

Disease type/risk	First Author	Study Title Complete Citation	Date	Abstract	Human	Human cell	Animal	Animal cell
	Rossi, A.	Rossi, A.; Serraino, I.; Dugo, P.; Di Paola, R.; Mondello, L.; Genovese, T.; Morabito, D.; Dugo, G.; Sautebin, L.; Caputi, A. P.; Cuzzocrea, S., Protective effects of anthocyanins from blackberry in a rat model of acute lung inflammation. <i>Free Radic Res</i> 2003 , <i>37</i> , (8), 891-900.	2003	Anthocyanins are a group of naturally occurring phenolic compounds related to the coloring of plants, flowers and fruits. These pigments are important as quality indicators, as chemotaxonomic markers and for their antioxidant activities. Here, we have investigated the therapeutic efficacy of anthocyanins contained in blackberry extract (cyanidin-3-O-glucoside represents about 80% of the total anthocyanin contents) in an experimental model of lung inflammation induced by carrageenan in rats. Injection of carrageenan into the pleural cavity elicited an acute inflammatory response characterized by fluid accumulation which contained a large number of neutrophils as well as an infiltration of polymorphonuclear leukocytes in lung tissues and subsequent lipid peroxidation, and increased production of nitrite/nitrate (NOx) and prostaglandin E2 (PGE2). All parameters of inflammation were attenuated in a dose-dependent manner by anthocyanins (10, 30 mg kg(-1) 30 min before carrageenan). Furthermore, carrageenan induced an upregulation of the adhesion molecule ICAM-1, nitrotyrosine and poly (ADP-ribose) synthetase (PARS) as determined by immunohistochemical analysis of lung tissues. The degree of staining was lowered by anthocyanins treatment. Thus, the anthocyanins contained in the blackberry extract exert multiple protective effects in carrageenan-induced pleurisy.			X	
	Freese, R.	Freese, R.; Vaarala, O.; Turpeinen, A. M.; Mutanen, M., No difference in platelet activation or inflammation markers after diets rich or poor in vegetables, berries and apple in healthy subjects. <i>European Journal of Nutrition</i> 2004 , <i>43</i> , (3), 175-182.	2004	Background: High intake of vegetables and fruits is associated with decreased risk of coronary heart disease. Part of these cardioprotective effects may be mediated via the antithrombotic effects of compounds found in vegetables and fruits, such as flavonoids. Aim of the study: To study the effects of high and low intake of vegetables, berries and apple on platelet function and inflammatory markers. Methods: The study was a randomised, controlled parallel human dietary intervention with healthy female and male volunteers (n = 77, 19-52 y). Nineteen healthy volunteers served as controls. The volunteers consumed one of four strictly controlled isocaloric 6-week diets containing either 810 or 196 g/10 MJ of vegetables, berries and apple and rich either in linoleic acid (11% of energy, en%) or oleic acid (12 en%). Blood and three 24-hour urine samples were collected at the beginning and at the end of the study period for analyses of various markers of platelet function and inflammation. Results: No differences between the treatment groups were seen in platelet count or volume, markers of platelet activation (ex vivo aggregation to ADP and thrombin receptor activating peptide, protein kinase C activity, urinary 2,3-dinor-thromboxane B-2 excretion, plasma P-selectin), plasma intercellular adhesion molecule-1, sensitive C-reactive protein, or antiphospholipid antibodies. Conclusions: The results indicate that in healthy volunteers 6-week diets differing markedly in the amounts of vegetables, berries and apple do not differ in their effects on platelets or inflammation.	X			

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	Pergola, C.	<p>Pergola, C.; Rossi, A.; Dugo, P.; Cuzzocrea, S.; Sautebin, L.,</p> <p>Inhibition of nitric oxide biosynthesis by anthocyanin fraction of blackberry extract.</p> <p>Nitric Oxide 2006, 15, (1), 30-9.</p>	2003	<p>Anthocyanins are natural colorant belonging to the flavonoid family, widely distributed among flowers, fruits, and vegetables. Some flavonoids have been found to possess anticarcinogenic, cytotoxic, cytostatic, antioxidant, and anti-inflammatory properties. Since increased nitric oxide (NO) plays a role in inflammation, we have investigated whether the pharmacological activity of the anthocyanin fraction of a blackberry extract (cyanidin-3-O-glucoside representing about 88% of the total anthocyanin content) was due to the suppression of NO synthesis. The markedly increased production of nitrites by stimulation of J774 cells with lipopolysaccharide (LPS) for 24 h was concentration-dependently inhibited by the anthocyanin fraction (11, 22, 45, and 90 microg/ml) of the extract. Moreover, this inhibition was dependent on a dual mechanism, since the extract attenuated iNOS protein expression and decreased the iNOS activity in lungs from LPS-stimulated rats. Inhibition of iNOS protein expression appeared to be at the transcriptional level, since the extract and similarly cyanidin-3-O-glucoside (10, 20, 40, and 80 microg/ml, amounts corresponding to the concentrations present in the extract) decreased LPS-induced NF-kappaB activation, through inhibition of I-kappaBalpha degradation, and reduced ERK-1/2 phosphorylation in a concentration-dependent manner. In conclusion, our study demonstrates that at least some part of the anti-inflammatory activity of blackberry extract is due to the suppression of NO production by cyanidin-3-O-glucoside, which is the main anthocyanin present in the extract. The mechanism of this inhibition seems to be due to an action on the expression/activity of the enzyme. In particular, the protein expression was inhibited through the attenuation of NF-kappaB and/or MAPK activation.</p>			X	X