$-OCH_3$	-H	Peonidin
$-OCH_3$	-OH	Petunidin
$-OCH_3$	$-OCH_3$	Malvidin

Anthocyanins basic structure

Fig. 1. Anthocyanins structure.

plants, the six major classes of anthocyanins are cyanidin (50 %), delphinidin (12 %), pelargonidin (12 %), peonidin (12 %), petunidin (7 %) and malvidin (7%) [10]. Among them, the first three are non-methylated anthocyanins, which are the most widely distributed in nature [11].

Anthocyanins are found in red, blue, purple and other brightly coloured plants, mainly in certain fruits (such as blueberry, grape, blackberry), grains (such as black rice, black beans, purple corn), vegetables (such as red cabbage, eggplant) and other (such as *Lycium ruthenicum*). In recent years, with the in-depth research of anthocyanins, the content, structure and biological activities of anthocyanins in various plants have been gradually discovered (Tab. 1). The proportion of cyanidins in anthocyanins is highest in most fruits and grains. Cyanidin-3-glucoside (Cy3G) content is the highest in blackberry, mulberry, black rice, purple corn and purple wheat, accounting for 89 %, 65.8 %, 91.0 %, 37.1 %, 27.4–45.8 % of total anthocyanins content (*TAC*), respectively [36, 49, 44, 51]. Delphinidin-3-[(4”-*p*-coumaroyl)-rhamnosyl (1→6) glucoside]-5-glucoside is the main anthocyanins of eggplant, accounting for 69.1–87.7 % [64]. Pelargonidin-3-glucoside (Pg3G) is accounting for 80 % of strawberry. The highest level of petunidin-3-glucoside (Pt3G) is in black bean and *Lycium ruthenicum* – 40.0–56.0 % and 35.2 %, respectively [54, 66]. Anthocyanins in blueberry and grape are mainly composed of malvidin, which accounts for 41.0 % and 88.8 % of *TAC*, respectively [22, 28]. Anthocyanins from various sources differ in content, species and biological activities.

The existence of multiple phenolic hydroxyl groups in anthocyanins makes the stability of anthocyanins poor, but glycosylation or glycosyl acylation can improve their stability. The smallest unit of anthocyanins combines with various sugars or organic acids to produce different types of anthocyanin derivatives, which is one of the reasons of the molecular diversity of anthocyanins [67]. In the glycosylation reaction, when anthocyanins bind only one sugar, they are generally bound to the C3 position of the anthocyanin skeleton. When combined with two sugars, those are usually bound to the hydroxyl groups of the C3 and C5 positions, sometimes combined at the C3 and C7 positions. Glucose, galactose, arabinose, rhamnose and xylose are common sugars that combine with anthocyanins. The most common anthocyanin derivatives in nature are 3-glucoside, 3,5-diglucoside and 3,7-diglucoside [68]. Among them, Cy3G is one of the most common anthocyanins [69]. In glycosyl acylation reaction, organic acids generally bind to the sugar at the C3 position of anthocyanins, and the two acids are simultaneously bound to the sugars of C3 and C5 positions. Research showed that the structure of anthocyanins from various sources are different and the degree, position as well as quantity of glycosylation and glycosyl acylation are different [67].

At present, co-pigmentation of organic acids is an important way to promote stabilization of anthocyanins. Common organic acids include malonic acid, acetic acid, malic acid, caffeic acid, ferulic acid, gallic acid, sinapic acid and *p*-coumaric acid [70]. He et al. [71] elucidated the mechanism of co-pigmentation between *Vitis amurensis* Rupr. anthocyanins (0.1 $mg\cdot ml^{-1}$) and organic acids (0.87 $mg\cdot ml^{-1}$, ferulic acid : D-gluconic acid : caffeic acid : vanillic acid = 1.5 : 2.5 : 2.5 : 0.5, w/w/w/w) promoted by high hydrostatic pressure (*HHP*; 300 MPa, 2 min). Research on *HHP* co-pigmentation showed that the anthocyanin derivatives are newly formed owing to appropriate modifications that increases the co-pigmentation rate (42.1 %), photo-thermal stability and potential antioxidant activities in vivo and in vitro.

Tab. 1. Biological activities and improving effects on human health of anthocyanins.

Source	*TAC* [mg·kg-1]	Anthocyanin	Ratio [%]	Activity	Ref.
Fruits					
Blackcurrant	2 780–5 702 (FW)	Delphinidin-3-rutinoside	55.4–31.1	Antioxidant	[12]
		Cyanidin-3-rutinoside	69.7–26.4		
		Delphinidin-3-glucoside	35.0–16.2		
		Cyanidin-3-glucoside	15.5		
	–	–	–	Anti-inflammatory	[13]
	–	–	–	Bacteriostatic	[14]
	–	–	–	Anticancer	[15]
	–	–	–	Anti-diabetes	
	–	–	–	Anti-obesity	
Mulberry	257–5 697 (FW)	Cyanidin-3-glucoside	65.7	Antioxidant	[16, 17]
		Cyanidin-3-rutinoside	27.2		
		Delphinidin-3-rutinoside	1.8		
	–	–	–	Anticancer	[18]
	–	–	–	Protection of organs	[19]
	–	–	–	Anti-diabetes	[20]
	–	–	–	Anti-obesity	[21]
Blueberry	1 080–3 000 (FW)	Malvidin (malvidin-3-galactoside, malvidin-3-glucoside)	41.0	Antioxidant	[22]
		Delphinidin (delphinidin-3-galactoside)	33.1		
		Petunidin	17.3		
	–	–	–	Anti-inflammatory	[13]
	–	–	–	Bacteriostatic	[4]
	–	–	–	Anticancer	[23]
	–	–	–	Protection organs	[24]
	–	–	–	Anti-diabetes	[25]
	–	–	–	Anti-obesity	[25]
	–	–	–	Vision protection	[26]
	–	–	–	Improvement of neurodegenerative diseases	[25]
Grape	680–2 210 (FW)	Malvidin (malvidin-3-glucoside, malvidin-3,5-diglucoside)	88.8	Antioxidant	[27, 28]
		Peonidin (peonidin-3-glucoside, peonidin-3,5-diglucoside)	12.0–62.5		
		Cyanidin (cyanidin-3,5-diglucoside)	8.7–60.0		
	–	–	–	Anticancer	[29]
	–	–	–	Bacteriostatic	[28]
	–	–	–	Improvement of neurodegenerative diseases	[30]
Raspberry	137–1 776 (FW)	Cyanidin-3-sophoroside	59.9	Antioxidant	[11]
		Cyanidin-3-O-(2''-O-glucosyl) rutinoside	19.2	Anti-inflammatory	
		Cyanidin-3-glucoside	12.6	Anticancer	
		Cyanidin-3-rutinoside	7.0	–	[11]
	–	–	–	Anti-diabetes	[31]
Cherry	545–1 714 (FW)	Cyanidin-3-glucosylrutinoside	42.0	Antioxidant	[32, 33]
		Cyanidin-3-rutinoside	35.4		
		Peonidin-3-rutinoside	5.2		
		Peonidin-3-glucoside	0.9		
		Cyanidin-3-glucoside	0.4		
		Cyanidin-3-sophoroside	0.4		
	–	–	–	Anti-inflammatory	[32]
	–	–	–	Anticancer	[32]
	–	–	–	Bacteriostatic	[34]
	–	–	–	Protection organs	[32]

Tab. 1. *continued*

Source	*TAC* [mg·kg⁻¹]	Anthocyanin	Ratio [%]	Activity	Ref.
Cherry	–	–	–	Anti-diabetes	[32]
	–	–	–	Anti-obesity	[32]
	–	–	–	Improvement of neurodegenerative diseases	[32]
Blackberry	1 070–1 240 (FW)	Cyanidin-3-glucoside	89	Antioxidant	[35, 36]
		Cyanidin-3-dioxaloylglucoside	7.5		
		Cyanidin-3-malonylglucoside	2.7		
		Cyanidin-3-xyloside	0.9		
		Cyanidin-3-rutinoside	0.2		
	–	–	–	Anti-inflammatory	[35]
	–	–	–	Anticancer	[37]
	–	–	–	Anti-diabetes	[38]
	–	–	–	Anti-obesity	
Strawberry	157–276 (FW)	Pelargonidin-3-glucoside	80.0	Antioxidant	[39, 40]
		Pelargonidin-3-rutinoside	6.0	Anti-inflammatory	
		Cyanidin-3-glucoside	3.8	Anticancer	
Sugarcane	11–132 (DW)	Cyanidin-3-glucoside	0–72.4	Antioxidant	[41]
		Malvidin-3-*p*-coumaroyl-rhamnoside-5-glucoside	0–72.0		
		Cyanidin-3,5-diglucoside	9.4–55.7		
		Cyanidin-3-caffeoyl-glucoside-5-glucoside	0–44.3		
		Malvidin-3-caffeoyl-glucoside	13.5		
Hawthorn	13–21 (FW)	Cyanidin-3-galactoside	76.9–86.5	Antioxidant	[42]
		Cyanidin-3-glucoside	9.2–11.5		
Cereals					
Black rice	416 920 (DW)	Cyanidin-3-glucoside	91.0	Antioxidant	[43, 44]
		Peonidin-3-glucoside	7.1		
		Cyanidin-3-rutinoside	0.9		
		Cyanidin-3,5-diglucoside	0.9		
	–	–	–	Anticancer	[45]
	–	–	–	Bacteriostatic	[46]
	–	–	–	Protection organs	[47]
	–	–	–	Improvement of neurodegenerative diseases	[48]
Purple wheat	442–22 127 (DW)	Cyanidin-3-glucoside	27.4–45.8	Antioxidant	[49]
		Cyanidin-3-(6-malonyl glucoside)	19.2–35.3		
		Cyanidin-3-rutinoside	6.5–20.0		
		Peonidin-3-glucoside	6.4–20.2		
		Peonidin-3-(6-malonylglucoside)	4.3–4.4		
	–	–	–	Anticancer	[29]
Purple corn	391–4743 (DW)	Cyanidin-3-glucoside	37.1	–	[50, 51]
		Cyanidin-3-(6’’-malonylglucoside)	29.4		
		Peonidin-3-glucoside	8.2		
		Delphinidin-3-glucoside-5-rhamnoside	8.0		
		Pelargonidin-3-glucoside	6.6		
		Pelargonidin-3-(6’’-malonylglucoside)	5.9		
	–	–	–	Anti-inflammatory	[52]
	–	–	–	Anticancer	[51]
	–	–	–	Protection organs	[53]
Black bean	1 700–2 500 (DW)	Petunidin-3-glucoside	40.0–56.0	Anti-diabetes	[54, 55]
		Delphinidin-3-glucoside	34.0		
		Petunidin-3-glycoside	29.0		
		Malvidin-3-glucoside	10.0–24.0		

Tab. 1. *continued*

Source	*TAC* [mg·kg-1]	Anthocyanin	Ratio [%]	Activity	Ref.
Black bean		Pelargonidin	6.0		
	–	–	–	Antioxidant	[56]
	–	–	–	Anti-inflammatory	[56]
	–	–	–	Anticancer	
	–	–	–	Anti-obesity	
	–	–	–	Vision protection	[57]
	–	–	–	Improvement of neurodegenerative diseases	[58]
Purple sweet potato	804–1 459 (DW)	Cyanidin-3-caffeoyl-*p*-hydroxybenzoylsophoroside-5-glucoside	4.3–43.3	Antioxidant	[59]
		Peonidin-3-caffeoyl-*p*-hydroxybenzoylsophoroside-5-glucoside	5.0–27.7		
		Cyanidin-3-(6''-caffeoyl sophoroside)-5-glucoside	1.4–26.8	Anti-diabetes	
		Peonidin-3-p-hydroxybenzoyl sophoroside-5-glucoside	1.5–22.2		
	–	–	–	Anti-inflammatory	[60]
	–	–	–	Protection organs	[6]
	–	–	–	Improvement of neurodegenerative diseases	[60]
Vegetables					
Red cabbage	770–3 220 (FW)	Cyanidin-3-diglucoside-5-glucoside	20.0–23.0	Antioxidant	[61]
		Cyanidin-3-(sinapoyl) (sinapoyl)-diglucoside-5-glucoside	11.2		
		Cyanidin-3-(*p*-coumaroyl)-diglucoside-5-glucoside	8.2	Antioxidant	[61]
		Cyanidin-3-(feruloyl) (sinapoyl)-diglucoside-5-glucoside	7.8		
		Cyanidin-3-(sinapoyl)-diglucoside-5-glucoside	7.8		
	–	–	–	Anti-inflammatory	[62]
	–	–	–	Anticancer	[61]
	–	–	–	Bacteriostatic	[34]
Eggplant	658–857 (FW)	Delphinidin-3-[(4''-*p*-coumaroyl)-rhamnosyl (1→6) glucoside]-5-glucoside	69.1–87.7	Antioxidant	[63, 64]
		Delphinidin-3-glucoside	–	Anticancer	
		Delphinidin-3-rutinoside	–		
Others					
Lycium ruthenicum	147 430 (FW)	Petunidin (petunidin-3-glucoside)	63.6	Antioxidant	[65, 66]
		Delphinidin (delphinidin-3-glucoside)	31.4	Anti-inflammatory	

TAC – total anthocyanins content, expressed per kilogram of fresh weight (FW) or dry weight (DW).
Ratio represent proportion in total anthocyanin content.
(–) – no data.

Biological activities

Anthocyanins from various sources have different structures, so there are some differences in biological activities and beneficial effects on human health (Tab. 1).

Antioxidant activity

Excessive free radicals in human body can induce oxidation of lipids, proteins, DNA, RNA and sugars, and even cause cancer, neurodegenerative diseases and autoimmune diseases, which threat human health [1, 13]. Antioxidation refers to an oxidation reaction that effectively inhibits free radicals to restore the dynamic balance of free radicals in human body. Anthocyanins currently belong to the most effective natural antioxidants and free radical scavengers, their ability to scavenge free radicals being 30–50 times higher than that of vitamin C or vitamin E [2]. Studies showed that the antioxidant activities of anthocyanins are closely related to their structural characteristics, including the species of anthocyanins, the positions and quantities of glycosylation or glycosyl acylation [10], as well as the scavenging activities of six anthocyanins against superoxide free radicals. The order of scavenging activity of superoxide free radicals was found to be delphinidin > petunidin > cyanidin > malvidin > peonidin > pelargonidin [41, 72].

Zhao et al. [41] characterized and quantified anthocyanins in the epidermis of three sugarcane varieties, including ROC 22, Guitang 21 and Haitang 22. The results showed that *TAC* of ROC 22 was 110.6 ± 3.1 mg·kg^{-1}·DW. This variety mainly contains Cy3G and cyanidin-3,5-diglucoside (Cy3,5G), accounting for 97 % of *TAC*. *TAC* of Guitang 21 was as high as 132.0 ± 4.8 mg·kg^{-1}·DW, with malvidin-3-p-coumaroyl-rhamnoside-5-glucoside (72.0 %) as the dominant component. *TAC* of Haitang 22 was only 10.8 ± 1.4 mg·kg^{-1}·DW, this variety mainly containing Cy3,5G and cyanidin-3-caffeoyl-glucoside-5-glucoside. By comparing the antioxidant activity indexes of anthocyanins it was found that ROC 22 had the highest total antioxidant activity, followed by Guitang 21 and the lowest was Haitang 22. The comparison of ROC 22 and Haitang 22 showed that the anthocyanin antioxidant activity was positively correlated with the content. ROC 22 and Guitang 21 showed that the antioxidant activity of cyanidins was stronger than that of malvidins.

Jing et al. [63] evaluated the scavenging ability of reactive oxygen species (ROS) of delphinidin-3-[(4”-trans-p-coumaroyl)-rhamnosyl (1→6) glucoside]-5-glucoside (also known as nasunin) extracted from eggplant peel and delphinidin-3-glucoside (Dp3G), delphinidin-3-rutinoside (Dp3R), delphinidin-3-sambubioside, delphinidin-3,5-diglucoside (Dp3,5G) and delphinidin-3-rutinoside-5-glucoside from market standard products in HT-29 and HCT-116 cell lines. It was found that Dp3G, 3-sambubioside and 3-rutinoside glycosylated on C3 position had higher ROS clearance rate than Dp3,5G and delphinidin-3-rutinoside-5-glucoside glycosylated both on C3 and C5 positions, while nasunin had the lowest ROS clearance rate. The results showed that delphinidin derivatives glycosylated only on C3 had higher ROS-scavenging activity than those glycosylated on both C3 and C5. He et al. [71] showed that high hydrostatic pressure can promote rapid formation of stabilized anthocyanins from anthocyanins and organic acids, thereby enhancing the photo-thermal stability of anthocyanins and exhibiting satisfactory antioxidant activity in vivo and in vitro.

Anti-inflammatory activity

Inflammation is caused by proinflammatory cytokines and mediators in human body. Reducing the secretion of proinflammatory cytokines can be used to treat inflammation and related diseases such as rheumatoid arthritis, atherosclerosis, glomerulonephritis, gastroenteritis and others. As an anti-inflammatory factor, anthocyanins can inhibit inflammation by reducing the expression of inflammatory cytokines interleukin 6 (IL-6) and interleukin-1β (IL-1β) [3].

Zhang et al. [66] gavaged gouty arthritis model rats induced by monosodium uric with anthocyanins extract from *Lycium barbarum* and Pt3G standard. The results showed that 200 mg·kg^{-1} anthocyanins extract and 40 mg·kg^{-1} Pt3G could significantly reduce the levels of tumor necrosis factor-α (TNF-α), cyclooxygenase-1, IL-1β, interleukin-18 (IL-18), and prostaglandin E2 in serum, which indicates that anthocyanins extract and Pt3G had anti-inflammatory effects. Duarte et al. [40] gavaged pleurisy model mice using various doses of strawberry anthocyanins extract and Pg3G monomer. The results indicated that anthocyanins can treat inflammation by reducing total leukocyte influx, neutrophil migration to the pleural cavity, myeloperoxidase, adenosine deaminase activities, nitric oxide, TNF-α, IL-6 levels, and the therapeutic effect is dose-dependent. The treatment effect of 10 mg·kg^{-1} Pg3G was better than of 400 mg·kg^{-1} strawberry anthocyanins extract, which indicates that Pg3G had better anti-inflammatory effect than the crude extract. Lee et al. [13] found that blueberry, blackberry and blackcurrant anthocyanins extracts can play an anti-inflammatory role by reducing the level of

IL-1β mRNA, markedly attenuating LPS-induced nuclear factor κB (NF-κB) p65 translocation to the nucleus, and inhibiting the expression and secretion of pro-inflammatory factors.

Bacteriostatic activity

Anthocyanins can inhibit a variety of bacteria such as *Listeria monocytogenes*, *Staphylococcus aureus*, *Salmonella enteritidis* or *Vibrio parahaemolyticus*, which are causative agents of food-borne diseases. Kim et al. [46] showed that the black rice anthocyanins extract mainly containing Cy3G can reduce the degree of Helicobacter pylori infection in Mongolian gerbils and can have certain bacteriostatic effect. The bacteriostatic effect of 50 mg·kg^{-1} was significantly stronger than that of 10 mg·kg^{-1}, indicating that the bacteriostatic effect was positively correlated with the dosage. Sun et al. [4] found that blueberry anthocyanins can enter the cell inner membrane, reduce the activities of alkaline phosphatase, adenosine triphosphatase (ATPase) and superoxide dismutase (SOD) in *L. monocytogenes, Staph. aureus, S. enteritidis* and *V. parahaemolyticus*, hinder the transfer of information and energy, or control the self-protection ability of pathogens to express bacteriostasis. Demirdöven et al. [34] determined that the anthocyanins from red cabbage and sour cherry pomace had good bacteriostatic properties by detecting the minimum inhibitory concentrations regarding *Escherichia coli, Staph. aureus, L. monocytogenes, S.* Typhimurium and *Bacillus cereus*.

ACTIVITIES ON HUMAN HEALTH

Anti-cancer activity

Cancer cells can quickly invade the surrounding healthy tissues and proliferate in large numbers, causing a fatal threat to human body [73]. Anthocyanins can inhibit cancer cells by inhibiting cell invasion, resisting cell proliferation and promoting cell apoptosis. It was found that the anti-cancer effects of anthocyanins from various sources are closely related to their species and glycosylation positions.

Chen et al. [18, 45] studied the inhibitory effects of black rice and mulberry anthocyanins on the invasion of human hepatocellular carcinoma cells (SKHep-1) and human lung cancer cells (A549). The results indicated that Cy3G and peonidin-3-glucoside (Pn3G) from black rice had anticancer effect by inhibiting SKHep-1 cell invasion and motility, together with reducing secretion of matrix metalloproteinase-9 and urokinase-type plasminogen activator (u-PA), which were dose-dependent on anthocyanins. Among them, Pn3G inhibited cell motility and invasion only at > 100 μmol·l^{-1}, while the effective concentration of Cy3G was 50 μmol·l^{-1}, suggesting that the anticancer effect of cyanidins was stronger than that of peonidins. Cy3G and cyanidin-3-rutinoside (Cy3R) from mulberry were found to play the anticancer role by inhibiting A549 cell invasion and motility, reducing the activity of u-PA and matrix metalloproteinase-2, together with activating NF-κB and c-Jun. Studies showed that Cy3G can inhibit cell-collagen interactions, but Cy3R had no such effect. Research showed that various anthocyanins glycosylated at the C3 position had different anticancer effects. Mazewski et al. [29] evaluated the antiproliferative effect on human colorectal cancer cells HCT-116 and HT-29 using Pn3G, Cy3G and Pg3G. Among them, Cy3G and Pn3G had a good antiproliferative effect in a dose-dependent manner, but Pg3G had no inhibitory effect. This indicated that the inhibitory effects of cyanidins and peonidins are significantly higher than pelargonidins.

Anthocyanins and organs injury

Liver is an important detoxification organ in human body. A large number of studies showed that anthocyanins can protect alcoholic-induced liver fibrosis by improving energy metabolism and adenosine 5'-monophosphate (AMP)-activated protein kinase (AMPK) autophagy signal pathway. Anthocyanins can also reduce liver oxidative stress and inflammatory cytokines to decrease liver fibrosis, which have a good protective effect on liver injury [6]. Relevant reports indicated that the protective effect of anthocyanins on liver may be closely related to the structure and content of anthocyanins.

Wan et al. [19] gavaged ethanol-mediated high-fat diet model mice with 200 mg·kg^{-1}·body weight (BW) Cy3G from mulberry. The results indicated that Cy3G improved chronic alcoholic liver injury by increasing AMPK phosphorylation and autophagy, together with improving energy metabolism. Chen et al. [74] showed that the main components of blueberry anthocyanins, including malvidin-3-galactoside, Dp3R and Cy3G, can protect human embryonic-liver cells by reducing oxidative stress injury caused by CCl4 metabolism, inhibiting mitochondrial swelling and caspase-3 activation, together with blocking cell apoptosis. They could also effectively protect the liver by promoting cell proliferation. Studies showed that, within the experimental range (2.5–10 mg·l^{-1}), the hepatoprotective effect was directly proportional to the concentration of anthocyanins. Hou et al.

[47] gavaged black rice anthocyanins at various doses to model mice induced by CCl4, and the results showed that anthocyanins reduced liver injury in a dose-dependent manner by reducing aminotransferase activity in serum and enhancing SOD as well as glutathione peroxidase (GPx) activities. Cy3G showed much stronger hepatoprotective activity than Pn3G at the same concentration, indicating that cyanidins have stronger hepatoprotective effect than peonidins.

Anthocyanins also showed protective effects on kidney and lung injury. Popović et al. [24] showed that blueberry anthocyanins could significantly reduce the consumption of antioxidant enzymes (catalase (CAT), peroxidase, SOD, GPx, glutathione S-transferase, glutathione reductase, glutathione), and the damage of proximal and distal renal tubules in CCl4-induced acute renal injury model rats. This strong antioxidant activity was attributed to the presence of hydrogen atoms on Dp3G, which are hydroxyl-unstable and highly active free radicals. Liu et al. [75] gavaged radiation-induced lung injury model rats with blueberry anthocyanins. It was found that blueberry anthocyanins can improve lung injury by ameliorating radiation-induced anti-obesity, lung/body weight ratio, radiation-induced lung inflammation and lung collagen deposition. In vitro, anthocyanins protect cells from radiation-induced death by regulating the expression of B-cell lymphoma-2, Bax and caspase-3.

Anthocyanins and diabetes

Diabetes is a metabolic disease characterized by hyperglycemia. Long-term hyperglycemia can lead to chronic damage and dysfunction of kidney, heart, blood vessel, nerve and other tissues, threatening human health. Anthocyanins can prevent diabetes and improve related complications by enhancing glycogen content in cells, glucose uptake and consumption, regulating insulin secretion, reducing insulin resistance or increasing insulin secretion [20]. Comprehensive studies showed that the antidiabetic function of anthocyanins is related to the species and their different glycosyl acylation positions, while the effect is dose-dependent.

Chen et al. [76] studied anthocyanins extract from black soybean seed coat and found that Cy3G monomer can enhance the ability of glucose uptake in skeletal muscle cells of L6 rats by activating protein kinase B/glucose transporter protein 4 (Akt/GLUT4) signal pathway. In 150 $\mu g \cdot ml^{-1}$ anthocyanins extract and 40 $\mu mol \cdot l^{-1}$ (approximately 20 $\mu g \cdot ml^{-1}$) Cy3G treatment groups, the uptake level of fluorescent glucose analogue (2-NBDG) increased 1.81-times and 1.90-times, respectively (compared with the control group), which indicated that Cy3G has better antidiabetic function than a crude extract. Yan et al. [20] treated HepG2 cell model induced by high sugar and palmitic acid with mulberry anthocyanins. The results showed that anthocyanins can play an antidiabetic role by alleviating insulin resistance, increasing glycogen content in cells, glucose consumption and uptake. The increase of glucose consumption in 50 $\mu g \cdot ml^{-1}$ and 250 $\mu g \cdot ml^{-1}$ groups was 18.8 % and 31.8 %, respectively, which indicates that the antidiabetic function was positively correlated with anthocyanins dosage.

Jang et al. [59] compared the effects of purple sweet potato anthocyanins (cyanidin-3-caffeoyl-*p*-hydroxybenzoyl-sophoroside-5-glucoside (PEAK9), peonidin-3-caffeoyl sophoroside-5-glucoside (PEAK11) and peonidin-3-(6''-caffeoyl-6'''-feruloyl sophoroside)-5-glucoside (PEAK14)) on glucose production in HepG2 cells. The results showed that the lowering effect on glucose production was PEAK9 > PEAK11 > PEAK14, which indicated that cyanidins have better hypoglycemic effect than peonidins. The comparison of PEAK11 and PEAK14 showed that different glycosyl acylation forms on C3 have different hypoglycemic effects. PEAK9 and PEAK14 were administered intragastrically to hyperglycemia model mice. PEAK9 reduced blood glucose and had antidiabetic effects by inhibiting liver glucose output and expressing strong free radical-scavenging activity, but PEAK14 had no obvious effect. Results further indicated that the antidiabetic function of cyanidins is higher than that of peonidins. The exact mechanism of anthocyanins-mediated insulin secretion, regulation of β cells and maintenance of glucose homeostasis, as well as the antidiabetic mechanism of anthocyanins monomer as well as its metabolic transformation and absorption, need to be further studied.

Anthocyanins and obesity

According to the Lancet Obesity Commission, obesity is driving global growth in type 2 diabetes, cardiovascular diseases and multiple cancers [77]. It has been reported that anthocyanins can play a good anti-obesity role in vivo and in vitro by increasing energy consumption, inhibiting lipid absorption and food intake, and regulating lipid metabolism and intestinal microflora [7], which are related to the structure and content of anthocyanins in food.

Matsukawa et al. [78] treated 3T3-L1 adipocytes with Cy3G, which prevented obesity by regulating lipid metabolism. The results showed that the regulation effects of anthocyanins on lipid metabolism were achieved by increasing the expression of UCP-1, PGC-1α and C/EBPβ, enhancing the content of multilocular lipid droplets, mitochondria and beige adipocytes, and promoting the differentiation of preadipocytes. The anti-obesity effect of 100 $\mu mol \cdot l^{-1}$ anthocyanins was significantly stronger than 50 $\mu mol \cdot l^{-1}$, indicating that the anti-obesity effects of Cy3G are positively correlated with its dose.

YOU et al. [21] treated BAT-cMyc cells with Cy3G and Cy3R from mulberry, which showed that anthocyanins can promote carbohydrate and fat metabolism by improving mitochondrial function and increasing the number of mitochondria in brown adipose tissue. Cy3G and Cy3R had different effects on tumor suppressor genes (C/EBPα, C/EBPβ) and adipogenesis regulator (PPARγ) in BAT-cMyc cells. Cy3G significantly enhanced the expression of C/EBPα gene, but Cy3R did not. Cy3R significantly increased the expression of C/EBPβ gene, but Cy3G did not. The protein expression levels of PPARγ2 in Cy3G and Cy3R groups increased 2.17- and 2.28-times, respectively. This might be due to different effects of anthocyanins with different glycoside ligands. Therefore, their mechanism of action regarding effects on obesity needs to be further studied.

Anthocyanins and eye diseases

Studies have confirmed that anthocyanins have a strong antioxidant effect, which can help eliminate toxic chemicals and free radicals in the retina, thereby protecting vision and eyes [26]. LEE et al. [79] used anthocyanins from *Vaccinium uliginosum* L. to treat blue light-induced retinal pigment epithelial cells loaded with photosensitizers. The results showed that anthocyanins could reduce blue light damage to cells through antioxidant effects and improve the state of damaged cells by inhibiting oxidation of photosensitizers, thereby reducing cell death. SONG et al. [26] fed blueberry anthocyanins to diabetic model rats (20, 40, 80 $mg \cdot kg^{-1}$). The results showed that anthocyanins increased the activity of glutathione and GPx, and reduced malondialdehyde and ROS levels in a dose-dependent manner, thereby improving the antioxidant capacity of the retina. They could also up-regulate IL-1β and vascular endothelial growth factor to exert anti-inflammatory function and protect retinal cells from diabetes-induced damage. PAIK et al. [57] fed retinal degeneration model rats (50 $mg \cdot kg^{-1}$) with anthocyanins from black soybeans seed coat. The results indicated that anthocyanins can reduce the structural and functional damage of rat retinal neurons. The also had anti-inflammatory effects and protected retinal photoreceptors by inhibiting inflammation, thereby preventing retinal degeneration.

Anthocyanins and neurodegenerative diseases

With the aging of the world's population and the growth of life pressure, the incidence of neurodegenerative diseases is increasing year by year, and the affected population is becoming younger, mainly including Alzheimer's disease, vascular dementia and sleep deprivation cognitive impairment. There is no effective treatment available for neurodegenerative diseases. It was reported that anthocyanins can improve cognitive impairment caused by neurodegenerative diseases by regulating oxidative stress in neurons, inhibiting neuroinflammation and improving vascular function [8].

PACHECO et al. [30] gavaged 200 $mg \cdot kg^{-1}$ grape skin anthocyanins to sporadic dementia of Alzheimer's type rats induced by streptozotocin. The results indicated that anthocyanins can reduce memory impairment by improving oxidative damage in brain together with restoring the activity of acetylcholinesterase and Na^{+}-K^{+}-ATPase ion pump in model rats, as well as by enhancing the level of antioxidant enzymes (SOD, CAT and GPx). THUMMAYOT et al. [80] found that Cy3G can reduce neurotoxicity of Aβ25-35-induced human neuroblastoma cells by decreasing cell viability, intracellular ROS production and intracellular calcium release, together with reducing the expression levels of calpain and cleaved caspase-12. The mechanism of anthocyanins at improving neurodegenerative diseases needs a lot of further research.

CONCLUSION

The structure and content of anthocyanins in fruits, cereals and vegetables are reviewed. Most of anthocyanins in plants are mainly cyanidins and Cy3G is the main structure. Certainly, anthocyanins content and structure are affected by various factors such as plant variety, production region or climate. There is an interesting phenomenon that the natural formation of anthocyanins requires light, while the formation mechanism of anthocyanins in the absence of light, such as in case of purple potato, black rice or purple corn, remains to be studied. Co-pigmentation can improve stability and antioxidant activity of anthocyanins. The effect of structure and content of anthocyanins and co-pigments, pH, temperature, pressure and other factors on the co-pigmentation effect, the mechanism of stabilization and the bioactivity of the stabilized anthocyanins need to be studied.

The relationship between anthocyanin structure, biological activities and disease improvement is discussed. Anthocyanins have dose-dependent antioxidant, anti-inflammatory and bacteriostatic effects, playing a role in improving cancer, diabetes, obesity and eye diseases. The antioxidant activities of anthocyanins decrease in an order of delphinidin > petunidin > cyanidin > malvidin > peonidin > pelargonidin, and the antioxidant activity of anthocyanins glycosylated only on C3 position is higher than that of anthocyanins glycosylated on both C3 and C5 positions. The anticancer effects of cyanidins and peonidins are stronger than those of malvidins, and the hepatoprotective and antidiabetic effects of cyanidins are stronger than those of peonidins. The anticancer and anti-obesity effects of various anthocyanins glycosylated on C3 position are different. At present, some achievements have been made in the research of anthocyanins. However, the research on the molecular structure of anthocyanins and the mechanism by which they exert their biological activities such as anticancer, anti-diabetes, anti-inflammation and improving neurodegenerative diseases still needs to be further explored. In addition, in-depth research on the biological activities of stabilized anthocyanins and their protective effects on human health is required. Although anthocyanins are ubiquitous in fruits and vegetables, the content of anthocyanins digested by human body is low, which cannot achieve the effective concentration of biological activity. Therefore, the metabolism of anthocyanins and improvement of their bioavailability need to be further explored. Solution of the above problems will promote further development and application of anthocyanins.

Abbreviations

Cy3G – cyanidin-3-glucoside; *TAC* – total anthocyanins content; Pg3G – pelargonidin-3-glucoside; Pt3G – petunidin-3-glucoside; Cy3,5G – cyanidin-3,5-diglucoside; ROS – reactive oxygen species; Dp3G – delphinidin-3-glucoside; Dp3R – delphinidin-3-rutinoside; Dp3,5G – delphinidin-3,5-diglucoside; HT-29 and HCT-116 – human colon cancer cell lines; IL-6 – interleukin 6; IL-1β – interleukin-1β; TNF-α: tumor necrosis factor-α; IL-18 – interleukin-18; LPS – lipopolysaccharide; NF-κB – nuclear factor κB; ATPase – adenosine triphosphatase; SOD – superoxide dismutase; SKHep-1 – human hepatocellular carcinoma cells; A549 – human lung cancer cells; Pn3G – peonidin-3-glucosid; u-PA – urokinase-type plasminogen activator; Cy3R – cyanidin-3-rutinoside; AMP – adenosine 5'-monophosphate; AMPK – activated protein kinase; CAT – catalase; GPx – glutathione peroxidase; Akt/GLUT4 – Protein Kinase B/glucose transporter protein 4, 2-NBDG – 2-[N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl) amino]-2-deoxy-D-glucose; HepG2 – hcuman hepatoellular carcinomas,; PEAK9 – cyanidin-3-caffeoyl-p-hydroxybenzoyl-sophoroside-5-glucoside; PEAK11 – peonidin-3-caffeoyl sophoroside-5-glucoside; PEAK14 – peonidin-3-(6"-caffeoyl-6"'-feruloyl sophoroside)-5-glucoside; UCP-1 – uncoupling protein-1; PGC-1α – peroxisome proliferator-activated receptor-γ coactivator-1α; C/EBPβ – CCAAT/enhancer binding protein β; BAT-cMyc cells – one type of mouse primary immortalized brown adipocyte; C/EBPα – CCAAT/enhancer binding protein α; PPARγ – peroxisome proliferator-activated receptor γ; Aβ25-35: amyloid β-protein 25-35.

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REFERENCES

1. Gowd, V. – Ji, Z. – Chen, W.: Anthocyanins as promising molecules and dietary bioactive components against diabetes – A review of recent advances. Trends in Food Science and Technolgy, *68*, 2017, pp. 1–13. DOI: 10.1016/j.tifs.2017.07.015.
2. Mendoza-Wilson, A. M – Castro-Arredondo, S. I. – Balandrán-Quintana, R. R.: Computational study of the structure – free radical scavenging relationship of procyanidins. Food Chemistry, *161*, 2014, pp. 155–161. DOI: 10.1016/j.foodchem.2014.03.111.
3. Aboonabi, A. – Singh, I. – Meyer, R. R.: Cytoprotective effects of berry anthocyanins against induced oxidative stress and inflammation in primary human diabetic aortic endothelial cells. Chemico-Biological Interactions, *317*, 2020, article 108940. DOI: 10.1016/j.cbi.2020.108940.
4. Sun, X. – Zhou, T. – Wei, C. – Lan, W. – Zhao, Y. – Pan, Y. – Wu, V. C. H.: Antibacterial effect and mechanism of anthocyanin rich Chinese wild blueberry extract on various foodborne pathogens. Food Control, *94*, 2018, pp. 155–161. DOI: 10.1016/j.foodcont.2018.07.012.
5. Mazewski, C. – Liang, K. – de Mejia, E. G.: Inhibitory potential of anthocyanin-rich purple and red corn extracts on human colorectal cancer cell proliferation in vitro. Journal of Functional Foods, *34*,

2017, pp. 254–265. DOI: 10.1016/j.jff.2017.04.038.
6. Cai, Z. – Song, L. – Qian, B. – Xu, W. – Ren, J. – Jing, P. – Oey, I.: Understanding the effect of anthocyanins extracted from purple sweet potatoes on alcohol-induced liver injury in mice. Food Chemistry, *245*, 2018, pp. 463–470. DOI: 10.1016/j.foodchem.2017.10.119.
7. Xie, L. – Su, H. – Sun, C. – Zheng, X. – Chen, W.: Recent advances in understanding the anti-obesity activity of anthocyanins and their biosynthesis in microorganisms. Trends in Food Science and Technology, *72*, 2018, pp. 13–24. DOI: 10.1016/j.tifs.2017.12.002.
8. dos Santos, N. M. – Batista, P. B. – Batista, Â. G. – Júnior, M. R. M.: Current evidence on cognitive improvement and neuroprotection promoted by anthocyanins. Current Opinion in Food Science, *26*, 2019, pp. 71–78. DOI: 10.1016/j.cofs.2019.03.008.
9. Fang, J.: Classification of fruits based on anthocyanin types and relevance to their health effects. Nutrition, *31*, 2015, pp. 1301–1306. DOI: 10.1016/j.nut.2015.04.015.
10. Ali, H. M. – Almagribi, W. – Al-Rashidi, M. N.: Antiradical and reductant activities of anthocyanidins and anthocyanins, structure–activity relationship and synthesis. Food Chemistry, *194*. 2016, pp. 1275–1282. DOI: 10.1016/j.foodchem.2015.09.003.
11. Teng, H. – Fang, T. – Lin, Q. – Song, H. – Liu, B. – Chen, L.: Red raspberry and its anthocyanins: Bioactivity beyond antioxidant capacity. Trends in Food Science and Technology, *66*, 2017, pp. 153–165. DOI: 10.1016/j.tifs.2017.05.015.
12. Stanys, V. – Bendokas, V. – Rugienius, R. – Sasnauskas, A. – Frercks, B. – Mažeikienė, I. – Šikšnianas, T.: Management of anthocyanin amount and composition in genus *Ribes* using interspecific hybridization. Scientia Horticulturae, *247*, 2019, pp. 123–129. DOI: 10.1016/j.scienta.2018.12.014.
13. Lee, S. G. – Kim, B. – Yang, Y. – Pham, T. X. – Park, Y. K. – Manatou, J. – Koo, S. I. – Chun, O. K. – Lee, J. Y.: Berry anthocyanins suppress the expression and secretion of proinflammatory mediators in macrophages by inhibiting nuclear translocation of NF-κB independent of NRF2-mediated mechanism. Journal of Nutritional Biochemistry, *25*, 2014, pp. 404–411. DOI: 10.1016/j.jnutbio.2013.12.001.
14. Zhao, M. – Bai, J. – Bu, X. – Tang, Y. – Han, W. – Li, D. – Wang, L. – Yang, Y. – Xu, Y.: Microwave-assisted aqueous two-phase extraction of phenolic compounds from *Ribes nigrum* L. and its antibacterial effect on foodborne pathogens. Food Control, *119*, 2021, article 107449. DOI: 10.1016/j.foodcont.2020.107449.
15. Wu, G. – Hui, X. – Liang, J. – Liu, H. – Chen, H. – Gong, X. – Brennan, M. A. – Zeng, X. A. – Guo, X. – Brennan, C. S.: Combination of rehydrated whey protein isolate aqueous solution with blackcurrant concentrate and the formation of encapsulates via spray-drying and freeze-drying: Alterations to the functional properties of protein and their anticancer properties. Food Chemistry, *355*, 2021, article 129620. DOI: 10.1016/j.foodchem.2021.129620.
16. Farahani, M. – Salehi-Arjmand, H. – Khadivi, A. – Akramian, M.: Chemical characterization and antioxidant activities of *Morus alba* var. *nigra* fruits. Scientia Horticulturae, *253*, 2019, pp. 120–127. DOI: 10.1016/j.scienta.2019.04.040.
17. Khalifa, I. – Zhu, W. – Li, K. – Li, C.: Polyphenols of mulberry fruits as multifaceted compounds: Compositions, metabolism, health benefits, and stability – A structural review. Journal of Functional Foods, *40*, 2018, pp. 28–43. DOI: 10.1016/j.jff.2017.10.041.
18. Chen, P. N. – Chu, S. C. – Chiou, H. L. – Kuo, W. H. – Chiang, C. L. – Hsieh, Y. S.: Mulberry anthocyanins, cyanidin 3-rutinoside and cyanidin 3-glucoside, exhibited an inhibitory effect on the migration and invasion of a human lung cancer cell line. Cancer Letters, *235*, 2006, pp. 248–259. DOI: 10.1016/j.canlet.2005.04.033.
19. Wan, T. – Wang, S. – Ye, M. – Ling, W. – Yang, L.: Cyanidin-3-O-β-glucoside protects against liver fibrosis induced by alcohol via regulating energy homeostasis and AMPK/autophagy signaling pathway. Journal of Functional Foods, *37*, 2017, pp. 16–24. DOI: 10.1016/j.jff.2017.07.033.
20. Yan, F. – Dai, G. – Zheng, X.: Mulberry anthocyanin extract ameliorates insulin resistance by regulating PI3K/AKT pathway in HepG2 cells and db/db mice. Journal of Nutritional Biochemistry, *36*, 2016, pp. 68–80. DOI: 10.1016/j.jnutbio.2016.07.004.
21. You, Y. – Liang, C. – Han, X. – Guo, J. – Ren, C. – Liu, G. – Huang, W. – Zhan, J.: Mulberry anthocyanins, cyanidin 3-glucoside and cyanidin 3-rutinoside, increase the quantity of mitochondria during brown adipogenesis. Journal of Functional Foods, *36*, 2017, pp. 348–356. DOI: 10.1016/j.jff.2017.07.007.
22. Li, D. – Meng, X. – Li, B.: Profiling of anthocyanins from blueberries produced in China using HPLC-DAD-MS and exploratory analysis by principal component analysis. Journal of Food Composition and Analysis, *47*, 2016, pp. 1–7. DOI: 10.1016/j.jfca.2015.09.005.
23. Zhou, F. – Wang, T. – Zhang, B. – Zhao, H.: Addition of sucrose during the blueberry heating process is good or bad? Evaluating the changes of anthocyanins/anthocyanidins and the anticancer ability in HepG-2 cells. Food Research International, *107*, 2018, pp. 509–517. DOI: 10.1016/j.foodres.2018.02.071.
24. Popović, D. – Kocić, G. – Katić, V. – Jović, Z. – Zarubica, A. – Veličković, L.J. – Nikolić, V. – Jović, A. – Kundalić, B. – Rakić, V. – Ulrih, N. P. – Skrt, M. – Sokolović, D. – Dinić, L. – Stojanović, M. – Milosavljević, A. – Veličković, F. – Sokolović, D.: Protective effects of anthocyanins from bilberry extract in rats exposed to nephrotoxic effects of carbon tetrachloride. Chemico-Biological Interactions, *304*, 2019, pp. 61–72. DOI: 10.1016/j.cbi.2019.02.022.
25. Shao, X. – Zhao, B. – Wang, B. – Zhao, B. – Zhu, Y. – Yuan, Z. – Zhang, J.: Neuroprotective effects of blueberry anthocyanins against perfluorooctanoic sulfonate on planarian *Dugesia japonica*. Ecotoxicology and Environmental Safety, *175*, 2019, pp. 39–47. DOI: 10.1016/j.ecoenv.2019.03.023.

26. Song, Y. – Huang, L. – Yu, J.: Effects of blueberry anthocyanins on retinal oxidative stress and inflammation in diabetes through Nrf2/HO-1 signaling. Journal of Neuroimmunology, *301*, 2016, pp. 1–6. DOI: 10.1016/j.jneuroim.2016.11.001.
27. Pérez-Navarro, J. – Izquierdo-Cañas, P. M. – Mena-Morales, A. – Martínez-Gascueña, J. – Chacón-Vozmediano, J. L. – García-Romero, E. – Hermosín-Gutiérrez, I. – Gómez-Alonso, S.: Phenolic compounds profile of different berry parts from novel *Vitis vinifera* L. red grape genotypes and Tempranillo using HPLC-DAD-ESI-MS/MS: A varietal differentiation tool. Food Chemistry, *295*, 2019, pp. 350–360. DOI: 10.1016/j.foodchem.2019.05.137.
28. Trikas, E. D. – Melidou, M. – Papi, R. M. – Zachariadis, G. A. – Kyriakidis, D. A.: Extraction, separation and identification of anthocyanins from red wine by-product and their biological activities. Journal of Functional Foods, *25*, 2016, pp. 548–558. DOI: 10.1016/j.jff.2016.06.033.
29. Mazewski, C. – Liang, K. – de Mejia, E. G.: Comparison of the effect of chemical composition of anthocyanin-rich plant extracts on colon cancer cell proliferation and their potential mechanism of action using *in vitro, in silico*, and biochemical assays. Food Chemistry, *242*, 2018, pp. 378–388. DOI: 10.1016/j.foodchem.2017.09.086.
30. Pacheco, S. M. – Soares, M. S. P. – Gutierres, J. M. – Gerzson, M. F. B. – Carvalho, F. B. – Azambuja, J. H. – Schetinger, M. R. C. – Stefanello, F. M. – Spanevello, R. M.: Anthocyanins as a potential pharmacological agent to manage memory deficit, oxidative stress and alterations in ion pump activity induced by experimental sporadic dementia of Alzheimer's type. Journal of Nutritional Biochemistry, *56*, 2018, pp. 193–204. DOI: 10.1016/j.jnutbio.2018.02.014.
31. Noratto, G. D. – Chew, B. P. – Atienza, L. M.: Red raspberry (*Rubus idaeus* L.) intake decreases oxidative stress in obese diabetic (db/db) mice. Food Chemistry, *227*, 2017, pp. 305–314. DOI: 10.1016/j.foodchem.2017.01.097.
32. Blando, F. – Oomah, B. D.: Sweet and sour cherries: Origin, distribution, nutritional composition and health benefits. Trends in Food Science and Technology, *86*. 2019. pp. 517–529. DOI: 10.1016/j.tifs.2019.02.052.
33. Kirakosyan, A. – Gutierrez, E. – Solano, B. R. – Seymour, E. M. – Bolling, S. F.: The inhibitory potential of Montmorency tart cherry on key enzymes relevant to type 2 diabetes and cardiovascular disease. Food Chemistry, *252*, 2018, pp. 142–146. DOI: 10.1016/j.foodchem.2018.01.084.
34. Demirdöven, A. – Karabiyikli, Ş. – Tokatli, K. – Öncül, N.: Inhibitory effects of red cabbage and sour cherry pomace anthocyanin extracts on food borne pathogens and their antioxidant properties. LWT – Food Science and Technology, *63*, 2015, pp. 8–13. DOI: 10.1016/j.lwt.2015.03.101.
35. de Velde, F. V. – Grace, M. H. – Esposito, D. – Pirovani, M. É. – Lila, M. A.: Quantitative comparison of phytochemical profile, antioxidant, and anti-inflammatory properties of blackberry fruits adapted to Argentina. Journal of Food Composition and Analysis, *47*, 2016, pp. 82–91. DOI: 10.1016/j.jfca.2016.01.008.
36. Weber, F. – Boch, K. – Schieber, A.: Influence of copigmentation on the stability of spray dried anthocyanins from blackberry. LWT – Food Science and Technology, *75*, 2017, pp. 72–77. DOI: 10.1016/j.lwt.2016.08.042.
37. Shi, N. – Riedl, K. M. – Schwartz, S. J. – Zhang, X. – Clinton, S. K. – Mazewski, T.: Efficacy comparison of lyophilised black raspberries and combination of celecoxib and PBIT in prevention of carcinogen-induced oesophageal cancer in rats. Journal of Functional Foods, *27*, 2016, pp. 84–94. DOI: 10.1016/j.jff.2016.08.044.
38. Johnson, M. H. – Wallig, M. – Vital, D. A. L. – de Mejia, E. G.: Alcohol-free fermented blueberry–blackberry beverage phenolic extract attenuates diet-induced obesity and blood glucose in C57BL/6J mice. Journal of Nutritional Biochemistry, *31*, 2016, pp. 45–59. DOI: 10.1016/j.jnutbio.2015.12.013.
39. Chaves, V. C. – Calvete, E. – Reginatto, F. H.: Quality properties and antioxidant activity of seven strawberry (*Fragaria x ananassa* duch) cultivars. Scientia Horticulturae, *225*, 2017, pp. 293–298. DOI: 10.1016/j.scienta.2017.07.013.
40. Duarte, L. J. – Chaves, V. C. – dos Santos Nascimento, M. V. P. – Calvete, E. – Li, M. – Ciraolo, E. – Ghigo, A. – Hirsch, E. – Simões, C. M. O. – Reginatto, F. H. – Dalmarco, E. M.: Molecular mechanism of action of pelargonidin-3-O-glucoside, the main anthocyanin responsible for the anti-inflammatory effect of strawberry fruits. Food Chemistry, *247*, 2018, pp. 56–65. DOI: 10.1016/j.foodchem.2017.12.015.
41. Zhao, Z. – Yan, H. – Zheng, R. – Khan, M. S. – Fu, X. – Tao, Z. – Zhang, Z.: Anthocyanins characterization and antioxidant activities of sugarcane (*Saccharum officinarum* L.) rind extracts. Industrial Crops and Products, *113*, 2018, pp. 38–45. DOI: 10.1016/j.indcrop.2018.01.015.
42. Liu, S. – Chang, X. – Liu, X. – Shen, Z.: Effects of pretreatments on anthocyanin composition, phenolics contents and antioxidant capacities during fermentation of hawthorn (*Crataegus pinnatifida*) drink. Food Chemistry, *212*, 2016, pp. 87–95. DOI: 10.1016/j.foodchem.2016.05.146.
43. Hao, J. – Zhu, H. – Zhang, Z. – Yang, S. – Li, H.: Identification of anthocyanins in black rice (*Oryza sativa* L.) by UPLC/Q-TOF-MS and their in vitro and in vivo antioxidant activities. Journal of Cereal Science, *64*, 2015, pp. 92–99. DOI: 10.1016/j.jcs.2015.05.003.
44. Hou, Z. – Qin, P. – Zhang, Yan. – Cui, S. – Ren, G.: Identification of anthocyanins isolated from black rice (*Oryza sativa* L.) and their degradation kinetics. Food Research International, *50*, 2013, pp. 691–697. DOI: 10.1016/j.foodres.2011.07.037.
45. Chen, P. N. – Kuo, W. H. – Chiang, C. L. – Chiou, H. L. – Hsieh, Y. S. – Chu, S. C.: Black rice anthocyanins inhibit cancer cells invasion via repressions of MMPs and u-PA expression. Chemico-

Biological Interactions, *163*, 2006, pp. 218–229. DOI: 10.1016/j.cbi.2006.08.003.
46. Kim, S. H. – Woo, H. J. – Lee, M. H. – Park, M. – Nagendran, T. – Rhee, K. J. – Lee, D. – Jin, Y. B. – Choi, S. W. – Seo, W. D. – Kim, J. B.: Antimicrobial effects of black rice extract on *Helicobacter pylori* infection in Mongolian gerbil. Journal of Cereal Science, *85*, 2019, pp. 1–5. DOI: 10.1016/j.jcs.2018.11.002.
47. Hou, F. – Zhang, R. – Zhang, M. – Su, D. – Wei, Z. – Deng, Y. – Zhang, Y. – Chi, J. – Tang, X.: Hepatoprotective and antioxidant activity of anthocyanins in black rice bran on carbon tetrachloride-induced liver injury in mice. Journal of Functional Foods, *5*, 2013, pp. 1705–1713. DOI: 10.1016/j.jff.2013.07.015.
48. Vargas, C. G. – da Silva Junior, J. D. – Rabelo, T. K. – Moreira, J. C. F. – Gelain, D. P. – Rodrigues, E. – Augusti, P. R. – de Oliveira Rios, A. – Flôres, S. H.: Bioactive compounds and protective effect of red and black rice brans extracts in human neuron-like cells (SH-SY5Y). Food Research International, *113*, 2018, pp. 57–64. DOI: 10.1016/j.foodres.2018.06.069.
49. Abdel-Aal, E. S. M. – Hucl, P. – Rabalski, I.: Compositional and antioxidant properties of anthocyanin-rich products prepared from purple wheat. Food Chemistry, *254*, 2018, pp. 13–19. DOI: 10.1016/j.foodchem.2018.01.170.
50. Li, Q. – Somavat, P. – Singh, V. – Chatham, L. – de Mejia, E. G.: A comparative study of anthocyanin distribution in purple and blue corn coproducts from three conventional fractionation processes. Food Chemistry, *231*, 2017, pp. 332–339. DOI: 10.1016/j.foodchem.2017.03.146.
51. Wang, D. – Lei, Y. – Ma, Y. – Zhang, L. – Zhao, X.: Inhibition of ALV-A-induced apoptosis in DF-1 cells via inactivation of nuclear transcription factor κB by anthocyanins from purple corn (*Zea mays* L.). Journal of Functional Foods, *10*, 2014, pp. 274–282. DOI: 10.1016/j.jff.2014.06.022.
52. Chen, C. – Somavat, P. – Singh,V. – de Mejia, E. G.: Chemical characterization of proanthocyanidins in purple, blue, and red maize coproducts from different milling processes and their anti-inflammatory properties. Industrial Crops and Products, *109*, 2017, pp. 464–475. DOI: 10.1016/j.indcrop.2017.08.046.
53. Petroni, K. – Trinei, M. – Fornari, M. – Calvenzani, V. – Marinelli, A. – Micheli, L. A. – Pilu, R. – Matros, A. – Mock, H. P. – Tonelli, C. – Giorgio, M.: Dietary cyanidin 3-glucoside from purple corn ameliorates doxorubicin-induced cardiotoxicity in mice. Nutrition, Metabolism and Cardiovascular Diseases, *27*, 2017. pp. 462–469. DOI: 10.1016/j.numecd.2017.02.002.
54. Prietto, L. – Mirapalhete, T. C. – Pinto, V. Z. – Hoffmann, J. F. – Vanier, N. L. – Lim, L. T. – Dias, A. R. G. – da Rosa Zavareze, E.: pH-sensitive films containing anthocyanins extracted from black bean seed coat and red cabbage. LWT – Food Science and Technolog, *80*, 2017, pp. 492–500. DOI: 10.1016/j.lwt.2017.03.006.
55. Mojica, L. – Berhow, M. – de Mejia, E. G.: Black bean anthocyanin-rich extracts as food colorants: Physicochemical stability and antidiabetes potential. Food Chemistry, *229*, 2017, pp. 628–639. DOI: 10.1016/j.foodchem.2017.02.124.
56. Kim, S. Y. – Wi, H. R. – Choi, S. – Ha, T. J. – Lee, B. W. – Lee, M.: Inhibitory effect of anthocyanin-rich black soybean testa (*Glycine max* (L.) Merr.) on the inflammation-induced adipogenesis in a DIO mouse model. Journal of Functional Foods, *14*, 2015, pp. 623–633. DOI: 10.1016/j.jff.2015.02.030.
57. Paik, S. S. – Jeong, E. – Jung, S. W. – Ha, T. J. – Kang, S. – Sim, S. – Jeon, J. H. – Chun, M. H. – Kim I. B.: Anthocyanins from the seed coat of black soybean reduce retinal degeneration induced by N-methyl-N-nitrosourea. Experimental Eye Research, *97*, 2012, pp. 55–62. DOI: 10.1016/j.exer.2012.02.010.
58. Badshah, H. – Kim, T. H. – Kim, M. O.: Protective effects of anthocyanins against amyloid beta-induced neurotoxicity in vivo and in vitro. Neurochemistry International, *80*, 2015, pp. 51–59. DOI: 10.1016/j.neuint.2014.10.009.
59. Jang, H. H. – Kim, H. W. – Kim, S. Y. – Kim, S. M. – Kim, J. B. – Lee, Y. M.: In vitro and in vivo hypoglycemic effects of cyanidin 3-caffeoyl-p-hydroxybenzoylsophoroside-5-glucoside, an anthocyanin isolated from purple-fleshed sweet potato. Food Chemistry, *272*, 2019, pp. 688–693. DOI: 10.1016/j.foodchem.2018.08.010.
60. Shan, Q. – Zheng, Y. – Lu, J. – Zhang, Z. – Wu, D. – Fan, S. – Hu, B. – Cai, X. – Cai, H. – Liu, P. – Liu, F.: Purple sweet potato color ameliorates kidney damage via inhibiting oxidative stress mediated NLRP3 inflammasome activation in high fat diet mice. Food and Chemical Toxicology, *69*, 2014, pp. 339–346. DOI: 10.1016/j.fct.2014.04.033.
61. Wiczkowski, W. – Topolska, J. – Honke, J.: Anthocyanins profile and antioxidant capacity of red cabbages are influenced by genotype and vegetation period. Journal of Functional Foods, *7*, 2014, pp. 201–211. DOI: 10.1016/j.jff.2014.02.011.
62. Tong, T. – Niu, Y. H. – Yue, Y. – Wu, S. – Ding, H.: Beneficial effects of anthocyanins from red cabbage (*Brassica oleracea* L. var. *capitata* L.) administration to prevent irinotecan-induced mucositis. Journal of Functional Foods, *32*, 2017, pp. 9–17. DOI: 10.1016/j.jff.2017.01.051.
63. Jing, P. – Qian, B. – Zhao, S. – Qi, X. – Ye, L. – Giusti, M. M. – Wang, X.: Effect of glycosylation patterns of Chinese eggplant anthocyanins and other derivatives on antioxidant effectiveness in human colon cell lines. Food Chemistry, *172*, 2015, pp. 183–189. DOI: 10.1016/j.foodchem.2014.08.100.
64. Todaro, A. – Cimino, F. – Rapisarda, P. – Catalano, A. E. – Barbagallo, R. N. – Spagna, G.: Recovery of anthocyanins from eggplant peel. Food Chemistry, *114*, 2009, pp. 434–439. DOI: 10.1016/j.foodchem.2008.09.102.
65. Zhang, G. – Chen, S. – Zhou, W. – Meng, J. – Deng, K. – Zhou, H. – Hu, N. – Suo, Y.: Rapid qualitative and quantitative analyses of eighteen phenolic compounds from *Lycium ruthenicum* Murray by

UPLC-Q-Orbitrap MS and their antioxidant activity. Food Chemistry, *269*, 2018, pp. 150–156. DOI: 10.1016/j.foodchem.2018.06.132.
66. Zhang, G. – Chen, S. – Zhou, W. – Meng, J. – Deng, K. – Zhou, H. – Hu, N. – Suo, Y.: Anthocyanin composition of fruit extracts from *Lycium ruthenicum* and their protective effect for gouty arthritis. Industrial Crops and Products, *129*, 2019, pp. 414–423. DOI: 10.1016/j.indcrop.2018.12.026.
67. Ongkowijoyo, P. – Luna-Vital, D. A. – de Mejia, E. G.: Extraction techniques and analysis of anthocyanins from food sources by mass spectrometry: An update. Food Chemistry, *250*, 2018, pp. 113–126. DOI: 10.1016/j.foodchem.2018.01.055.
68. Sinopoli, A. – Calogero, G. – Bartolotta, A.: Computational aspects of anthocyanidins and anthocyanins: A review. Food Chemistry, *297*, 2019, article 124898. DOI: 10.1016/j.foodchem.2019.05.172.
69. Zhu, F.: Anthocyanins in cereals: Composition and health effects. Food Research International, *109*, 2018, pp. 232–249. DOI: 10.1016/j.foodres.2018.04.015.
70. Zhao, C. L. – Yu, Y. Q. – Chen, Z. J. – Wen, G. S. – Wei, F. G. – Zheng, Q. – Wang, C. D. – Xiao, X. L.: Stability-increasing effects of anthocyanin glycosyl acylation. Food Chemistry, *214*, 2017, pp. 119–128. DOI: 10.1016/j.foodchem.2016.07.073.
71. He, Y. – Wen, L. K. – Yu, H. S. – Zheng, F. – Wang, Z. T. – Xu, X. W. – Zhang, H. – Cao, Y. – Wang, B. X. – Chu, B. J. – Hao, J. Y.: Effects of high hydrostatic pressure-assisted organic acids on the copigmentation of *Vitis amurensis Rupr* anthocyanins. Food Chemistry, *268*, 2018, pp. 15–26. DOI: 10.1016/j.foodchem.2018.06.052.
72. Rahman, M. M. – Ichiyanagi, T. – Komiyama, T. – Hatano, Y. – Konishi, T. Superoxide radical-and peroxynitrite-scavenging activity of anthocyanins; structure-activity relationship and their synergism. Free Radical Research, *40*, 2006, pp. 993–1002. DOI: 10.1080/10715760600815322.
73. Cianciosi, D. – Varela-Lopez, A. – Forbes-Hernandez, T. Y. – Gasparrini, M. – Afrin, S. – Reboredo-Rodriguez, P. – Zhang, J. J. – Quiles, J. L. – Nabavi, S. F. – Battino, M. – Giampieri, F.: Targeting molecular pathways in cancer stem cells by natural bioactive compounds. Pharmacological Research, *135*, 2018, pp. 150–165. DOI: 10.1016/j.phrs.2018.08.006.
74. Chen, J. – Zhao, Y. – Tao, X. – Zhang, M. – Sun, A.: Protective effect of blueberry anthocyanins in a CCL4-induced liver cell model. LWT – Food Science and Technology, *60*, 2015, pp. 1105–1112. DOI: 10.1016/j.lwt.2014.10.010.
75. Liu, Y. – Tan, D. – Tong, C. – Zhang, Y. – Xu, Y. – Liu, X. – Gao, Y. – Hou, M.: Blueberry anthocyanins ameliorate radiation-induced lung injury through the protein kinase RNA-activated pathway. Chemico-Biological Interactions, *242*, 2015, pp. 363–371. DOI: 10.1016/j.cbi.2015.11.001.
76. Chen, Z. – Li, W. – Guo, Q. – Xu, L. – Santhanam, R. K. – Gao, X. – Chen, Y. – Wang, C. – Panichayupakaranant, P. – Chen, H.: Anthocyanins from dietary black soybean potentiate glucose uptake in L6 rat skeletal muscle cells via up-regulating phosphorylated Akt and GLUT4. Journal of Functional Foods, *52*, 2019, pp. 663–669. DOI: 10.1016/j.jff.2018.11.049.
77. Swinburn, B. – Dietz, W. – Kleinert, S.: A Lancet Commission on obesity. Lancet, *386*, 2015, pp. 1716–1717. DOI: 10.1016/S0140-6736(15)00722-9.
78. Matsukawa, T. – Villareal, M. O. – Motojima, H. – Isoda, H.: Increasing cAMP levels of preadipocytes by cyanidin-3-glucoside treatment induces the formation of beige phenotypes in 3T3-L1 adipocytes. Journal of Nutritional Biochemistry, *40*, 2017, pp. 77–85. DOI: 10.1016/j.jnutbio.2016.09.018.
79. Lee, B. L. – Kang, J. H. – Kim, H. M. – Jeong, S. H. – Jang, D. S. – Jang, Y. P. – Choung, S. Y.: Polyphenol-enriched *Vaccinium uliginosum* L. fractions reduce retinal damage induced by blue light in A2E-laden ARPE19 cell cultures and mice. Nutrition Research, *36*, 2016, pp. 1402–1414. DOI: 10.1016/j.nutres.2016.11.008.
80. Thummayot, S. – Tocharus, C. – Suksamrarn, A. – Tocharus, J.: Neuroprotective effects of cyanidin against Aβ-induced oxidative and ER stress in SK-N-SH cells. Neurochemistry International, *101*, 2016, pp. 15–21. DOI: 10.1016/j.neuint.2016.09.016.

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