

**Supplementary Table 1** Anti-inflammatory effects of anthocyanidins enriched plant and fruit (cell and animal study).

Food	Model	Model	Route of administration/dosage	Result	Ref.
Blueberry	Assessment of cecal microbiota activity and colon morphology	mdr1a/mice	Oral: 10%	↑Concentrations of butyric acid ↓concentrations of succinic acid ↑Colon crypt size and number of goblet cells per crypt ↓Number of Clostridium perfringens, Enterococcus spp. and Lactobacillus spp.	[1]
	TNBS-induced UC	Female-C57BL/6 mice	Oral: 10, 20 and 40 mg/ kg	↓Weight gain ↓Mortality ↓Diarrhea score ↓Shortening of the colons owing to inflammation and hydropsia ↓Mucosal congestion, erosion and thickening of the colon wall ↑Goblet cells and IL-10 ↓NO, MPO, IL-12, TNFα and IFN-γ	[2]
	DSS-induced UC	Rat	Oral: 5 g/rat	↓Disease activity index ↓MPO activity ↓MDA ↓Bacterial translocation ↓Aerobic and anaerobic bacterial count ↓MCP-1and GRO/CINC-1 (not significant) ↑Cecal SCFA	[3]
Barberry	Acetic acid-induced UC	Male Wistar rats	Oral: 375, 750, and 1500 mg/kg Rectal: 750 and 1500 mg/kg	↓Ulcer area and macroscopic ulcer index ↓Colon wet weight/length ratio ↓Inflammatory cells infiltration ↓Epithelial necrosis and lesions ↑Colon crypt size and number of goblet cells per crypt	[4]
Sunrouge	DSS-induced UC	Male-specific pathogenfree ICR mice	Oral: 0.16 mg/day	↑Survival rates ↓Body weight loss ↑Length of colorectum ↓Spleen hypertrophy ↑Anthocyanin concentrations in tissues and serum ↑ALT, no difference in TNFα, IL-1b and IL-6	[5]
Cranberry	DSS-induced UC	Male BALB/c mice	Oral: 0.1 and 1% extract powder, 1.5% dried whole cranberry powder	↓Colon length ↓MPO activity ↓TNFα and IL-1b serum level ↓TNFα and IL-1b gene expression ↓Disease activity index ↓Structural damage in colonic mucosa ↓Inflammatory cells infiltration	[6]
Bilberry	DSS-induced UC	BALB/c mice	Oral: 20% dried bilberry 1 and 10% anthocyanin extract	↓Secretion of IFN-γ, TNFα and IL-6 ↓Intestinal inflammation ↓Histological scores ↓Colon shortening ↓leukocytes infiltration ↓Apoptotic epithelial cells	[7]
	Intestinal oxidative stress induced by ischemia reperfusion	Male BALB/c mice	Oral: 1.62 g/mouse	↓MDA ↓Mucosal injury in the ileum	[8]
Cooked navy and black bean	DSS-induced UC	C57BL/6 mice	Oral: 20% navy bean or black bean	↑Cecal SCFA concentrations ↓mRNA expression of colonic inflammatory cytokines (IL-6, IL-9, IFN-γ and IL-17A) ↑Anti-inflammatory IL-8, IL-10, Tlr4 and FasL	[9]

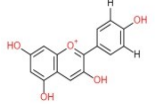
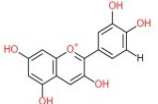
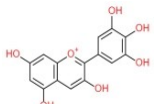
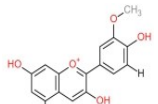
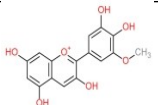
				↓Serum levels of IL-1b, TNFa, IFN-g and IL-17a ↑Cecal SCFA and fecal phenolic compound concentrations ↑Histological injury score and apoptosis ↑Serum ORAC, reversed splenic tissue weight increase	
Black raspberry	DSS-induced UC	C57BL/6J male mice	Oral: 5% black raspberry diets	↓Staining of macrophages and neutrophils ↓NFkB p65 nuclear localization in the colon ↓Ulceration in the mucosa, submucosa and muscularis on day 28 ↓Protein expression of DNMT3B, HDAC1, HDAC2 and MBD2 ↓HDAC1 mRNA expression in spleen, ↓mRNA expression of DNMT3B, HDAC1, HDAC2 and MBD2 in bone marrow ↑Methylation and mRNA expression of dkk3, dkk2 and apc ↓B-catenin nuclear localization	[10]

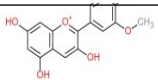
ALT: Alanine transaminase; DNMT: Deoxyribonucleic acid methyltransferase; DSS: Dextran sodium sulfate; FasL: Fas ligand; GRO/CINC-1: Growth-regulated oncogene/cytokine induced neutrophil chemoattractants-1; HDAC: Histone deacetylases; iNOS: Inducible nitric oxide synthase; MBD: Methyl-binding domain; MCP-1: Monocyte chemoattractant protein-1; MDA: Malondialdehyde; MPO: Myeloperoxidase; NO: Nitric oxide; ORAC: Oxygen radical absorbance capacity; p-Ikba: Phospho-Ikba; PMN: Polymorphonuclear; SCFA: Short-chain fatty acids; Tlr4: Toll-like receptor 4; TNBS: 2,4,6-Trinitrobenzene sulfonic acid; UC: Ulcerative colitis.

#### Notes and references:

1. Paturi, G., et al., *Influence of dietary blueberry and broccoli on cecal microbiota activity and colon morphology in mdr1a(-/-) mice, a model of inflammatory bowel diseases*. Nutrition, 2012. **28**(3): p. 324-30.
2. Xiao, X., et al., *Preventive effects of cranberry products on experimental colitis induced by dextran sulphate sodium in mice*. Food Chem, 2015. **167**: p. 438-46.
3. Osman, N., et al., *Probiotics and blueberry attenuate the severity of dextran sulfate sodium (DSS)-induced colitis*. Dig Dis Sci, 2008. **53**(9): p. 2464-73.
4. Minaiyan, M., et al., *Comparative Study of Berberis vulgaris Fruit Extract and Berberine Chloride Effects on Acetic Acid-Induced Colitis in Rats*. Iran J Pharm Res, 2011. **10**(1): p. 97-104.
5. Akiyama, S., et al., *Effects of anthocyanin-rich tea "Sunrouge" on dextran sodium sulfate-induced colitis in mice*. Biofactors, 2012. **38**(3): p. 226-33.
6. Rossi, A., et al., *Protective effects of anthocyanins from blackberry in a rat model of acute lung inflammation*. Free Radic Res, 2003. **37**(8): p. 891-900.
7. Biedermann, L., et al., *Bilberry ingestion improves disease activity in mild to moderate ulcerative colitis - an open pilot study*. J Crohns Colitis, 2013. **7**(4): p. 271-9.
8. Jakešević, M., et al., *Effects of bilberry (Vaccinium myrtillus) in combination with lactic acid bacteria on intestinal oxidative stress induced by ischemia-reperfusion in mouse*. J Agric Food Chem, 2013. **61**(14): p. 3468-78.
9. Zhang, C., et al., *Cooked navy and black bean diets improve biomarkers of colon health and reduce inflammation during colitis*. Br J Nutr, 2014. **111**(9): p. 1549-63.
10. Wang, L.S., et al., *Dietary black raspberries modulate DNA methylation in dextran sodium sulfate (DSS)-induced ulcerative colitis*. Carcinogenesis, 2013. **34**(12): p. 2842-50.

**Supplementary Table 2** Anti-inflammatory activity/ potential of the six most common anthocyanidins.

Anthocyanidins	Structure	Model	Concentration/dose	Signaling pathways and downstream genes	Pharmacological activity	Ref.
Pelargonidin		Murine J774 macrophages	100 $\mu\text{mol L}^{-1}$	$\downarrow$ iNOS, $\downarrow$ NF $\kappa$ B	Anti-inflammatory activity	[1]
Cyanidin		In vitro enzyme inhibition assay	IC <sub>50</sub> = 90 $\mu\text{mol L}^{-1}$ IC <sub>50</sub> = 60 $\mu\text{mol L}^{-1}$	$\downarrow$ COX-1 $\downarrow$ COX-2	Anti-inflammatory potential	[2]
		In vitro enzyme inhibition assay	40 $\mu\text{mol L}^{-1}$	$\downarrow$ COX-1* $\downarrow$ COX-2*	Anti-inflammatory potential	[3]
		In vitro enzyme inhibition assay	0.15-1.2 $\mu\text{mol L}^{-1}$	$\downarrow$ PLA2 A	Anti-inflammatory potential	[4]
		LPS-induced RAW 264.7 cells	1-5 $\mu\text{mol L}^{-1}$	$\downarrow$ COX-2 $\downarrow$ ERK1/2 $\downarrow$ IL-1 $\downarrow$ iNOS, $\downarrow$ I $\kappa$ B- $\alpha$ $\downarrow$ JNK1/2 $\downarrow$ NF- $\kappa$ B $\downarrow$ p38 $\downarrow$ TNF- $\alpha$	Anti-inflammatory activity	[5]
Delphinidin		In vitro enzyme inhibition assay	0.15-1.2 mmol L <sup>-1</sup>	$\downarrow$ PLA2	Anti-inflammatory potential	[6]
		LPS-activated murine macrophage RAW264 cells	25-100 $\mu\text{mol L}^{-1}$	$\downarrow$ AP-1 $\downarrow$ C/EBP $\delta$ $\downarrow$ c-Jun $\downarrow$ COX-2 $\downarrow$ ERK1/2 $\downarrow$ I $\kappa$ B- $\alpha$ $\downarrow$ JNK1/2 $\downarrow$ NF- $\kappa$ B $\downarrow$ p38	Anti-inflammatory activity	[7]
Peonidin		In vitro enzyme inhibition assay	0.15-2.1 $\mu\text{mol L}^{-1}$	$\downarrow$ PLA2	Anti-inflammatory potential	[6]
		TPS-stimulated JB6 P+ mouse epidermal cells	5-20 $\mu\text{mol L}^{-1}$	$\downarrow$ COX-2 $\downarrow$ ERK1/2 A	Anti-inflammatory activity	[8]
Petunidin		In vitro enzyme inhibition assay	0.15-2.1 $\mu\text{mol L}^{-1}$	$\downarrow$ PLA2	Anti-inflammatory	[6]

					potential	
Malvidin		In vitro enzyme inhibition assay	0.15-2.1 $\mu\text{mol L}^{-1}$	$\downarrow$ PLA2	Anti-inflammatory potential	[6]
		In vitro enzyme inhibition assay	40 $\mu\text{mol L}^{-1}$	$\downarrow$ COX-1 $\downarrow$ COX-2	Anti-inflammatory potential	[3]

$\downarrow$ inhibition. \*, the most potent inhibitor when compared to other anthocyanidins. AP: activator protein; COX: cyclooxygenase; C/EBP: CCAAT/enhancer-binding protein; ERK: extracellular signal-regulated kinase; iNOS: inducible nitric oxid synthase; I $\kappa$ B: inhibitor of nuclear factor kappa B kinase; IL: interleukin; JNK: c-Jun N-terminal kinase; NF- $\kappa$ B: nuclear factor kappa B; PLA: phospholipase A; p38: p38 kinase; TNF: tumor necrosis factor;

## Notes and references:

1. Hämäläinen, M., et al., *Anti-inflammatory effects of flavonoids: genistein, kaempferol, quercetin, and daidzein inhibit STAT-1 and NF-kappaB activations, whereas flavone, isorhamnetin, naringenin, and pelargonidin inhibit only NF-kappaB activation along with their inhibitory effect on iNOS expression and NO production in activated macrophages.* Mediators Inflamm, 2007. **2007**: p. 45673.
2. Wang, H., et al., *Antioxidant and antiinflammatory activities of anthocyanins and their aglycon, cyanidin, from tart cherries.* J Nat Prod, 1999. **62**(2): p. 294-6.
3. Seeram, N.P., Y. Zhang, and M.G. Nair, *Inhibition of proliferation of human cancer cells and cyclooxygenase enzymes by anthocyanidins and catechins.* Nutr Cancer, 2003. **46**(1): p. 101-6.
4. Muñoz-Espada, A.C. and B.A. Watkins, *Cyanidin attenuates PGE2 production and cyclooxygenase-2 expression in LNCaP human prostate cancer cells.* J Nutr Biochem, 2006. **17**(9): p. 589-96.
5. Min, S.W., S.N. Ryu, and D.H. Kim, *Anti-inflammatory effects of black rice, cyanidin-3-O-beta-D-glycoside, and its metabolites, cyanidin and protocatechuic acid.* Int Immunopharmacol, 2010. **10**(8): p. 959-66.
6. Dreiseitel, A., et al., *sPhospholipase A(2) is inhibited by anthocyanidins.* J Neural Transm (Vienna), 2009. **116**(9): p. 1071-7.
7. Hou, D.X., et al., *Anthocyanidins inhibit cyclooxygenase-2 expression in LPS-evoked macrophages: structure-activity relationship and molecular mechanisms involved.* Biochem Pharmacol, 2005. **70**(3): p. 417-25.
8. Kwon, J.Y., et al., *Peonidin inhibits phorbol-ester-induced COX-2 expression and transformation in JB6 P+ cells by blocking phosphorylation of ERK-1 and -2.* Ann N Y Acad Sci, 2007. **1095**: p. 513-20.

**Supplementary Table 3****All of the biological processes of the most common anthocyanidins treated IBD**

GO-BP	Category	Description	Count	%	Log10(P)
GO:0033674	GO biological processes	Positive regulation of kinase activity	15	34.09	-12.995
GO:1901699	GO biological processes	Cellular response to nitrogen compound	15	34.09	-12.531
GO:0034614	GO biological processes	Cellular response to reactive oxygen species	10	22.73	-12.374
GO:1904645	GO biological processes	Response to amyloid-beta	7	15.91	-10.918
GO:2000377	GO biological processes	Regulation of reactive oxygen species metabolic process	9	20.45	-10.166
GO:0034762	GO biological processes	Regulation of transmembrane transport	12	27.27	-9.576
GO:0006690	GO biological processes	Icosanoid metabolic process	7	15.91	-8.738
GO:0060326	GO biological processes	Cell chemotaxis	9	20.45	-8.502
GO:0019221	GO biological processes	Cytokine-mediated signaling pathway	12	27.27	-7.960
GO:0045124	GO biological processes	Regulation of bone resorption	5	11.36	-7.911
GO:0097237	GO biological processes	cellular response to toxic substance	8	18.18	-7.84
GO:0050878	GO biological processes	regulation of body fluid levels	9	20.45	-6.6
GO:0045907	GO biological processes	positive regulation of vasoconstriction	4	9.09	-6.44
GO:0008610	GO biological processes	lipid biosynthetic process	10	22.73	-6.35
GO:0030155	GO biological processes	regulation of cell adhesion	10	22.73	-6.34
GO:0045927	GO biological processes	positive regulation of growth	7	15.91	-6.23

GO:0031334	processes GO biological processes	positive regulation of protein complex assembly	7	15.91	-6.13
GO:0031623	GO biological processes	receptor internalization	5	11.36	-5.72
GO:0050727	GO biological processes	regulation of inflammatory response	8	18.18	-5.51
GO:0035690	GO biological processes	cellular response to drug	7	15.91	-5.34

**All of the KEGG pathways of the most common anthocyanidins treated IBD**

KEGG	Category	Description	Count	%	Log10(P)
hsa01521	KEGG pathway	EGFR tyrosine kinase inhibitor resistance	8	18.18	-11.86
hsa04611	KEGG pathway	Platelet activation	7	15.91	-8.64
hsa04913	KEGG pathway	Ovarian steroidogenesis	5	11.36	-7.52
hsa05206	KEGG pathway	MicroRNAs in cancer	8	18.18	-7.25
hsa04520	KEGG pathway	Adherens junction	5	11.36	-6.71
hsa05202	KEGG pathway	Transcriptional misregulation in cancer	6	13.64	-6.08
hsa00590	KEGG pathway	Arachidonic acid metabolism	4	9.09	-5.32
hsa04921	KEGG pathway	Oxytocin signaling pathway	5	11.36	-5.1
hsa04022	KEGG pathway	cGMP-PKG signaling pathway	5	11.36	-4.96
hsa02010	KEGG pathway	ABC transporters	3	6.82	-4.16
hsa04080	KEGG pathway	Neuroactive ligand-receptor interaction	5	11.36	-3.86
hsa04972	KEGG pathway	Pancreatic secretion	3	6.82	-3.16
hsa04010	KEGG pathway	MAPK signaling pathway	3	6.82	-1.96