


## Neuste Studie über Aronia-Beeren mit wichtigsten Markern (oxidiertes LDL, Prostaglandine, hochsensitives CRP, MCP-1) für entzündliche Gefässerkrankungen (Bluthochdruck, Schlaganfall, Herzinfarkt): hoch signifikant!!

[Atherosclerosis](#). 2007 Feb 20; [Epub ahead of print]  FULL-TEXT ARTICLE [Links](#)

Combination therapy of statin with flavonoids rich extract from chokeberry fruits enhanced reduction in cardiovascular risk markers in patients after myocardial infraction (MI).

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Recent studies have shown, that chronic flavonoids treatment improves vascular function and cardiovascular remodeling by decreasing superoxide anion production as well as by increasing NO realize from endothelial cells. A progressive decrease in systolic blood pressure and reduction of low-density lipoprotein oxidation (Ox-LDL) has also been reported. However, none of these studies were done in patient with coronary artery disease treated with statins. This was a double-blind, placebo-controlled, parallel trial. Forty-four patients (11 women and 33 men, mean age 66 years) who survived myocardial infraction and have received statin therapy for at least 6 months (80% dose of 40mg/day simvastatin) were included in the study. The subjects were randomised to receive either 3x 85mg/day of chokeberry flavonoid extract (*Aronia melanocarpa* E) or placebo for a period of 6 weeks. The study extract was a commercially-available (OTC) product of the following declared composition: anthocyanins (about 25%), polymeric procyanidines (about 50%) and phenolic acids (about 9%). Compared to placebo (ANOVA and Tukey's test), flavonoids significantly reduced serum 8-isoprostans ( $p < 0.000$ ) and Ox-LDL levels ( $p < 0.000$ ) (by 38 and 29%, respectively), as well as hsCRP ( $p < 0.007$ ) and MCP-1 ( $p < 0.001$ ) levels (by 23 and 29%, respectively). In addition, significant increase in adiponectin ( $p < 0.03$ ) levels and reduction in systolic and diastolic blood pressure by a mean average of 11 and 7.2mmHg, respectively were found. CONCLUSION: In view of the fact that chokeberry flavonoids reduce the severity of inflammation, regardless of statins, they can be used clinically for secondary prevention of ischaemic heart disease.

## Artikel über Möglichkeiten zur Wirkungsverstärkung von Anthocyanen über Pharmakokinetische Tricks in der Galenik über Phytinsäure: Verbesserungsmöglichkeit für Pascoe Aronia??

[J Agric Food Chem.](#) 2007 Mar 21;55(6):2489-96. Epub 2007 Feb 24.



[Links](#)

### Enhanced absorption of anthocyanins after oral administration of phytic acid in rats and humans.

- [Matsumoto H,](#)
- [Ito K,](#)
- [Yonekura K,](#)
- [Tsuda T,](#)
- [Ichiyanagi T,](#)
- [Hirayama M,](#)
- [Konishi T.](#)

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Many studies on the bioavailability of polyphenols have been reported. However, the relative urinary excretions of AC are also low, ranging from 0.004% to 0.1%. By contrast, other polyphenols show higher urinary excretion levels. Here, we studied the enhancing effects of phytic acid (IP6) on absorption of blackcurrant anthocyanins (BCAs) in rats and humans. In rats after oral administration of BCAs (as 241 mg of AC/kg body weight) in IP6 (0%, 0.25%, 0.5%, 1%, 2.5%) solution, the ACs recovery in urine was increased dependent on IP6 dose. These results suggest that the IP6 enhances gastrointestinal absorption of ACs. At the further analysis of IP6 enhancement effect in rat, whereas BCAs were normally passed through the stomach and duodenum within 2 h, in IP6 group, after 2-6 h post-administration, stomach and jejunum content's weights were specifically heavy, and large amounts of ACs were also detected in stomach, duodenum, and jejunum. These results suggested that the mixture of BCAs and IP6 reduced the gastrointestinal motility. Prolongation of ACs residue in gastrointestinal tract then caused the enhancing effects of IP6 on absorption of AC. In the human study, each subject was orally administrated a BCA beverage containing BCA concentrate (AC 4 mg/kg body weight), 1% of IP6, and 1% of sodium citrate as a pH stabilizer. Both the plasma level and the urinary excretion of AC were increased as compared to BCA administration without IP6. AC intake with IP6 may increase the bioavailability of AC to the comparative level as other polyphenols. Yet, phytic acid, being a strong chelator of important minerals, contributes to mineral deficiencies. An interference with iron uptake has been reported. Safety tests are therefore necessary before high dose IP6 can be used in foods.

## **Pascoe-Aronia kann auch bei Übergewicht und Diabetes sinnvoll eingesetzt werden:**

### **Klare Hinweise hier an Ratten-Experimenten mit Genchips (Microarrays) gemacht!!!**

[Biochem Pharmacol.](#) 2006 Apr 14;71(8):1184-97. Epub 2006 Feb 17.

**ELSEVIER**  
FULL-TEXT ARTICLE

[Links](#)

#### **Microarray profiling of gene expression in human adipocytes in response to anthocyanins.**

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- [Ueno Y,](#)
- [Yoshikawa T,](#)
- [Kojo H,](#)
- [Osawa T.](#)

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Adipocyte dysfunction is strongly associated with the development of obesity and insulin resistance. It is accepted that the regulation of adipocytokine secretion or the adipocyte specific gene expression is one of the most important targets for the prevention of obesity and amelioration of insulin sensitivity. Recently, we demonstrated that anthocyanins, which are pigments widespread in the plant kingdom, have the potency of anti-obesity in mice and the enhancement adipocytokine secretion and its gene expression in adipocytes. In this study, we have shown the gene expression profile in human adipocytes treated with anthocyanins (cyanidin 3-glucoside; C3G or cyanidin; Cy). The human adipocytes were treated with 100 microM C3G, Cy or vehicle for 24 h. The total RNA from the adipocytes was isolated and carried out GeneChip microarray analysis. Based on the gene expression profile, we demonstrated the significant changes of adipocytokine expression (up-regulation of adiponectin and down-regulation of plasminogen activator inhibitor-1 and interleukin-6). Some of lipid metabolism related genes (uncoupling protein2, acylCoA oxidase1 and perilipin) also significantly induced in both common the C3G or Cy treatment groups. These studies have provided an overview of the gene expression profiles in human adipocytes treated with anthocyanins and demonstrated that anthocyanins can regulate adipocytokine gene expression to ameliorate adipocyte function related with obesity and diabetes that merit further investigation.

**Gene expression profile of isolated rat adipocytes treated with anthocyanins.**

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Adipocyte dysfunction is strongly associated with the development of obesity and insulin resistance. It is accepted that the regulation of adipocytokine secretion or the adipocyte specific gene expression is one of the most important targets for the prevention of obesity and amelioration of insulin sensitivity. Recently, we demonstrated that anthocyanins, which are pigments widespread in the plant kingdom, have the potency of anti-obesity in mice and the enhancement adipocytokine secretion and adipocyte gene expression in adipocytes. In this study, we have shown for the first time the gene expression profile in isolated rat adipocytes treated with anthocyanins (cyanidin 3-glucoside; C3G or cyanidin; Cy). The rat adipocytes were treated with 100  $\mu$ M C3G, Cy or vehicle for 24 h. The total RNA from the adipocytes was isolated and carried out GeneChip microarray analysis. A total of 633 or 427 genes was up-regulated (>1.5-fold) by the treatment of adipocytes with C3G or Cy, respectively. The up-regulated genes include lipid metabolism and signal transduction-related genes, however, the altered genes were partly different between the C3G- and Cy-treated groups. Based on the gene expression profile, we demonstrated the up-regulation of hormone sensitive lipase and enhancement of the lipolytic activity by the treatment of adipocytes with C3G or Cy. These data have provided an overview of the gene expression profiles in adipocytes treated with anthocyanins and identified new responsive genes with potentially important functions in adipocytes related with obesity and diabetes that merit further investigation.

**Anthocyanin enhances adipocytokine secretion and adipocyte-specific gene expression in isolated rat adipocytes.**

- [Tsuda T,](#)
- [Ueno Y,](#)
- [Aoki H,](#)
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Adipocyte dysfunction is strongly associated with the development of obesity and insulin resistance. It is accepted that the regulation of adipocytokine secretion or the adipocyte-specific gene expression is one of the most important targets for the prevention of obesity and amelioration of insulin sensitivity. In this study, we demonstrated that anthocyanins (cyanidin or cyanidin 3-glucoside) have the potency of a unique pharmacological function in isolated rat adipocytes. Treated adipocytes with anthocyanins enhanced adipocytokine (adiponectin and leptin) secretion and up-regulated the adipocyte specific gene expression without activation of PPARgamma in isolated rat adipocytes. The gene expression of adiponectin was also up-regulated in white adipose tissue in mice fed an anthocyanin supplemented diet. As one of the possible mechanisms, AMP-activated protein kinase activation would be associated with these changes, nevertheless, the AMP:ATP ratio was significantly decreased by administration of the anthocyanins. These data suggest that anthocyanins have a potency of unique therapeutic advantage and also have important implications for preventing obesity and diabetes.

**Effects of novel plant antioxidants on platelet superoxide production and aggregation in atherosclerosis.**

- [Ryszawa N,](#)
- [Kawczynska-Drozd A,](#)
- [Pryjma J,](#)
- [Czesnikiewicz-Guzik M,](#)
- [Adamek-Guzik T,](#)
- [Naruszewicz M,](#)
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Superoxide anion is produced in human platelets predominantly by Nox2-dependent NADPH oxidases. In vitro experiments have shown that it might play a role in modulating platelet functions. The relationship between platelet superoxide production and aggregation remains poorly defined. Accordingly, we aimed to study superoxide production and aggregation in platelets from subjects with significant cardiovascular risk factors (hypertension, hypercholesterolemia, smoking and diabetes mellitus) and from control individuals. Moreover, we studied the effects of novel polyphenol-rich extracts of *Aronia melanocarpa* (chokeberry) berries on platelet function in vitro. Superoxide production was significantly increased in patients with cardiovascular risk profile when compared to controls, while platelet aggregation in response to either collagen or thrombin were borderline higher, and did not reach statistical significance. Interestingly, no relationship was observed between platelet aggregation ex vivo and platelet superoxide production in either of studied groups. No correlation was found between endothelial function (measured by FMD) and platelet aggregation ex vivo either. Polyphenol-rich extracts of *A. melanocarpa* berries caused a significant concentration dependent decrease in superoxide production only in patients with cardiovascular risk factors, while no effect was observed in the control group. *A. melanocarpa* extracts abolished the difference in superoxide production between risk factor patients and controls. *A. melanocarpa* extracts exerted significant concentration dependent anti-aggregatory effects in both studied groups, which indicated that these effects may be independent of its ability to modulate superoxide production. The anti-aggregatory effects of chokeberry extracts were similar irrespective of aggregation inducing agent (collagen or thrombin). Moreover, they appear to be independent of platelet NO release as NOS inhibition by L-NAME did not lead to their abrogation.

**Antihyperlipidemic effect of Aronia melanocarpa fruit juice in rats fed a high-cholesterol diet.**

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- [Kuzmanov K,](#)
- [Mihova V,](#)
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Aronia melanocarpa fruit juice (AMFJ) used in our experiment was very rich in phenolic substances (709.3 mg gallic acid equivalents/100 ml juice). Anthocyanins (106.8 mg cyanidin-3-glucoside equivalents/100 ml juice) were the main flavonoid group. The aim of this study was to assess the influence of AMFJ on plasma lipids and lipoprotein profile, and histopathology of liver and aorta in rats with dietary-induced hyperlipidemia. AMFJ was administered by gavage for 30 days at doses of 5, 10 and 20 ml/kg body weight to rats fed a standard diet (SD) or a 4% cholesterol-containing diet (4% ChD). The 4% ChD caused a significant elevation of plasma total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG). AMFJ did not significantly influence plasma lipids in rats fed the SD and significantly hindered the elevation of plasma TC, LDL-C and TG in rats fed the 4% ChD. High-density lipoprotein cholesterol (HDL-C) levels were not significantly influenced either by the 4% ChD or by AMFJ. Neither the cholesterol feeding, nor AMFJ treatment induced any histopathological changes in rat liver and aorta. In conclusion, AMFJ showed an antihyperlipidemic effect in rats with hyperlipidemia and could be valuable in reducing this factor of cardiovascular risk.

**Effect of Aronia melanocarpa fruit juice on indomethacin-induced gastric mucosal damage and oxidative stress in rats.**

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Aronia melanocarpa fruits are rich in phenolic substances-mainly flavonoids from the anthocyanin subclass. The anthocyanins are water-soluble plant pigments with antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, gastroprotective and other activities. We studied the effect of A. melanocarpa fruit juice (AMFJ) on indomethacin-induced gastric mucosal damage in rats and its possible relation to the oxidative status. AMFJ (5, 10 and 20 ml kg<sup>-1</sup>) was applied orally as a pretreatment 1 h before the subcutaneous administration of indomethacin (30 mg kg<sup>-1</sup>). Gastric ulcer formation was estimated morphometrically and histopathologically 4h after the indomethacin administration. Malondialdehyde (MDA) in rat plasma and gastric mucosa and also reduced glutathione (GSH) and oxidized glutathione (GSSG) in gastric mucosa were determined and used as biochemical markers of the oxidative status. AMFJ-pretreatment diminished the number and area of indomethacin-induced gastric lesions. Histopathological examination of rat stomachs demonstrated that AMFJ induced an increase in gastric mucus production and a reduction of the depth and severity of indomethacin-induced mucosal lesions. AMFJ dose-dependently reduced the elevated indomethacin plasma and gastric MDA levels and at the doses of 10 and 20 ml kg<sup>-1</sup> they were not significantly different from the control values. Neither indomethacin-treatment, nor AMFJ-pretreatment had a significant influence on GSH and GSSG gastric mucosal levels. These results demonstrated that indomethacin-induced gastric mucosal damage was accompanied by the development of oxidative stress, evidenced by the accumulation of MDA. AMFJ-pretreatment decreased the gastric lesions caused by indomethacin. It could be suggested that this effect of AMFJ was probably due to the increased mucus production and interference with oxidative stress development as evidenced by the decreased plasma and gastric mucosal MDA.



**Up-regulation of tumor suppressor carcinoembryonic antigen-related cell adhesion molecule 1 in human colon cancer Caco-2 cells following repetitive exposure to dietary levels of a polyphenol-rich chokeberry juice.**

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Consumption of berries and red fruits rich in polyphenols may contribute to the reduction of colon cancer through mechanisms not yet understood. In this study, we investigated the response of subconfluent Caco-2 cells (a human colon carcinoma model) to repetitive exposure (2 h a day for a 4-day period) of a subtoxic dose of a chokeberry (*Aronia melanocarpa*) juice containing mixed polyphenols. To mimic physiological conditions, we subjected the chokeberry juice to in vitro gastric and pancreatic digestion. The effects on viability, proliferation and cell cycle were determined, and changes in the expression of genes in response to the chokeberry treatment were screened using Affymetrix oligonucleotide microarrays. Exposure to the chokeberry juice inhibited Caco-2 cell proliferation by causing G(2)/M cell cycle arrest. We detected changes in the expression of a group of genes involved in cell growth and proliferation and cell cycle regulation, as well as those associated to colorectal cancer. A selection of these genes was further confirmed by quantitative RT-PCR. Among these, the tumor suppressor carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1), whose expression is known to be reduced in the majority of early adenomas and carcinomas, was up-regulated by the treatment both at the mRNA and protein levels (as shown by flow cytometry analysis). CEACAM1, with a significant regulatory role on cell proliferation of particular interest at early stages of cancer development, may be a potential target for chemoprevention by food components such as those present in polyphenol-rich fruits.

**Anthocyanin-rich extracts inhibit multiple biomarkers of colon cancer in rats.**

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- [Malik M,](#)
- [Zhao C,](#)
- [He J,](#)
- [Kwon Y,](#)
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The aim of the present study was to investigate the chemoprotective activity of anthocyanin-rich extracts (AREs) from bilberry (*Vaccinium myrtillus* L.), chokeberry (*Aronia meloncarpa* E.), and grape (*Vitis vinifera*) by assessing multiple biomarkers of colon cancer in male rats treated with a colon carcinogen, azoxymethane. Fischer 344 male rats were fed the AIN-93 diet (control) or AIN-93 diet supplemented with AREs for 14 wk. Biomarkers that were evaluated included the number and multiplicity of colonic aberrant crypt foci (ACF), colonic cell proliferation, urinary levels of oxidative DNA damage, and expression of cyclooxygenase (COX) genes. To assess the bioavailability, levels of anthocyanins in serum, urine, and feces were evaluated. Total ACF were reduced ( $P < 0.05$ ) in bilberry, chokeberry, and grape diet groups compared with the control group. The number of large ACF was also reduced ( $P < 0.05$ ) in bilberry and chokeberry ARE-fed rats. Colonic cellular proliferation was decreased in rats fed bilberry ARE and chokeberry ARE diets. Rats fed bilberry and grape ARE diets had lower COX-2 mRNA expression of gene. High levels of fecal anthocyanins and increased fecal mass and fecal moisture occurred in ARE-fed rats. There was also a significant reduction ( $P < 0.05$ ) in fecal bile acids in ARE-fed rats. The levels of urinary 8-hydroxyguanosine were similar among rats fed different diets. These results support our previous in vitro studies suggesting a protective role of AREs in colon carcinogenesis and indicate multiple mechanisms of action.

**Intact anthocyanins and metabolites in rat urine and plasma after 3 months of anthocyanin supplementation.**

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- [Magnuson BA,](#)
- [Lala G,](#)
- [Tian Q,](#)
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Anthocyanins are polyphenols responsible for most red to purple colors in plants. Human consumption of these pigments is increasing because of their potential health benefits and use as natural colorants. With more than 600 different anthocyanins found in nature, the impact of chemical structure on their absorption and metabolism needs to be investigated. Urine and plasma samples were collected from 32 rats receiving control diet or chokeberry-, bilberry-, and grape-enriched (3.85 g cyanidin 3-galactoside equivalent/kg) diet for 14 wk. Below 2 micromol/l of anthocyanins and relatively higher levels of presumable metabolites were detected by high-performance liquid chromatography-photodiode array in the plasma. In the urine the total concentration of intact anthocyanins and methylated derivatives ranged from 17.4 (bilberry) to 52.6 (chokeberry) nmol/l. The type and number of anthocyanin glycosylations affected the absorption remarkably. Detection of an acylated anthocyanin in plasma and urine suggests bioavailability of these anthocyanin derivatives that are commonly found in commercially available colorants.