

# **Aronia melanocarpa research bibliography**

*—draft—*

**Keywords:** *Alzheimer, Antibacterial, Antiviral, Anti-inflammatory, Anxiolytic, Cadmium intoxication, Cancer, Cardiovascular, Diabetes, Gastric, Gut, Hemorrhoids, Lead poisoning, Liver, Metabolism, Metabolic syndrome, Muscle recovery, ORAC, Pancreas, Respiratory, Weight gain*

# 1

## Alzheimer

(cholinesterase inhibitor, rats)

Amadeo Gironés-Vilaplana, Patrícia Valentão, Paula B. Andrade, Federico Ferreres, Diego A. Moreno, Cristina García-Viguera

Phytochemical profile of a blend of black chokeberry and lemon juice with cholinesterase inhibitory effect and antioxidant potential

Food Chemistry 134(4) 15 October 2012, pp. 2090–2096

In this study, black chokeberry concentrate was added (5% w/v) to lemon juice, since previous reports suggested potential health benefits of this blend. The phytochemical composition, antioxidant capacity (scavenging of DPPH, superoxide and hydroxyl radicals, and hypochlorous acid), and inhibitory activity against cholinesterase of the new blend were determined and compared with those of lemon juice and chokeberry in citric acid (5%). The chokeberry concentrate, rich in cyanidin-glycosides, quercetin derivatives, and 3-O-caffeoylquinic acid, and lemon juice, possessing flavones, flavanones, quercetin derivatives, and hydroxycinnamic acids, were characterised. The new drink showed a higher antioxidant effect than the chokeberry or lemon controls for all the tested methods, except for hypochlorous acid, in which lemon juice displayed higher activity. Both the lemon juice and chokeberry controls inhibited acetylcholinesterase and butyrylcholinesterase, and this effect was increased in the new mixtures. The results of the different radical scavenging assays indicate that the lemon–black chokeberry (5% w/v) mixture was more antioxidative than the respective controls separately. Moreover, their inhibition of cholinesterase is of interest regarding neurodegenerative disorders such as Alzheimer’s disease, Parkinson’s disease, or senile dementia. Highlights: New beverage rich in bioactive compounds of lemon juice and chokeberry concentrate. New lemon juice and chokeberry blend showed higher antioxidant activity than individual sources, except for HOCl. Lemon juice and chokeberry mixture beverage inhibited cholinesterase activity. The new blend has potential for food product development and nutrition.

<http://www.sciencedirect.com/science/article/pii/S0308814612006474>

## 2

### **Antibacterial**

**(viruses, flu, humans, rats)**

Valcheva-Kuzmanova SV, Belcheva A

Current knowledge of Aronia melanocarpa as a medicinal plant

Folia Med (Plovdiv). 2006;48(2):11-7

Aronia melanocarpa, native to eastern North America, has become popular in Eastern Europe and Russia. Aronia melanocarpa fruits are one of the richest plant sources of phenolic substances, mainly anthocyanins – glycosides of cyanidin. Anthocyanins are water soluble pigments accounting for the dark blue and even black color of the fruits. Administered orally they can be absorbed as intact glycosides. Aronia melanocarpa fruit juice and anthocyanins derived from the fruits have been studied intensively for the last 15 years. Most of the effects of Aronia melanocarpa anthocyanins are due to their high antioxidative activity. Our investigations have demonstrated a remarkable hepatoprotective, a very good gastroprotective and a pronounced anti-inflammatory effect of Aronia melanocarpa fruit juice in rats as well as a bacteriostatic activity in vitro against Staphylococcus aureus and Escherichia coli and an antiviral activity against type A influenza virus. Research of other authors has demonstrated that Aronia melanocarpa anthocyanins can normalize the carbohydrate metabolism in diabetic patients and in streptozotocin-diabetic rats, have an in vitro antimutagenic activity and exhibit a distinct immunomodulatory activity in human lymphocyte cultures and in patients with breast cancer, suppress the growth of human HT-29 colon cancer cells, inhibit the N-nitrosamine formation in rats and decrease the toxicity and accumulation of cadmium in liver and kidneys. Currently, there are no data in literature about any unwanted and toxic effects of Aronia melanocarpa fruits, juice and extracts.

<http://www.ncbi.nlm.nih.gov/pubmed/17408071>

## 3

### **Antibacterial**

**(gastrointestinal pathogens, humans)**

Puupponen-Pimiä R, Nohynek L, Alakomi HL, Oksman-Caldentey KM

The action of berry phenolics against human intestinal pathogens

Biofactors 4/2005; 23: 243–251.

Phenolic compounds present in berries selectively inhibit the growth of human gastrointestinal pathogens. Especially cranberry, cloudberry, raspberry, strawberry and bilberry possess clear antimicrobial effects against e.g. salmonella and staphylococcus. Complex phenolic polymers, such as ellagitannins, are strong antibacterial agents present in cloudberry, raspberry and strawberry. Berry phenolics seem to affect the growth of different bacterial species with different mechanisms. Adherence of bacteria to epithelial surfaces is a prerequisite for colonization and infection of many pathogens. Antimicrobial activity of berries may also be related to anti-adherence activity of the berries. Utilization of enzymes in berry processing increases the amount of phenolics and antimicrobial activity of the berry products. Antimicrobial berry compounds are likely to have many important applications in the future as natural antimicrobial agents for food industry as well as for medicine.

<http://iospress.metapress.com/content/3gebj8ang2lu8k1g/>

## 4

### **Antibacterial**

#### **(bacterial growth, in vitro)**

Marie Bräunlich, Ole A. Økstad, Rune Slimestad, Helle Wangensteen, Karl E. Malterud and Hilde Barsett

Effects of Aronia melanocarpa Constituents on Biofilm Formation of Escherichia coli and Bacillus cereus

Molecules 2013, 18(12), 14989-14999; doi:10.3390/molecules181214989

Many bacteria growing on surfaces form biofilms. Adaptive and genetic changes of the microorganisms in this structure make them resistant to antimicrobial agents. Biofilm-forming organisms on medical devices can pose serious threats to human health. Thus, there is a need for novel prevention and treatment strategies. This study aimed to evaluate the ability of Aronia melanocarpa extracts, subfractions and compounds to prevent biofilm formation and to inhibit bacterial growth of Escherichia coli and Bacillus cereus in vitro. It was found that several aronia substances possessed anti-biofilm activity, however, they were not toxic to the species screened. This non-toxic inhibition may confer a lower potential for resistance development compared to conventional antimicrobials.

<http://www.mdpi.com/1420-3049/18/12/14989>

<http://www.mdpi.com/1420-3049/18/12/14989/pdf>

## 5

### Antiviral

#### (rats)

Park S, Kim JI, Lee I, Lee S, Hwang MW, Bae JY, Heo J, Kim D, Han SZ, Park MS

Aronia melanocarpa and its components demonstrate antiviral activity against influenza viruses

Biochem Biophys Res Commun. 2013 Oct 11; 440(1):14-9. doi: 10.1016/j.bbrc.2013.08.090. Epub 2013 Sep 5.

The influenza virus is highly contagious in human populations around the world and results in approximately 250,000-500,000 deaths annually. Vaccines and antiviral drugs are commonly used to protect susceptible individuals. However, the antigenic mismatch of vaccines and the emergence of resistant strains against the currently available antiviral drugs have generated an urgent necessity to develop a novel broad-spectrum anti-influenza agent. Here we report that Aronia melanocarpa (black chokeberry, Aronia), the fruit of a perennial shrub species that contains several polyphenolic constituents, possesses in vitro and in vivo efficacy against different subtypes of influenza viruses including an oseltamivir-resistant strain. These anti-influenza properties of Aronia were attributed to two constituents, ellagic acid and myricetin. In an in vivo therapeutic mouse model, Aronia, ellagic acid, and myricetin protected mice against lethal challenge. Based on these results, we suggest that Aronia is a valuable source for antiviral agents and that ellagic acid and myricetin have potential as influenza therapeutics.

<http://www.ncbi.nlm.nih.gov/pubmed/24012672>

## 6

### Anti-inflammatory

#### (inflammatory bowel disease, mice)

U Conn: Efficacy of Aronia (chokeberry) polyphenols to inhibit Th17 in vitro and in a mouse model of inflammatory bowel diseases (IBD)

Research is currently being done on the use of Aronia berries to treat inflammatory bowel disease (IBD). IBD affects 1.4 million Americans, Children with IBD have increased risk of nutrient deficiencies, muscle wasting, and poor bone development.

Chokeberry (*Aronia melanocarpa*), a native Connecticut specialty crop, is a promising fruit to develop as an IBD intervention. Our overall hypothesis is that chokeberry polyphenols and their metabolites attenuate IBD by limiting Th17 cell differentiation and cytokine release. In adoptive transfer models of experimental colitis, Th17 cells play an important role in disease initiation. We have assembled a multi-disciplinary team at the University of Connecticut Health Center and Storrs consisting of Dr. Francisco Sylvester, a pediatric gastroenterologist, Dr. Mark Brand, a horticulturist, and Dr. Bradley Bolling, a nutritionist to 1) determine which polyphenol-rich chokeberry genotypes have the greatest effect on Th17 in vitro, and 2) characterize the effect of dietary chokeberry extract on Th17 using a mouse model of IBD.

<http://midatlanticonia.wordpress.com/2011/11/16/u-conn-efficacy-of-aronia-chokeberry-polyphenols-to-inhibit-th17-in-vitro-and-in-a-mouse-model-of-inflammatory-bowel-diseases-ibd/>

[<http://www.dietandhealth.uconn.edu/projects/efficacy-of-aronia-chokeberry-polyphenols-to-inhibit-th17-in-vitro-and-in-a-mouse-model-of-inflammatory-bowel-diseases-ibd/> - not working]

## 7

### **Anti-inflammatory**

**(anti-ocular/uveitis, rats)**

Ohgami K, Ilieva I, Shiratori K, Koyama Y, Jin XH, Yoshida K, Kase S, Kitaichi N, Suzuki Y, Tanaka T, Ohno S.

Anti-inflammatory effects of aronia extract on rat endotoxin-induced uveitis.

Invest Ophthalmol Vis Sci. 2005 Jan;46(1):275-81.

This study shows the anti-inflammatory power of Aronia: “the anti-inflammatory effect of 100 mg Aronia extract was as strong as that of 10 mg prednisolone”, “The anti-inflammatory action of Aronia extract was stronger than that of either quercetin or anthocyanin administered alone.”

**PURPOSE:** Aronia crude extract (ACE) with high levels of polyphenol compounds has been reported to have antioxidative effects in vitro and in vivo. In this study, attention was focused on the antioxidant effect of ACE. The purpose of the present study was to investigate the effect of ACE on endotoxin-induced uveitis (EIU) in rats. In addition, the endotoxin-induced expression of the inducible nitric oxide synthase (iNOS) and cyclooxygenase (COX)-2 proteins was investigated in a mouse macrophage cell line (RAW 264.7) treated with ACE in vitro, to clarify the anti-inflammatory effect. **METHODS:** EIU was induced in male Lewis rats by a footpad

injection of lipopolysaccharide (LPS). Immediately after the LPS inoculation, 1, 10, or 100 mg ACE or 10 mg prednisolone was injected intravenously. After 24 hours, the aqueous humor was collected from both eyes, and the number of infiltrating cells, protein concentration, nitric oxide (NO), prostaglandin (PG)-E<sub>2</sub>, and TNF-alpha levels in the aqueous humor were determined. RAW 264.7 cells treated with various concentrations of ACE were incubated with 10 µg/mL LPS for 24 hours. Levels of NO, PGE<sub>2</sub>, and TNF-alpha were determined by an enzyme-linked immunosorbent assay. The expression of iNOS and COX-2 proteins was analyzed by Western blot analysis. **RESULTS:** The number of inflammatory cells, the protein concentrations, and the levels of NO, PGE<sub>2</sub>, and TNF-alpha in the aqueous humor in the groups treated with ACE were significantly decreased in a dose-dependent manner. In addition, the anti-inflammatory effect of 100 mg ACE was as strong as that of 10 mg prednisolone. The anti-inflammatory action of ACE was stronger than that of either quercetin or anthocyanin administered alone. ACE also suppressed LPS-induced iNOS and COX-2 protein expressions in RAW 264.7 cells in vitro in a dose-dependent manner. **CONCLUSIONS:** The results suggest that ACE has a dose-dependent anti-ocular inflammatory effect that is due to the direct blocking of the expression of the iNOS and COX-2 enzymes and leads to the suppression of the production of NO, PGE<sub>2</sub>, and TNF-alpha.

<http://www.ncbi.nlm.nih.gov/pubmed/15623784>

## 8

### **Anti-inflammatory**

(rats)

Borissova P, Valcheva S, Belcheva A

Anti-inflammatory effect of flavonoids in the natural juice from *Aronia melanocarpa*, rutin and rutin-magnesium complex on an experimental model of inflammation induced by histamine and serotonin.

Acta Physiol Pharmacol Bulg 1994; 20: 25–30.

The anti-inflammatory effects of the anthocyan flavonoids in the natural juice from *Aronia melanocarpa* and of rutin-magnesium complex, the water-soluble derivative of rutin were studied in comparison with rutin. Two experimental models of inflammation were used. Inflammation of rat hind paw was induced either by 0.5% solution of histamine or by 0.01% solution of serotonin. The swelling of the rat paw was measured oncometrically by a pletismometer. The results showed that the anthocyan flavonoids from the natural juice of *Aronia melanocarpa* exerted more pronounced effects as compared to rutin in both models of inflammation. The rutin-magnesium complex did not exhibit any anti-inflammatory activity against histamine-

induced inflammation. Its effects against serotonin-induced inflammation were comparable to those of rutin.

<http://www.ncbi.nlm.nih.gov/pubmed/7892768>

9

Anti-inflammatory (aortic cells, humans)

D. Zapolska-Downar, D. Bryk, M. Małecki, K. Hajdukiewicz, D. Sitkiewicz

Aronia melanocarpa fruit extract exhibits anti-inflammatory activity in human aortic endothelial cells

Eur J Nutr. Aug 2012; 51(5): 563–572. doi: 10.1007/s00394-011-0240-1

Background: Altered expression of cell adhesion molecules (CAMs) has been implicated in a variety of chronic inflammatory conditions, including atherosclerosis. Regulation of adhesion molecule expression by specific redox-sensitive mechanisms has been reported. Additionally, it has been observed that the extract of Aronia melanocarpa (*A. Melanocarpa*) fruits, rich in polyphenols, exhibits potent anti-oxidant properties and displays cardioprotective activity. Methods and results: Human aortic endothelial cells (HAECs) were pretreated with various concentrations (primarily 50 µg/mL) of Aronia Melanocarpa fruit extract prior to treatment with TNFα (10 ng/mL) for various periods of time. The surface protein and mRNA expression of ICAM-1 and VCAM-1 were determined using flow cytometry and real-time RT-PCR, respectively. Adhesion of peripheral blood mononuclear leucocytes (PBMLs) to TNFα-treated HAECs was evaluated by an adhesion assay. Activation of NF-κB was evaluated by measuring NF-κB p65 phosphorylation using flow cytometry. ROS production was determined by reduction in fluorescent 2',7'-dichlorofluorescein diacetate (DCFH-DA). Tested *A. Melanocarpa* extract significantly inhibited the expression of ICAM-1 and VCAM-1, attenuated the phosphorylation of NF-κB p65 and decreased intracellular ROS production in TNFα-treated HAECs. Conclusion: We conclude that *A. Melanocarpa* fruit extract exhibits anti-inflammatory effects in HAECs by inhibiting the expression of endothelial CAMs, activation of NF-κB and production of ROS.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3397226/>

10

Anti-inflammatory (antioxidation, endothelial cells)

Han G L, Li C M, Mazza G, Yang X G

Effect of anthocyanin rich fruit extract on PGE2 produced by endothelial cells.

Wei Sheng Yan Jiu 2005; 34: 581-4

**OBJECTIVE:** To study the effect of anthocyanin rich fruit extract on PGE2 produced by endothelial cells. **METHODS:** Normal human endothelial cells, CRL-2606, were cultured in F12K medium (complemented with 10% FBS, 0.1 mg/ml heparin, 0.03 mg/ml ECGS, 50 µg/ml streptomycin and 500U/ml penicillin) in 5% CO2 with 95% air at 37 degrees C. When the cells grow close to confluence, anthocyanin rich fruit extract with/without 100 ng/ml of LPS were added to the medium. After 18 hours of incubation, cells were harvested and the supernatant were collected. Cell viability was assayed. After centrifugation, PGE2 concentration in the supernatant was measured with the STAT-Prostaglandin E2 EIA Kit. **RESULTS:** 300 µg/ml or higher Chokeberry extract showed cytotoxicity effect on CRL-2606 cells, the viability was lower than 60% and showed a dose-response manner. Under using dosage, Blackcurrant extract (100-700 µg/ml) and Blueberry extract (50 – 400 µg/ml) did not show any cytotoxicity. When stimulated by LPS, the production of PGE2 by endothelial cells were increased two fold. Blueberry extract inhibit such action. 100 µg/ml of Blueberry extract keeps the production of PGE2 in normal level. 700 µg/mL of Blackcurrant extract and 500 µg/ml Chokeberry extract also inhibit the releasing of PGE2. **CONCLUSION:** Anthocyanin rich fruit extract from Blueberry, Blackcurrant, and Chokeberry inhibit PGE2 produced by endothelial cells, there exist anti-inflammation and antioxidation.

<http://www.ncbi.nlm.nih.gov/pubmed/16329602>

11

Antioxidant (pomace)

Rajchl, A., Čížková, H., Kapci, B., Voldřich, M., Capanoglu, E., Neradová, E.

Investigating the antioxidant potential of chokeberry (*Aronia melanocarpa*) products

Journal of Food and Nutrition Research 52(4), 07/2013

Several studies have reported on the flavonoid and phenolic acid contents of chokeberry. However, limited reports have been focused on the anthocyanins and antioxidant activity of chokeberry products, although chokeberries are generally consumed as processed. In order to determine the health-related constituents of different chokeberry products, total phenolics, flavonoids, anthocyanins and antioxidant activity were examined in fourteen chokeberry products. The highest total phenolics and anthocyanin contents were found in chokeberry pomace with the values of 63.1 g per kg expressed as gallic acid equivalents, and 4.5 g per kg expressed as cyanidin-3-glucoside equivalents. Total flavonoid content and total antioxidant activity analysed by three different methods (2,2-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS), diphenyl-(2,4,6-trinitrophenyl) iminoazanium (DPPH), and cupric ion reducing antioxidant capacity (CUPRAC)) were higher in dried chokeberries compared to the rest of the products. The

anthocyanin profile was determined by high performance liquid chromatography. Cyanidin-3-galactoside was found to be the major anthocyanin in all samples, but some differences were observed in the contents of individual anthocyanins.

<http://agris.fao.org/agris-search/search.do?recordID=SK2013000216>

12

Antioxidant (bioavailability)  
(in vitro, in vivo)

Petko N. Denev, Christo G. Kratchanov, Milan Ciz, Antonin Lojek and Maria G. Kratchanova

Bioavailability and Antioxidant Activity of Black Chokeberry (*Aronia melanocarpa*) Polyphenols: in vitro and in vivo Evidences and Possible Mechanisms of Action: A Review.

Comprehensive Reviews in Food Science and Food Safety, Volume 11, Issue 5, pages 471–489, September 2012, DOI: 10.1111/j.1541-4337.2012.00198.x

Black chokeberry (*Aronia melanocarpa*) is a distinctive berry with a high content of polyphenol compounds and possesses one of the highest in vitro antioxidant activities among fruits. The bioavailability of aronia polyphenols seems to be low, but there is ample evidence for chokeberry health benefits including antidiabetic, cardioprotective, hepatoprotective, antimutagenic, and anticarcinogenic effects. This review presents the available information for the bioavailability and antioxidant activity of chokeberry polyphenols and explains the possible mechanisms of action in vivo in the prevention and treatment of oxidative stress-related diseases. The review shows the available data for chokeberry antioxidant activity in vitro, in isolated cells and cell lines, and in vivo, in both human subjects and animals. It is evident that in vivo antioxidant action of chokeberry extends far beyond radical scavenging and includes suppression of reactive oxygen and nitrogen species formation, inhibition of prooxidant enzymes, restoration of antioxidant enzymes, and probably cellular signaling to regulate the level of antioxidant compounds and enzymes. The original contribution of this work is that it compiles the available information up to date and outlines the gaps and future directions in the assessment of chokeberry antioxidant action in vivo.

<http://onlinelibrary.wiley.com/doi/10.1111/j.1541-4337.2012.00198.x/abstract>

<http://onlinelibrary.wiley.com/doi/10.1111/j.1541-4337.2012.00198.x/full>

13

Antioxidant (anthocyanidins, pelargonidin, cyanidin, delphinidin, peonidin, petunidin, malvidin)

Kähkönen Marja P, Hopia AI, Vuorela HJ, Rauha J, Pihlaja K, Kujala TS, Heinonen M

Antioxidant activity of plant extracts containing phenolic compounds

J Agric Food Chem 1999;47: 3954 – 3962. DOI: 10.1021/jf990146l

The antioxidative activity of a total of 92 phenolic extracts from edible and nonedible plant materials (berries, fruits, vegetables, herbs, cereals, tree materials, plant sprouts, and seeds) was examined by autoxidation of methyl linoleate. The content of total phenolics in the extracts was determined spectrometrically according to the Folin-Ciocalteu procedure and calculated as gallic acid equivalents (GAE). Among edible plant materials, remarkable high antioxidant activity and high total phenolic content (GAE > 20 mg/g) were found in berries, especially aronia and crowberry. Apple extracts (two varieties) showed also strong antioxidant activity even though the total phenolic contents were low (GAE < 12.1 mg/g). Among nonedible plant materials, high activities were found in tree materials, especially in willow bark, spruce needles, pine bark and cork, and birch phloem, and in some medicinal plants including heather, bog-rosemary, willow herb, and meadowsweet. In addition, potato peel and beetroot peel extracts showed strong antioxidant effects. To utilize these significant sources of natural antioxidants, further characterization of the phenolic composition is needed.

<http://pubs.acs.org/doi/abs/10.1021/jf990146l>

14

Antioxidant (reduction of oxidative stress, red blood cells, humans)

Pilaczynska-Szczesniak L, Skarpanska-Steinborn A, Deskur E, Basta P, Horoszkiewicz-Hassan M

The influence of chokeberry juice supplementation on the reduction of oxidative stress resulting from an incremental rowing ergometer exercise

Int J Sport Nutr Exerc Metab 2005; 15: 48-58

The aim of the study was to investigate the influence of an increased intake of anthocyanins, contained in chokeberry juice, on the redox parameters in rowers performing a physical exercise during a 1-month training camp. The athletes were randomly assigned to receive 150 mL of chokeberry juice daily, containing 23 mg/100 mL of anthocyanins (supplemented group), or placebo (control group). Before and after the supplementation period, the subjects performed an incremental rowing exercise test. Blood samples were taken from the antecubital vein before each exercise test, 1 min after the test, and following a 24-h recovery period. After the supplementation period, TBARS concentrations in the samples collected 1 min after the exercise test and following a 24-h recovery period were significantly lower in the

subjects receiving chokeberry juice than in the control group. In the supplemented group, glutathione peroxidase activity was lower in the samples collected 1 min after the exercise test, and superoxide dismutase activity was lower in the samples taken following a 24-h recovery, as compared to the subjects receiving placebo. These findings indicate that an increased intake of anthocyanins limits the exercise-induced oxidative damage to red blood cells, most probably by enhancing the endogenous antioxidant defense system.

<http://journals.humankinetics.com/ijsnem-back-issues/IJSNEMVolume15Issue1February/TheInfluenceofChokeberryJuiceSupplementationontheReductionofOxidativeStressResultingfromanIncrementalRowingErgometerExercise>

<http://journals.humankinetics.com/AcuCustom/Sitename/Documents/DocumentItem/4671.pdf>

15

Antioxidant (oxidative stress, clinical)

C. Chrubasik, G. Li, S. Chrubasik

The clinical effectiveness of chokeberry: a systematic review

Phytotherapy Research 24(8), pp.p 1107–1114, August 2010. DOI: 10.1002/ptr.3226

Products derived from the black chokeberry, *Aronia melanocarpa*, are claimed to be beneficial in disorders or diseases associated with oxidative stress. The claims are based on evidence from in vitro studies and animal experiments. The active principle – a mixture of procyanidins, anthocyanins and phenolic acids – constitutes one of the most potent natural antioxidants. We carried out a systematic review of the quality of the clinical trials on chokeberry products that had been published up to December 2009, and used conventionally established criteria to assess the strength of the evidence for their clinical effectiveness. Thirteen studies were identified. The quality of most of the trials and, correspondingly, the evidence of effectiveness for *Aronia* products is poor. Though laboratory and clinical data indicate that chokeberry products may well be useful as “functional food” for disorders or diseases related to oxidative stress, these promising indications need to be confirmed in more rigorous studies before putative therapeutic uses can be confidently recommended for chokeberry products.

<http://onlinelibrary.wiley.com/doi/10.1002/ptr.3226/abstract>

[http://hal.archives-ouvertes.fr/docs/00/55/24/32/PDF/PEER\\_stage2\\_10.1002%252Fptr.3226.pdf](http://hal.archives-ouvertes.fr/docs/00/55/24/32/PDF/PEER_stage2_10.1002%252Fptr.3226.pdf)

16

Antioxidant (oxidative stress, rats)

Faff J, Frankiewicz-Jozko A

Effect of anthocyanins from Aronia melanocarpa on the exercise-induced oxidative stress in rat tissues

Biol Sport 2003; 20: 15-23.

We investigated the effect of the extract from fruits of Aronia melanocarpa (AM), containing the anthocyanin antioxidants on the lipid peroxidation index (TBARS) and the content of reduced glutathione (GSH) in rat tissues at rest and after exercising until exhaustion on a treadmill. For four consecutive days the animals were given AM through a gastric probe at 0.7 mg/ kg body mass (related to the content of the active substance). Control rats received 0.9% NaCl solution. Samples of the liver (L), heart (H), and white (WG) and red (RG) portions of the gastrocnemius muscle were collected from the animals at rest and immediately after the exercise. No effect of AM on TBARS was detected in the resting animals. The exercise, however, led to the significant elevation of the value of this index ( $P < 0.05$ ) in each of the tested tissues obtained from the control animals, and in the liver and heart of the AM-fed rats. The TBARS content in RG was significantly lower ( $P < 0.05$ ) in the latter compared to the former group of the animals. After administration of AM in rest, the GSH content tended to decrease in the examined tissues. Following the exercise, the significant reduction ( $P < 0.05$ ) in the GSH content was detected in all the tested tissues obtained from the control group. In contrast, no effect of the exercise on the GSH content was found in the AM-fed rats. After exercising, the higher GSH content ( $P < 0.05$ ) in the RG and H as well as the tendency to higher GSH content in WG and L were detected in rats given AM as compared to the control animals. The obtained results suggest that administration of AM markedly mitigates the exercise-induced reduction in the GSH content and elevation of TBARS in the tissues of the investigated animals.

<http://biolsport.com/abstracted.php?level=5&ICID=6701>

<http://biolsport.com/fulltxt.php?ICID=6701>

17

Antioxidant (oxidative damage, cancer, heart disease, diabetes, hypertension, hypercholesterolemia, treatment, prevention)

Magdalena Zielińska, Halina Gryglicka, Kamil K. Hozyasz

Chokeberry – clinical perspectives

Pediatrica Polska 88(5), Sept.-Oct. 2013, pp. 452–458.

Aronia melanocarpa contain particularly high amounts of procyanidins, anthocyanins, and phenolic acids. These antioxidants reduce the oxidative damage of human cells that can lead to cancer, heart disease, diabetes, hypertension, hypercholesterolemia. The black chokeberry may be used in the treatment and prevention of numerous civilization diseases.

<http://www.sciencedirect.com/science/article/pii/S0031393913000814>

18

Antioxidant (intoxication, protective antioxidative agent, mice)

Kowalczyk E, Charyk K, Fijalkowski P, Niedworok J, Blaszczyk J, Kowalski J.

Protective influence of natural anthocyanins of Aronia melanocarpa on selected parameters of antioxidative status in experimental intoxication with sulphide-2-chloroethyl-3-chloropropyl

Pol J Environ Stud 2004; 13: 339-41.

Sulphide-2-chloroethyl-3-chloropropyl is an alkylating agent. It possesses mutagenic and carcinogenic properties, participates in oxidative processes and can induce lipid peroxidation. The aim of our investigation was to define antioxidative activity of natural anthocyanins after single experimental intoxication with sulphide-2-chloroethyl-3-chloropropyl in mice. Catalase activity in hemolysate, thiobarbituric acid reacting substances (TBARS) concentration in hemolysate and selected organs were determined. The study confirms increased lipid peroxidation as a result of sulphide-2-chloroethyl-3-chloropropyl intoxication, but natural anthocyanines derived from Aronia Melanocarpa also seem to play a protective role as an antioxidative agent.

<http://www.pjoes.com/pdf/13.3/339-341.pdf>

19

Antioxidant (antiradical activity, anthocyanins)

Jun-ichiro Nakajima, Ippei Tanaka, Shujiro Seo, Mami Yamazaki, Kazuki Saito

Profiling and Radical Scavenging Activity of Anthocyanins in Various Berries

J Biomed Biotechnol. Dec 1, 2004; 2004(5): 241–247. doi:  
10.1155/S1110724304404045

Anthocyanin extracts of two blueberries, Vaccinium myrtillus (bilberry) and Vaccinium ashei (rabbiteye blueberry), and of three other berries, Ribes nigrum (black currant), Aronia melanocarpa (chokeberry), and Sambucus nigra (elderberry), were

analyzed by high-performance liquid chromatography coupled with photodiode array detection and electrospray ionization – mass spectrometry (LC/PDA/ESI-MS). Both bilberry and rabbiteye blueberry contained 15 identical anthocyanins with different distribution patterns. Black currant, chokeberry, and elderberry contained 6, 4, and 4 kinds of anthocyanins, respectively. The radical scavenging activities of these berry extracts were analyzed by using 2,2-diphenyl-1-picrylhydrazyl (DPPH). All these extracts showed potent antiradical activities.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1082896/>

<http://www.pubmedcentral.nih.gov/picrender.fcgi?artid=1082896&blobtype=pdf>

20

Antioxidant (anthocyanins, antioxidant activity, in vitro)

Marja P. Khknen, Marina Heinonen

Antioxidant Activity of Anthocyanins and Their Aglycons

J. Agric. Food Chem., 2003, 51 (3), pp 628–633. DOI: 10.1021/jf025551i

The antioxidant activity of the six common anthocyanidins, pelargonidin, cyanidin, delphinidin, peonidin, petunidin, and malvidin, and their glycosidic forms was evaluated in three lipid-containing models [human low-density lipoprotein (LDL) and bulk and emulsified methyl linoleate]. In addition, the radical scavenging activity of the compounds against the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical was studied. Most anthocyanins and their aglycons acted as strong antioxidants in emulsion and LDL. Many compounds showed an activity comparable to the well-known antioxidants  $\alpha$ -tocopherol, Trolox, catechin, and quercetin. In bulk methyl linoleate, anthocyanins and anthocyanidins possessed only a weak antioxidant activity or even oxidation-promoting activity. Depending on the anthocyanidin, different glycosylation patterns either enhanced or diminished the antioxidant power. For the most part, the activities of the glycosides and the aglycons did not differ remarkably in emulsion. In LDL the aglycons showed in general higher activities than the glycosides. In bulk oil, to the contrary, the glycosides were more effective than the aglycons.

<http://pubs.acs.org/doi/abs/10.1021/jf025551i>

21

Antioxidant (inhibitory effects)

Zafra-Stone S, Yasmin T, Bagchi M, Chatterjee A, Vinson JA, Bagchi D

Berry anthocyanins as novel antioxidants in human

Methods Find Exp Clin Pharmacol 2009, 31(1): 3. DOI:  
10.1358/mf.2009.31.1.1346608

The cytochrome P450 CYP2D6 isoform is involved in the metabolism of about 50% of all psychoactive drugs, including neuroleptic agents, selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors and tricyclic antidepressants. Therefore, inhibition of cytochrome P450 activity by foodstuffs has implications for drug safety. The present study addresses inhibitory effects of polyphenolic anthocyanins and their aglycons that are found in many dietary fruits and vegetables. Using a chemiluminescent assay, we obtained IC<sub>50</sub> values ranging from 55 μM to > 800 μM for 17 individual compounds. According to earlier data on furanocoumarins from grapefruit extract, CYP2D6 inhibition is achieved in the range of 190-900 nM. As the tested anthocyanins and anthocyanidins were shown to be about 1,000-fold less potent, they are unlikely to interfere with drug metabolism by CYP2D6. Further studies are warranted to examine the effects of the above flavonoids on other CYP isoforms for more detailed toxicity profiles.

[http://journals.prous.com/journals/servlet/xmlxsl/pk\\_journals.xml\\_summary\\_pr?p\\_JournalId=6&p\\_RefId=1346608&p\\_IsPs=N](http://journals.prous.com/journals/servlet/xmlxsl/pk_journals.xml_summary_pr?p_JournalId=6&p_RefId=1346608&p_IsPs=N)

22

Antioxidant (human blood platelets/breast cancer)  
in vitro

Olas, B. Wachowicz, P. Nowak, M. Kedzierska, A. Tomczak, A. Stochmal, W. Oleszek, A. Jeziorski, J. Piekarski

Studies on antioxidant properties of polyphenol-rich extract from berries of aronia melanocarpa in blood platelets

Journal of Physiology and Pharmacology 2008, 59, 4, 823–835

The antioxidant properties of extract from berries of *Aronia melanocarpa* (chokeberry) containing: anthocyanidines, phenolic acids and quercetine glycosides on oxidative/nitrative stress induced by peroxynitrite (ONOO<sup>-</sup>, a powerful physiological oxidant, nitrating species and inflammatory mediator) in human blood platelets were studied in vitro. The extract from *A. melanocarpa* (5-50 μg/mL) significantly inhibited platelet protein carbonylation (measured by ELISA method) and thiol oxidation estimated with 5,5'-dithio-bis(2-nitro-benzoic acid) (DTNB) induced by peroxynitrite (0.1 mM) (IC<sub>50</sub> – 35 μg/mL for protein carbonylation, and IC<sub>50</sub> – 33 μg/mL for protein thiol oxidation). The tested extract only slightly reduced platelet protein nitration (measured by C-ELISA method). The extract also caused a distinct reduction of platelet lipid peroxidation induced by peroxynitrite. Moreover, in our preliminary experiments we observed that the extract (50 μg/mL) reduced oxidative/nitrative stress in blood platelets from patients with breast cancer. The obtained results indicate that in vitro the extract from *A. melanocarpa* has the protective effects against

peroxynitrite-induced oxidative/nitrative damage to the human platelet proteins and lipids. The extract from *A. melanocarpa* seems to be also useful as an antioxidant in patients with breast cancer.

<http://jpp.krakow.pl/>

[http://www.jpp.krakow.pl/journal/archive/12\\_08/pdf/823\\_12\\_08\\_article.pdf](http://www.jpp.krakow.pl/journal/archive/12_08/pdf/823_12_08_article.pdf)

23

Antioxidant (anti-platelet, cardiovascular or inflammatory diseases, in vitro)

Olas B, Wachowicz B, Tomczak A, Erler J, Stochmal A, Oleszek W

Comparative anti-platelet and antioxidant properties of polyphenol-rich extracts from: berries of *Aronia melanocarpa*, seeds of grape and bark of *Yucca schidigera* in vitro

Platelets 2008; 19: 70-77.

The aim of the present study was to investigate and compare the anti-platelet action of extracts from three different plants: bark of *Yucca schidigera*, seeds of grape and berries of *Aronia melanocarpa* (chokeberry). Anti-platelet action of tested extracts was compared with action of well characterized antioxidative and anti-platelet commercial monomeric polyphenol-resveratrol. The effects of extracts on platelet adhesion to collagen, collagen-induced platelet aggregation and on the production of O<sub>2</sub>-\* in resting platelets and platelets stimulated by a strong platelet agonist-thrombin were studied. The in vitro experiments have shown that all three tested extracts (5-50 µg/ml) rich in polyphenols reduce platelet adhesion, aggregation and generation of O<sub>2</sub>-\* in blood platelets. Comparative studies indicate that all three plant extracts were found to be more reactive in reduction of platelet processes than the solution of pure resveratrol. The tested extracts due to their anti-platelet effects may play an important role as components of human diet in prevention of cardiovascular or inflammatory diseases, where blood platelets are involved.

<http://www.ncbi.nlm.nih.gov/pubmed/18231940>

24

Antioxidant (platelet superoxide production, cardiovascular risk factors, in vitro, ex vivo)

Ryszawa, A. Kawczynska-Drozd, J. Pryjma, M. Czesnikiewicz-Guzik, T. Adamek-Guzik, M. Naruszewicz, R. Korbut, T. J. Guzik

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

Journal of Physiology and Pharmacology 57(4), 12/2006

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. Platelet superoxide production is increased in subjects with cardiovascular risk factor profile, which may precede changes in platelet aggregation itself. Novel polyphenol rich extracts of A. melanocarpa berries exert significant anti-platelet effects ex vivo.

<http://www.jpp.krakow.pl/>

[http://www.jpp.krakow.pl/journal/archive/12\\_06/articles/08\\_article.html](http://www.jpp.krakow.pl/journal/archive/12_06/articles/08_article.html)

25

Antioxidant (oxidative stress, gastric mucosal, rats)

Valcheva-Kuzmanova S, Marazova K, Krasnaliev I, Galunska B, Borisova P, Belcheva A

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

Exp Toxicol Pathol 2005; 56:385. DOI: 10.1016/j.etp.2005.01.001

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(-1)) was applied orally as a pretreatment 1 h before the subcutaneous administration of indomethacin (30 mg kg(-1)). 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(-1) 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.

<http://www.sciencedirect.com/science/article/pii/S0940299305000047>

26

Anxiolytic (anxiety, locomotor, memory, rats)

Valcheva-Kuzmanova, S., Zhelyazkova-Savova, M.

Anxiolytic-like effect of Aronia melanocarpa fruit juice in rats

Methods Find Exp Clin Pharmacol 2009, 31(10): 651. DOI:  
10.1358/mf.2009.31.10.1423884

The main biologically active constituents of Aronia melanocarpa fruit juice (AMFJ) are polyphenolics, amongst them flavonoids, mainly anthocyanins. The aim of the present study was to investigate the effects of AMFJ (5 and 10 mL/kg) on anxiety using the social interaction test, on locomotor activity in the open field test and on working memory in the object recognition test in rats. AMFJ showed an anxiolytic-like effect which was demonstrated by a dose-dependent increase in the time of active social contacts between the test partners. The effects of both AMFJ doses were comparable to the effect of diazepam (1 mg/kg). AMFJ neither changed significantly

horizontal and vertical locomotor activity, nor did it adversely affect working memory.

[http://journals.prous.com/journals/servlet/xmlxsl/pk\\_journals.xml\\_summary\\_pr?p\\_JournalId=6&p\\_RefId=1423884&p\\_IsPs=N](http://journals.prous.com/journals/servlet/xmlxsl/pk_journals.xml_summary_pr?p_JournalId=6&p_RefId=1423884&p_IsPs=N)

27

Cadmium (intoxication, rats)

Kowalczyk E, Kopff A, Fijałkowski P, Kopff M, Niedworok J, Błaszczak J, Kedziora J, Tyślerowicz P

Effect of anthocyanins on selected biochemical parameters in rats exposed to cadmium.

Acta Biochim Pol 2003; 50: 543-548.

Cadmium is a dangerous occupational and environmental toxin. It accumulates in the human organism mainly in liver and kidneys. Cadmium half-life is about 10 years, so the symptoms of cadmium intoxication may occur several years after the exposure. Until now in treating intoxication with this metal chelating compounds have been used, burdened with numerous undesirable symptoms. In our investigations anthocyanins from *Aronia melanocarpa* were used to reduce the harmful results caused by cadmium. Administering anthocyanins with cadmium chloride resulted in a statistically significant decrease of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activity, concentration of bilirubin and urea in blood serum and decreased cadmium cumulation in liver and kidneys in relation to animals receiving cadmium chloride only.

[http://www.actabp.pl/#File?./html/2\\_2003/543.html](http://www.actabp.pl/#File?./html/2_2003/543.html)

[http://www.actabp.pl/pdf/2\\_2003/543.pdf](http://www.actabp.pl/pdf/2_2003/543.pdf)

28

Cancer (anthocyanins, cancer prevention)

Wang L, Stoner GD

Anthocyanins and their role in cancer prevention

Cancer Lett 2008; 269: 281–290. DOI: 10.1016/j.canlet.2008.05.020

The daily intake of anthocyanins in residents of the United States is estimated to be about 200 mg or about 9-fold higher than that of other dietary flavonoids. In this review, we summarize the latest developments on the anti-carcinogenic activities of

anthocyanins and anthocyanin-rich extracts in cell culture models and in animal model tumor systems, and discuss their molecular mechanisms of action. We also suggest reasons for the apparent lack of correlation between the effectiveness of anthocyanins in laboratory model systems and in humans as evidenced by epidemiological studies. Future studies aimed at enhancing the absorption of anthocyanins and/or their metabolites are likely to be necessary for their ultimate use for chemoprevention of human cancer.

<http://www.sciencedirect.com/science/article/pii/S0304383508003960>

<http://volcano.it/pubblicazioni/proprieta-anticancro-delle-antocianine.pdf>

29

Cancer (breast cancer)

Kędzierska M, Malinowska J, Kontek B, Kołodziejczyk-Czepas J, Czernek U, Potemski P, Piekarski J, Jeziorski A, Olas B.

Chemotherapy modulates the biological activity of breast cancer patients plasma: the protective properties of black chokeberry extract

Food Chem Toxicol. 2013 Mar; 53: 126-32. doi: 10.1016/j.fct.2012.11.042. Epub 2012 Dec 5.

In breast cancer patients (before and during anti-cancer therapy) oxidative/nitrative damage to various molecules is observed. Furthermore, anti-cancer treatments may also influence the hemostatic properties of blood platelets and plasma. The aim of our study was to assess the effect of oxidative/nitrative stress (estimated by measurements of the levels of carbonyl groups and 3-nitrotyrosine in proteins – ELISA and C-ELISA methods, respectively; lipid peroxidation and total antioxidant level – TAS) on the selected parameters of hemostatic activity of plasma (the process of fibrin polymerization and lysis) collected from breast cancer patients after surgery and after various phases of chemotherapy (doxorubicin and cyclophosphamide). Subsequently, we also evaluated the level of oxidative/nitrative stress and hemostatic activity in plasma from these patients in the presence of the commercial extract of *Aronia melanocarpa* (Aronox®) *in vitro*. Patients were hospitalized in Department of Oncological Surgery and Department of Chemotherapy in Medical University of Lodz, Poland. We observed increased levels of biomarkers of oxidative/nitrative stress in plasma from patients with breast cancer (before or after surgery and after various phases of chemotherapy) in comparison to healthy group. Our further experiments demonstrated the hemostatic activity of plasma from the investigated patients differs from hemostatic properties of plasma obtained from healthy volunteers. We also recognize the existence of a relationship between oxidative stress (measured by the level of carbonyl groups) and changes of hemostasis in breast cancer patients after I and IV phases of chemotherapy. Moreover, the obtained results showed that the commercial extract from *A. melanocarpa* berries significantly reduced, *in vitro*

system, the oxidative/nitrative stress and hemostasis changes in plasma from breast cancer patients, after surgery and different phases of chemotherapy. Considering the data presented in this study, we suggest that the oxidative/nitrative stress in plasma obtained from breast cancer patients (not only before or after the surgery, but also after various phases of doxorubicin and cyclophosphamide chemotherapy) may induce changes of hemostatic activity, which may contribute to thrombosis in these patients. Our results also suggest that the commercial extract of *A. melanocarpa* may be regarded as a promising new source of bioactive antioxidant natural compounds for breast cancer patients.

<http://www.ncbi.nlm.nih.gov/pubmed/23220617>

30

Cancer (breast, trial)

Yaneva MP, Botushanova AD, Grigorov LA, Kokov JL, Todorova EP, Krachanova MG

Evaluation of the immunomodulatory activity of *Aronia* in combination with apple pectin in patients with breast cancer undergoing postoperative radiation therapy

*Folia Med (Plovdiv)*. 2002; 44(1-2): 22-5.

The aim of the present study was to evaluate the immunomodulatory activity of *Aronia* in combination with apple pectin in patients with breast cancer in the course of postoperative radiation therapy. Monoclonal antibodies were used to assay specific T cell subsets. Tests were performed prior to and after 26 and 50 Gy of irradiation. The study comprised 42 women (19 to 65 years of age) receiving 15 g of apple pectin in combination with 20 ml of *Aronia* concentrate (Bioactive Substance Laboratory--Plovdiv) twice daily during postoperative irradiation. Irradiation was performed by a <sup>60</sup>Co-Rokus according to individualized treatment schedules. The following T lymphocyte populations were tested--CD3 total T lymphocytes, CD4 helper and inducer T cells, CD8 suppressor and cytotoxic T cells and NK cells. The levels of the polypeptide tissue antigen (TPA), an oncofetal protein, were tested in parallel. The TPA was used to assess treatment outcome in our patients. A group of 25 age-matched women with breast cancer served as controls. Immune status analysis of controls was performed prior to and following postoperative radiation. A total of 880 serum samples were tested. Assays of immunity parameters in the patients receiving *Aronia* in combination with apple pectin showed that CD4 and CD8 T cell counts increased significantly ( $P < 0.01$  and  $P < 0.05$  respectively). In control patients CD3 T cell levels lowered, the other T cell levels remained unchanged. Initially the number of NK cells was increased in both groups of patients. It remained constant throughout the course of the study. The normal levels of TPA in both groups of patients indicated a good treatment outcome due to the adequacy of surgery and in combination with radiation therapy.

<http://www.ncbi.nlm.nih.gov/pubmed/12422622>

31

Cancer (antimutagenic, anticarcinogenic, in vitro)

Gasiorowski K, Szyba K, Brokos B, Kolaczynska B, Jankowiak Włodarczyk M, Oszmianski J

Antimutagenic activity of anthocyanins isolated from Aronia melanocarpa fruits

Cancer Lett 1997; 119: 37-46

Anthocyanins belong to the flavonoid family and are ubiquitous in plants, especially in flower petals and fruit peels. We established that anthocyanins isolated from fruits of Aronia melanocarpa markedly inhibited the mutagenic activity of benzo(a)pyrene and 2-amino fluorene in the Ames test. In the Sister Chromatid Exchanges (SCEs) test with human blood-derived lymphocytes cultured in vitro, a significant decrease of SCEs frequency induced by benzo(a)pyrene was observed in the presence of anthocyanins. In the case of mitomycin C the effect of anthocyanins on SCEs frequency was smaller but still noticeable. Anthocyanins markedly inhibited the generation and release of superoxide radicals by human granulocytes. The results suggest that the antimutagenic influence of anthocyanins is exerted mainly by their free-radicals scavenging action as well as by the inhibition of enzymes activating promutagens and converting mutagens to the DNA-reacting derivatives. These preliminary data seem to be important in the aspect of a possible antimutagenic and anticarcinogenic potency of anthocyanins commonly present in fruits and vegetables.

[http://www.cancerletters.info/article/S0304-3835\(97\)00248-6/abstract](http://www.cancerletters.info/article/S0304-3835(97)00248-6/abstract)

32

Cancer (cytoprotective, carcinogenic process, in vitro, in vivo)

Duthie S J.

Berry phytochemicals, genomic stability and cancer: evidence for chemoprotection at several stages in the carcinogenic process

Mol Nutr Food Res 2007; 51: 665-74

Consumption of a diet high in plant-based foods is associated with a decreased risk of epithelial cell cancers at several sites. Cytoprotectants in fruits and vegetables include vitamins, minerals and numerous micronutrients. While there is little evidence uniquely linking berry consumption with lower cancer risk, berries contain high levels of compounds believed to reduce malignant transformation, including the polyphenol flavonoids and anthocyanins. There is strong and convincing evidence that berry

extracts and berry phytochemicals modulate biomarkers of DNA damage and indicators of malignant transformation in vitro and in vivo. Data from numerous cell culture and animal models indicate that berry components such as the anthocyanins are potent anticarcinogenic agents and are protective against genomic instability at several sites in the carcinogenic pathway. Anticarcinogenic mechanisms include modulation of carcinogen activation and detoxification, decreased DNA binding of the carcinogen, inhibition of oxidative DNA damage, alteration in cell signalling and malignant transformation and inhibition of cell invasiveness and metastasis. Exactly which berry constituents are cytoprotective remains uncertain and in the majority of in vitro and in vivo studies the concentration of extract or phytochemical employed is non-nutritional. Evidence for an anticarcinogenic effect in human studies is weak.

<http://www.ncbi.nlm.nih.gov/pubmed/17487926>

33

Cancer (cervical tumors, in vitro)

Rugină D, Sconța Z, Leopold L, Pinteș A, Bunea A, Socaciu C

Antioxidant activities of chokeberry extracts and the cytotoxic action of their anthocyanin fraction on HeLa human cervical tumor cells.

J Med Food. 2012 Aug; 15(8): 700-6. doi: 10.1089/jmf.2011.0246. Epub 2012 Jun 25.

The present study evaluates the antioxidant activity of two *Aronia melanocarpa* cultivars – Viking and Aron – and of *Aronia prunifolia* hybrid in relationship with their phytochemical composition regarding the contents of total phenolics, flavonoids, procyanidins, and monomeric anthocyanins. The antioxidant capacity of the mentioned extracts of chokeberries was evaluated through five complementary assays: 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid), H<sub>2</sub>O<sub>2</sub> scavenging potential, oxygen radical absorbance capacity, ferric reducing antioxidant power, and cupric ion reducing antioxidant capacity. *A. prunifolia* hybrid was found to have the highest antioxidant activity and to be the richest in polyphenols, procyanidins, and anthocyanins compared with the *A. melanocarpa* cultivars. A good correlation was observed between antioxidant activity and total procyanidin and anthocyanin content. Cyanidin glycosides inhibited HeLa human cervical tumor cell proliferation and increased generation of reactive oxygen species after 48 h of treatment, suggesting that they could be responsible for the antiproliferative activity. These results may be significant for industry concerning food quality and disease prevention.

<http://www.ncbi.nlm.nih.gov/pubmed/22846076>

34

Cancer (cytostatic inhibition, colon cancer)

Malik M, Zhao C W, Schoene N, Guisti M M, Moyer M P, Magnuson B A

Anthocyanin-rich extract from Aronia melanocarpa E. induces a cell cycle block in colon cancer but not normal colonic cells

Nutr Cancer 2003; 46: 186-96. DOI: 10.1207/S15327914NC4602\_12

Anthocyanin-rich extracts, potent antioxidants and commercially available food coloring agents, have been reported to inhibit growth of various cancer cell lines. We investigated the effect of semipurified anthocyanin-rich extract from fruits of Aronia melanocarpa, on normal colon and colon cancer cell lines. A 24-h exposure to 50 µg monomeric anthocyanin/ml of Aronia extract resulted in 60% growth inhibition of human HT-29 colon cancer cells. The treated cells showed a blockage at G1/G0 and G2/M phases of the cell cycle. The cell cycle arrest coincided with an increased expression of the p21WAF1 and p27KIP1 genes and decreased expression of cyclin A and B genes. Prolonged exposure to the extract resulted in no further change in the cell number, indicating a cytostatic inhibition of cell growth. NCM460 normal colon cells demonstrated <10% growth inhibition at the highest concentration of 50 µg/ml extract. A 35% decrease in the cyclooxygenase-2 gene expression was observed within 24 h of exposure of HT-29 cells but did not translate into decreased protein levels or protein activity. These results support the need for further research to identify the specific component(s) in this extract that suppress cancer cell growth and the genes affected by these natural compounds.

[http://www.tandfonline.com/doi/abs/10.1207/S15327914NC4602\\_12#.U6meOLHCfC8](http://www.tandfonline.com/doi/abs/10.1207/S15327914NC4602_12#.U6meOLHCfC8)

<http://www.encognitive.com/files/Anthocyanin-Rich%20Extract%20From%20Aronia%20meloncarpa%20E.%20Induces%20a%20Cell%20Cycle%20Block%20in%20Colon%20Cancer%20but%20Not%20Normal%20Colonic%20Cells.pdf>

35

Cancer (chemopreventive activity, inhibition of colon cancer)

Zhao C, Giusti M M, Malik M, Moyer M P, Magnuson B A

Effects of commercial anthocyanin-rich extracts on colonic cancer and nontumorigenic colonic cell growth

J Agric Food Chem 2004; 52: 6122-8

Commercially prepared grape (*Vitis vinifera*), bilberry (*Vaccinium myrtillus* L.), and chokeberry (*Aronia melanocarpa* E.) anthocyanin-rich extracts (AREs) were investigated for their potential chemopreventive activity against colon cancer. The growth of colon-cancer-derived HT-29 and nontumorigenic colonic NCM460 cells

exposed to semipurified AREs (10-75 µg of monomeric anthocyanin/mL) was monitored for up to 72 h using a sulforhodamine B assay. All extracts inhibited the growth of HT-29 cells, with chokeberry ARE being the most potent inhibitor. HT-29 cell growth was inhibited approximately 50% after 48 h of exposure to 25 µg/mL chokeberry ARE. Most importantly, the growth of NCM460 cells was not inhibited at lower concentrations of all three AREs, illustrating greater growth inhibition of colon cancer, as compared to nontumorigenic colon cells. Extracts were semipurified and characterized by high-pressure liquid chromatography, spectrophotometry, and colorimetry. Grape anthocyanins were the glucosylated derivatives of five different anthocyanidin molecules, with or without p-coumaric acid acylation. Bilberry contained five different anthocyanidins glycosylated with galactose, glucose, and arabinose. Chokeberry anthocyanins were cyanidin derivatives, monoglycosylated mostly with galactose and arabinose. The varying compositions and degrees of growth inhibition suggest that the anthocyanin chemical structure may play an important role in the growth inhibitory activity of commercially available AREs.

<http://www.ncbi.nlm.nih.gov/pubmed/15453676>

36

Cancer (chemoprevention, inhibited proliferation, colon cancer)

Bermudez-Soto M J, Larrosa M, Garcia-Cantalejo J M, Espin J C, Tomas-Barberan F A, Garcia-Conesa M

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

J Nutr Biochem 2007; 18: 259-71

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.

<http://www.ncbi.nlm.nih.gov/pubmed/16860979>

37

Cancer (chemoprotective, protective role in carcinogenesis, colon cancer, rats)

Lala G, Malik M, Zhao C W, He J, Kwon Y, Giusti M M et al.

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

Nutr Cancer 2006; 54: 84-93

The aim of the present study was to investigate the chemoprotective activity of anthocyanin-rich extracts (AREs) from bilberry (*Vaccinium myrtillus* L.), chokeberry (*Aronia melanocarpa* 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.

[http://www.tandfonline.com/doi/abs/10.1207/s15327914nc5401\\_10#.U6merLHCfC8](http://www.tandfonline.com/doi/abs/10.1207/s15327914nc5401_10#.U6merLHCfC8)

38

Cancer (colorectal cancer, review, meta-analysis)

Grodstein F, Newcomb PA, Stampfer MJ

Postmenopausal hormone therapy and the risk of colorectal cancer: a review and meta-analysis

Am J Med 1999; 106: 574–582.

Colorectal cancer is the fourth most common cancer and the second leading cause of cancer death in the United States. Accumulating evidence indicates that postmenopausal hormone therapy may reduce the risk of colorectal cancer in women. Through MEDLINE computer searches (January 1966 to September 1998) and a review of references, we identified English-language articles with quantitative data on the relation of postmenopausal hormone therapy to colorectal cancer. We reviewed the studies and made summary estimates of relative risks (RR) by weighting the results of each study in proportion to its precision, using a general variance-based, fixed-effects model. In our meta-analysis of 18 epidemiological studies of postmenopausal hormone therapy and colorectal cancer, we found a 20% reduction [RR = 0.80, 95% confidence interval (CI), 0.74 to 0.86] in risk of colon cancer and a 19% decrease (RR = 0.81, 95% CI, 0.72 to 0.92) in the risk of rectal cancer for postmenopausal women who had ever taken hormone therapy compared with women who never used hormones. Much of the apparent reduction in colorectal cancer was limited to current hormone users (RR = 0.66, 95% CI, 0.59 to 0.74). CONCLUSION: Observational studies suggest a reduced risk of colorectal cancer among women taking postmenopausal hormones. There is biological evidence to support this association.

<http://www.ncbi.nlm.nih.gov/pubmed/10335731>

39

Cancer (chemopreventive agent, intestinal carcinogenesis, mice)

Cooke D, Schwarz M, Boocock D, Winterhalter P, Steward W P, Gescher A J. et al.

Effect of cyanidin-3-glucoside and an anthocyanin mixture from bilberry on adenoma development in the ApcMin mouse model of intestinal carcinogenesis – relationship with tissue anthocyanin levels

Int J Cancer 2006; 119: 2213-20

Anthocyanins are dietary flavonoids, which can prevent carcinogen-induced colorectal cancer in rats. Here, the hypotheses were tested that Mirtoselect, an anthocyanin mixture from bilberry, or isolated cyanidin-3-glucoside (C3G), the most abundant anthocyanin in diet, interfere with intestinal adenoma formation in the ApcMin mouse, a genetic model of human familial adenomatous polyposis, and that consumption of C3G or Mirtoselect generates measurable levels of anthocyanins in the murine biophase. ApcMin mice ingested C3G or Mirtoselect at 0.03, 0.1 or 0.3% in the diet for 12 weeks, and intestinal adenomas were counted. Plasma, urine and intestinal mucosa were analyzed for presence of anthocyanins by high-pressure liquid chromatography with detection by UV spectrophotometry (520 nm) or tandem mass spectrometry (multiple reaction monitoring). Ingestion of either C3G or Mirtoselect reduced adenoma load dose-dependently. At the highest doses of C3G and Mirtoselect

adenoma numbers were decreased by 45% ( $p < 0.001$ ) or 30% ( $p < 0.05$ ), respectively, compared to controls. Anthocyanins were found at the analytical detection limit in the plasma and at quantifiable levels in the intestinal mucosa and urine. Anthocyanin glucuronide and methyl metabolites were identified in intestine and urine. Total anthocyanin levels in mice on C3G or Mirtoselect were 43 ng and 8.1  $\mu\text{g/g}$  tissue, respectively, in the intestinal mucosa, and 7.2 and 12.3  $\mu\text{g/ml}$  in the urine. The efficacy of C3G and Mirtoselect in the ApcMin mouse renders the further development of anthocyanins as potential human colorectal cancer chemopreventive agents worthwhile.

<http://onlinelibrary.wiley.com/doi/10.1002/ijc.22090/full>

40

Cancer (chemopreventive and chemotherapeutic, human lung carcinoma, inhibits tumor, in vitro, in vivo)

Ding M, Feng R, Wang S Y, Bowman L, Lu Y, Qian Y. et al.

Cyanidin-3-glucoside, a natural product derived from blackberry, exhibits chemopreventive and chemotherapeutic activity

J Biol Chem 2006; 281: 17 359-68

Epidemiological data suggest that consumption of fruits and vegetables has been associated with a lower incidence of cancer. Cyanidin-3-glucoside (C3G), a compound found in blackberry and other food products, was shown to possess chemopreventive and chemotherapeutic activity in the present study. In cultured JB6 cells, C3G was able to scavenge ultraviolet B-induced  $\cdot\text{OH}$  and radicals. In vivo studies indicated that C3G treatment decreased the number of non-malignant and malignant skin tumors per mouse induced by 12-O-tetradecanolyphorbol-13-acetate (TPA) in 7,12-dimethylbenz[a]anthracene-initiated mouse skin. Pretreatment of JB6 cells with C3G inhibited UVB- and TPA-induced transactivation of NF- $\kappa$ B and AP-1 and expression of cyclooxygenase-2 and tumor necrosis factor- $\alpha$ . These inhibitory effects appear to be mediated through the inhibition of MAPK activity. C3G also blocked TPA-induced neoplastic transformation in JB6 cells. In addition, C3G inhibited proliferation of a human lung carcinoma cell line, A549. Animal studies showed that C3G reduced the size of A549 tumor xenograft growth and significantly inhibited metastasis in nude mice. Mechanistic studies indicated that C3G inhibited migration and invasion of A549 tumor cells. These findings demonstrate for the first time that a purified compound of anthocyanin inhibits tumor promoter-induced carcinogenesis and tumor metastasis in vivo.

<http://www.jbc.org/content/281/25/17359.full>

41

Cancer (chemopreventive agent, intestinal carcinogenesis, mice)

Cooke D, Schwarz M, Boocock D, Winterhalter P, Steward W P, Gescher A J. et al.

Effect of cyanidin-3-glucoside and an anthocyanin mixture from bilberry on adenoma development in the ApcMin mouse model of intestinal carcinogenesis relationship with tissue anthocyanin levels

Int J Cancer 2006; 119: 2213-20

Anthocyanins are dietary flavonoids, which can prevent carcinogen-induced colorectal cancer in rats. Here, the hypotheses were tested that Mirtoselect, an anthocyanin mixture from bilberry, or isolated cyanidin-3-glucoside (C3G), the most abundant anthocyanin in diet, interfere with intestinal adenoma formation in the ApcMin mouse, a genetic model of human familial adenomatous polyposis, and that consumption of C3G or Mirtoselect generates measurable levels of anthocyanins in the murine biophase. ApcMin mice ingested C3G or Mirtoselect at 0.03, 0.1 or 0.3% in the diet for 12 weeks, and intestinal adenomas were counted. Plasma, urine and intestinal mucosa were analyzed for presence of anthocyanins by high-pressure liquid chromatography with detection by UV spectrophotometry (520 nm) or tandem mass spectrometry (multiple reaction monitoring). Ingestion of either C3G or Mirtoselect reduced adenoma load dose-dependently. At the highest doses of C3G and Mirtoselect adenoma numbers were decreased by 45% ( $p < 0.001$ ) or 30% ( $p < 0.05$ ), respectively, compared to controls. Anthocyanins were found at the analytical detection limit in the plasma and at quantifiable levels in the intestinal mucosa and urine. Anthocyanin glucuronide and methyl metabolites were identified in intestine and urine. Total anthocyanin levels in mice on C3G or Mirtoselect were 43 ng and 8.1  $\mu\text{g/g}$  tissue, respectively, in the intestinal mucosa, and 7.2 and 12.3  $\mu\text{g/ml}$  in the urine. The efficacy of C3G and Mirtoselect in the ApcMin mouse renders the further development of anthocyanins as potential human colorectal cancer chemopreventive agents worthwhile.

<http://onlinelibrary.wiley.com/doi/10.1002/ijc.22090/full>

42

Cancer (cancer prevention, gastric adenocarcinoma)

P.H. Shih, C.T. Yeh, G.C. Yen

Effects of anthocyanidin on the inhibition of proliferation and induction of apoptosis in human gastric adenocarcinoma cells

Food and Chemical Toxicology, 43(10), 10/2005, pp. 1557–1566. DOI: 10.1016/j.fct.2005.05.001

Anthocyanins are naturally occurring reddish pigments that abundant in fruits and

vegetables. To investigate the mechanistic basis for the anti-tumor properties of anthocyanins, five aglycone (cyanidin, delphinidin, malvidin, pelargonidin, and peonidin) and four glycosylated (cyaniding-3-glucoside, malvidin-3-glucoside, pelargonidin-3-glucoside and peonidin-3-glucoside) anthocyanins were used to examine their effects on cell cycle progression and induction of apoptosis in human gastric adenocarcinoma AGS cells. The data from cell viability assay showed that malvidin exhibited the most potent anti-proliferation effect on AGS cells in a time- and dose-dependent manner ( $P < 0.05$ ). This event is accompanied the arrest of AGS cells at the G0/G1 phase by malvidin at the tested concentrations of 0–200  $\mu\text{M}$ . Cellular uptake of anthocyanin and anthocyanidin was confirmed by HPLC analysis and the intracellular accumulation of malvidin ( $24.9 \pm 1.1 \mu\text{M}/\text{mg}$  protein) was observed when treatment of AGS cells with malvidin for 12 h. In addition, an accumulation of AGS cells in sub-G1 phase (20% and 30% increase for 100 and 200  $\mu\text{M}$  of malvidin, respectively) was observed as well as by the appearance of a fraction of cells with an aneuploid DNA content. The occurrence of apoptosis induced by malvidin was confirmed by morphological and biochemical features, including apoptotic bodies formation, caspase-3 activation and poly(ADP-ribose) polymerase proteolysis. Furthermore, the mitochondrial membrane potential of apoptotic cells after treatment with malvidin was significantly lost and resulted in the elevation of Bax/Bcl-2 ratio for 1.6-fold against control for 100  $\mu\text{M}$  treatment. In addition, the malvidin treatment significantly increased the p38 kinase expression and inhibited the ERK activity, and the effects of malvidin on caspase-3 activation were blocked, respectively, by the ERK and p38 inhibitors. These findings suggest that growth inhibition and cytotoxicity of AGS cells by malvidin is involved in the induction of apoptosis rather than necrosis.

<http://www.sciencedirect.com/science/article/pii/S0278691505001456>

<http://volcano.it/pubblicazioni/propriet%C3%A0-anticancro-delle-antocianine-2.pdf>

43

Cancer (cancer prophylaxis, inhibitory effect, rats)

Atanasova-Goranova V K, Dimova P I, Pevicharova G T

Effect of food products on endogenous generation of N-nitrosamines in rats

Br J Nutr. 1997 Aug; 78(2): 335-45.

An experiment was conducted to study the efficacy of two tomato pastes and aronia nectar (fruit juice + pulp from the black chokeberry, *Aronia melanocarpa* Elliot) as inhibitors of nitrosamine production in cancer prophylaxis programmes. White male rats of the Wistar strain were employed in an acute trial. Aminopyrin+sodium nitrite (APSN) were used as precursors for generation of endogenous nitrosamine. The animals were allocated to different dietary groups and fed by intubation with APSN or APSN + food products. Introduction of tomato paste (TP), high-beta-carotene tomato

paste (HCTP) and aronia nectar (AN) as inhibitors of N-nitrosamine formation exerted a positive effect on blood and liver variables which was demonstrated by decreased concentrations of glutamic-oxaloacetic transaminase (EC 2.6.1.1), glutamic-pyruvic transaminase (EC 2.6.1.2) and uric acid in serum and lipid content in hepatocytes. Animals treated with APSN developed dystrophic changes in liver such as centrolobular necrosis, intense exangia, and enlarged cells with two, often large, pyknotic nuclei, while the structure of livers of rats fed with TP, HCTP or AN was well protected and almost normal. TP had a particularly beneficial effect on serum total protein and albumin concentrations as had AN on the urea value. The inhibitory effect of the food products used is explained by their chemical nature including pH, ascorbic index (ascorbate:nitrate), lycopene and beta-carotene contents.

<http://www.ncbi.nlm.nih.gov/pubmed/9301422>

[http://journals.cambridge.org/abstract\\_S0007114597001384](http://journals.cambridge.org/abstract_S0007114597001384)

44

Cancer (leukemia, pro-apoptotic effect in humans, chemotherapeutic)

Tanveer Sharif, Mahmoud Alhosin, Cyril Auger, Carole Minker, Jong-Hun Kim, Nelly Etienne-Selloum, Pierre Bories, Hinrich Gronemeyer, Annelise Lobstein, Christian Bronner, Guy Fuhrmann, Valérie B. Schini-Kerth

Aronia melanocarpa Juice Induces a Redox-Sensitive p73-Related Caspase 3-Dependent Apoptosis in Human Leukemia Cells

PLoS ONE 7(3): e32526. doi:10.1371/journal.pone.0032526

Polyphenols are natural compounds widely present in fruits and vegetables, which have antimutagenic and anticancer properties. The aim of the present study was to determine the anticancer effect of a polyphenol-rich Aronia melanocarpa juice (AMJ) containing 7.15 g/L of polyphenols in the acute lymphoblastic leukemia Jurkat cell line, and, if so, to clarify the underlying mechanism and to identify the active polyphenols involved. AMJ inhibited cell proliferation, which was associated with cell cycle arrest in G2/M phase, and caused the induction of apoptosis. These effects were associated with an upregulation of the expression of tumor suppressor p73 and active caspase 3, and a downregulation of the expression of cyclin B1 and the epigenetic integrator UHRF1. AMJ significantly increased the formation of reactive oxygen species (ROS), decreased the mitochondrial membrane potential and caused the release of cytochrome c into the cytoplasm. Treatment with intracellular ROS scavengers prevented the AMJ-induced apoptosis and upregulation of the expression of p73 and active caspase 3. The fractionation of the AMJ and the use of identified isolated compounds indicated that the anticancer activity was associated predominantly with chlorogenic acids, some cyanidin glycosides, and derivatives of quercetin. AMJ treatment also induced apoptosis of different human lymphoblastic leukemia cells (HSB-2, Molt-4 and CCRF-CEM). In addition, AMJ exerted a strong

pro-apoptotic effect in human primary lymphoblastic leukemia cells but not in human normal primary T-lymphocytes. Thus, the present findings indicate that AMJ exhibits strong anticancer activity through a redox-sensitive mechanism in the p53-deficient Jurkat cells and that this effect involves several types of polyphenols. They further suggest that AMJ has chemotherapeutic properties against acute lymphoblastic leukemia by selectively targeting lymphoblast-derived tumor cells.

<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0032526>

45

Cancer (cancer prevention, chemoprevention)

Li-Shu Wang, Gary D. Stoner

Anthocyanins and their role in cancer prevention

Cancer Letters, 269(2), 10/2008, pp. 281–290

The daily intake of anthocyanins in residents of the United States is estimated to be about 200 mg or about 9-fold higher than that of other dietary flavonoids. In this review, we summarize the latest developments on the anti-carcinogenic activities of anthocyanins and anthocyanin-rich extracts in cell culture models and in animal model tumor systems, and discuss their molecular mechanisms of action. We also suggest reasons for the apparent lack of correlation between the effectiveness of anthocyanins in laboratory model systems and in humans as evidenced by epidemiological studies. Future studies aimed at enhancing the absorption of anthocyanins and/or their metabolites are likely to be necessary for their ultimate use for chemoprevention of human cancer.

<http://www.sciencedirect.com/science/article/pii/S0304383508003960>

<http://volcano.it/pubblicazioni/propriet%C3%A0-anticancro-delle-antocianine.pdf>

46

Cancer (cancer prevention, anti-platelet action, in vitro)

Seeram NP

Berry fruits for cancer prevention: current status and future prospects

J Agric Food Chem 2008; 56: 630–635.

The aim of the present study was to investigate and compare the anti-platelet action of extracts from three different plants: bark of *Yucca schidigera*, seeds of grape and berries of *Aronia melanocarpa* (chokeberry). Anti-platelet action of tested extracts was

compared with action of well characterized antioxidative and anti-platelet commercial monomeric polyphenol-resveratrol. The effects of extracts on platelet adhesion to collagen, collagen-induced platelet aggregation and on the production of O<sub>2</sub>-\* in resting platelets and platelets stimulated by a strong platelet agonist-thrombin were studied. The in vitro experiments have shown that all three tested extracts (5-50 µg/ml) rich in polyphenols reduce platelet adhesion, aggregation and generation of O<sub>2</sub>-\* in blood platelets. Comparative studies indicate that all three plant extracts were found to be more reactive in reduction of platelet processes than the solution of pure resveratrol. The tested extracts due to their anti-platelet effects may play an important role as components of human diet in prevention of cardiovascular or inflammatory diseases, where blood platelets are involved

<http://www.ncbi.nlm.nih.gov/pubmed/18211019>

47

Cancer (strongly inhibited cancer cell, chemoprevention)

Boivin D, Blanchette M, Barette S, Moghrabi A, Béliveau R

Inhibition of cancer cell proliferation and suppression of TNF-induced activation of NfkappaB by edible berry juice

Anti-cancer Res 2007; 27: 937-948.

Strawberry, raspberry, black currant, red currant, white currant, gooseberry, high-bush blueberry, low-bush blueberry, velvet leaf blueberry, serviceberry, blackberry, black chokeberry, sea buckthorn and cranberry were evaluated for antioxidant capacity, anti-proliferative activity, anti-inflammatory activity, induction of apoptosis and cell cycle arrest. Results: The growth of various cancer cell lines, including those of stomach, prostate, intestine and breast, was strongly inhibited by raspberry, black currant, white currant, gooseberry, velvet leaf blueberry, low-bush blueberry, sea buckthorn and cranberry juice, but not (or only slightly) by strawberry, high-bush blueberry, serviceberry, red currant, or blackberry juice. No correlation was found between the anti-proliferative activity of berry juices and their antioxidant capacity ( $p > 0.05$ ). The inhibition of cancer cell proliferation by berry juices did not involve caspase-dependent apoptosis, but appeared to involve cell-cycle arrest, as evidenced by downregulation of the expression of cdk4, cdk6, cyclin D1 and cyclin D3. Of the 13 berries tested, juice of 6 significantly inhibited the TNF-induced activation of COX-2 expression and activation of the nuclear transcription factor NFκB. Conclusion: These results illustrate that berry juices have striking differences in their potential chemopreventive activity and that the inclusion of a variety of berries in the diet might be useful for preventing the development of tumors.

<http://ar.iiarjournals.org/content/27/2/937.full.pdf>

48

Cardiovascular (cardioprotective activity)

Kowalczyk E, Krzesiński P, Fijałkowski P, Błaszczak J, Kowalski J

The use of anthocyanins in the treatment of cardiovascular diseases [in Polish]

Pol Merkur Lekarski 2005, 19(109): 108–110

Anthocyanins are common ingredients of human diet, and the rich source of them are: aronia fruits, black currant, raspberry, grapes and apples. Because of their chemical structure they are able to influence many active substances in human body having antioxidative, antiinflammatory and cardioprotective activity.

<http://europepmc.org/abstract/MED/16194041>

49

Cardiovascular diseases (polyphenols, endothelial cells, platelet inhibition, vasodilator)

Valérie B. Schini-Kerth, Nelly Étienne-Selloum, Thierry Chataigneau, Cyril Auger

Vascular Protection by Natural Product-Derived Polyphenols: In Vitro and In Vivo Evidence

Planta Med 2011; 77: 1161-1167. DOI <http://dx.doi.org/10.1055/s-0030-1250737>

Epidemiological studies have indicated that regular intake of fruit and vegetables and beverages such as red wine and tea, which contain high levels of polyphenols, is associated with a reduced risk of cardiovascular diseases. The beneficial effect of polyphenol-rich natural products has been attributable, at least in part, to their direct effect on blood vessels, and in particular on endothelial cells. Indeed, polyphenols from tea, grapes, berries, and plants have been shown to activate endothelial cells to increase the formation of potent vasoprotective factors including nitric oxide (NO) and endothelium-derived hyperpolarizing factor. Experimental and clinical studies have also indicated that chronic intake of several polyphenol-rich natural products is able to improve endothelial dysfunction and to decrease vascular oxidative stress associated with major cardiovascular diseases such as hypertension. Altogether, these observations suggest that polyphenol-rich sources of natural products have the potential to improve the function of blood vessels and, hence, to protect the vascular system.

Both experimental and clinical studies performed during the last 15 years support the view that several natural sources of polyphenols such as grape-derived products, berries, tea, and plants are able to improve the endothelial function both in vitro and in vivo mostly by stimulating the endothelial formation of NO, a potent vasodilator

and inhibitor of platelet activation.

<https://www.thieme-connect.de/products/ejournals/pdf/10.1055/s-0030-1250737.pdf>

50

Cardiovascular (cardiovascular diseases, antioxidant, anthocyanins, rats)

Kowalczyk E, Kopff A, Niedworok J, Kopff M, Jankowski A

Anthocyanins – an adjunct to cardiovascular therapy?

Kardiol Pol 2002; 57: 332-6

Anthocyanins are one of the most important water-soluble plant pigments. They belong to flavonoids and are derivatives of 2-phenyl-6-hydroxy-3-pyren. They have antioxidant and anti-inflammatory properties and, therefore, may be potentially used to combat oxidative stress, frequently present in cardiovascular diseases. AIM: To assess the effects of anthocyanins from chokeberry (*Aronia Melanocarpa*) on some parameters of oxidation-reduction balance in an animal model. METHODS: Of 20 male Wistar rats, 10 received for 3 months pure water, and the other rats 10-100 mg/l of anthocyanins from *Aronia melanocarpa*. Afterwards, blood samples were collected for assessment of the (1) content of substances reacting with thiobarbituric acid – TBARS, (2) antioxidant status and glutathione peroxidase activity, (3) concentration of sulphhydryl groups, and (4) nitrite concentration. RESULTS: Anthocyanins significantly reduced the content of TBARS and thiol protein groups and non-significantly increased glutathione peroxidase activity, total content of antioxidants and nitrite concentration. CONCLUSIONS: Anthocyanins from chokeberry decrease lipid peroxidation which may be potentially used to combat oxidative stress.

<http://www.ncbi.nlm.nih.gov/pubmed/12917728>

51

Cardiovascular (myocardial infarction, prevention of ischaemic heart disease, humans, clinical trial)

Naruszewicz M1, Laniewska I, Millo B, Dłużniewski M

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

Atherosclerosis. 2007 Oct; 194(2): e179-84. Epub 2007 Feb 21.

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 release 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 infarction and have received statin therapy for at least 6 months (80% dose of 40 mg/day simvastatin) were included in the study. The subjects were randomised to receive either 3\*85 mg/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 7.2 mmHg, 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.

<http://www.ncbi.nlm.nih.gov/pubmed/17320090>

52

Cardiovascular (anti-platelet effects, ex vivo)

Ryszawa N, Kawczynska-Drozd A, Pryjma J, Czesnikiewicz-Guzik M, Adamek-Guzik T, Naruszewicz M. et al.

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

J Physiol Pharmacol 2006; 57: 611-26

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. Platelet superoxide production is increased in subjects with cardiovascular risk factor profile, which may precede changes in platelet aggregation itself. Novel polyphenol rich extracts of *A. melanocarpa* berries exert significant anti-platelet effects ex vivo.

<http://jpp.krakow.pl/>

[http://jpp.krakow.pl/journal/archive/12\\_06/pdf/611\\_12\\_06\\_article.pdf](http://jpp.krakow.pl/journal/archive/12_06/pdf/611_12_06_article.pdf)

53

Cardiovascular (Heart Disease/Cholesterol of former smokers)

Uconn

Bradley Bolling has been awarded \$417,076 for his research of consumption of Aronia berries and its impact on cardiovascular disease in former smokers. “Our hypothesis is that dietary chokeberry polyphenols reduce cardiovascular disease risk in former smokers by improving cholesterol profiles and inhibiting inflammation and oxidative stress,” Bolling says.

<http://today.uconn.edu/blog/2012/01/uconn-researchers-awarded-state-grants-for-study-of-tobacco-related-disease>

54

Cardiovascular (hypercholesterolemia)

Anna Skoczyńska, Iwona Jêdrychowska, Rafa Porêba, Anna Affelska- Jercha, Barbara Turczyn, Anna Wojakowska, Ryszard Andrzejak

Influence of chokeberry juice on arterial blood pressure and lipid parameters in men with mild hypercholesterolemia

Pharmacological Reports 2007, 59, suppl. 1, 177-182

Fifty eight healthy men with the diagnosed mild hypercholesterolemia without pharmacological treatment were enrolled to the study in 2006. In all men biochemical measurements were carried out 4 times: at the beginning, after 6 weeks of regular chokeberry juice drinking, after 6 weeks without the juice drinking, then repeated after 6 weeks of chokeberry juice drinking. Laboratory tests included: total, low density lipoprotein (LDL), and high density lipoprotein (HDL) cholesterol and its subfractions: HDL and HDL<sup>2</sup>, triglycerides, lipid peroxides (LPO), C-reactive high sensitivity protein (hsCRP), homocysteine, fibrinogen, glucose and antioxidant vitamins. Regular chokeberry juice drinking resulted in reduction of total cholesterol level ( $p < 0.001$ ) and LDL cholesterol ( $p < 0.01$ ) and triglycerides ( $p < 0.001$ ), and increased HDL cholesterol ( $p < 0.001$ ) level. Moderate but significant decreases in the serum glucose ( $p < 0.05$ ), homocysteine ( $p < 0.001$ ) and fibrinogen ( $p < 0.01$ ) concentrations were also observed. These beneficial metabolic changes were associated with significant hypotensive effect of chokeberry juice drinking. Our studies showed that drinking of Aronia melanocarpa fruit juice may have a beneficial effect on reduction of cardiovascular risk.

[http://www.if-pan.krakow.pl/pjp/pdf/2007/s1\\_177.pdf](http://www.if-pan.krakow.pl/pjp/pdf/2007/s1_177.pdf)

55

Cardiovascular (hypercholesterolemia, in vivo)

Piotr Duchnowicz, Agnieszka Nowicka, Maria Koter-Michalak, Marlena Broncel

In vivo influence of extract from Aronia melanocarpa on the erythrocyte membranes in patients with hypercholesterolemia

Med Sci Monit 2012; 18(9): CR569-574. DOI: 10.12659/MSM.883353

Background: Hypercholesterolemia increases cholesterol concentration in erythrocyte membranes, which results in decrease of membrane fluidity and decreases the deformability of red blood cells. The fruits of Aronia melanocarpa contains many of polyphenols and other compounds that have beneficial health effects.

Material/Methods: The aim of the study was to estimate the influence of 2-month supplementation of extract from Aronia melanocarpa (100 mg Aronox, three times per day) on cholesterol concentration, lipid peroxidation, membrane fluidity, level of thiol groups and activity of ATPase in erythrocytes from patients with hypercholesterolemia. The study involved 25 patients with hypercholesterolemia without pharmacological treatment and 20 healthy individuals as a control group. Blood samples were collected before, and after 1 and 2 months of Aronia administration. Results: The 2-month Aronia supplementation resulted in a decrease of cholesterol concentration (by 22%) and a decrease of lipid peroxidation (by 40%), and an increase of membrane fluidity. No statistically significant increase of the concentration of thiol groups and of ATPase activity were observed. Conclusions: Our study shows that supplementation of extract from Aronia melanocarpa has a beneficial

effect on rheological properties of erythrocytes.

<http://medscimonit.com/abstract/index/idArt/883353>

56

Cardiovascular (hyperlipidemia)

S. Valcheva-Kuzmanova, K. Kuzmanov, S. Tsanova-Savova, V. Mihova, I. Krasnaliev, P. Borisova and A. Belcheva

Lipid-lowering effects of aronia melanocarpa fruit juice in rats fed cholesterol-containing diets

Hyperlipidemia characterized by an increase in low-density lipoprotein (LDL) cholesterol and a decrease in high-density lipoprotein cholesterol is one of the major risk factors for atherosclerosis and cardiovascular disease. Plant foods with high contents of phenolic phytochemicals are reported to be inversely correlated with plasma total cholesterol (TC) and LDL cholesterol. Aronia melanocarpa fruits are remarkably rich in phenolic substances. They are used for human consumption as juice, syrup, jam and wine. Our research demonstrated that A. melanocarpa fruit juice hindered the dietary-induced elevation of plasma TC, LDL cholesterol and triglycerides in rats. In view of the results from our experiment, we can suppose that the juice may be further tested for reducing hyperlipidemia in humans and possibly approved a valuable dietary supplement.

<http://onlinelibrary.wiley.com/doi/10.1111/j.1745-4514.2007.00132.x/abstract?>

57

Cardiovascular (blood pressure, clinical trial, infraction, statin, placebo, flavonoids)

Marek A. Naruszewicz

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

Official Journal of the European Atherosclerosis Society, 194(2), 10/2007, 179-184.

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 infarction and have received statin therapy for at least 6 months (80% dose of 40 mg/day simvastatin) were included in the study. The subjects were randomised to receive either 3× 85 mg/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 procyanidins (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 7.2 mmHg, 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.

<http://www.sciencedirect.com/science/article/pii/S0021915007000299>

<http://home.ueb.cas.cz/COST926/Naruszewicz2008.pdf>

58

Cardiovascular (blood pressure, oxidative stress, endothelin, metabolic syndrome)

Marlena Broncel, Marzena Koziróg, Piotr Duchnowicz, Maria Koter-Michala, Joanna Sikora, Julita Chojnowska-Jeziarska

*Aronia melanocarpa* extract reduces blood pressure, serum endothelin, lipid, and oxidative stress marker levels in patients with metabolic syndrome

Med Sci Monit. 2010 Jan;16(1):CR28-34.

It should be noted that non-anthocyanin components of *Aronia melanocarpa* might also play special biological roles. *Aronia melanocarpa* is rich not only in anthocyanins, but also in flavonols, phenolic acids, and procyanidins. The results of a study conducted in healthy volunteers revealed that epicatechin, catechin, and procyanidin induced nitric-oxide-dependent vasodilation (measured by plethysmography) [38]. Experiments on animals revealed that administration of the flavonoids epicatechin and epigallocatechin markedly lowered lymphatic cholesterol absorption in rats with a cannulated thoracic duct [40] and reduced the deposition of visceral fat and the concentration of hepatic triacylglycerol. The results of this study show that anthocyanins from *Aronia melanocarpa* may be of benefit to patients with MS as far as atherosclerosis prevention is concerned. It seems to result from anthocyanins' influence on blood pressure, ET-1 level, serum lipids, and oxidative status (GSH-Px, SOD, TBARS).

<http://www.basic.medscimonit.com/abstract/index/idArt/878315>

<http://www.aronslim.pl/data/aronia%20reduces%20blood%20pressure,...lipid%20in%20patients%20with%20metabolic%20syndrome.pdf>

59

Cardiovascular (blood clotting, in vitro)

Bijak M, Bobrowski M, Borowiecka M, Podsędek A, Golański J, Nowak P

Anticoagulant effect of polyphenols-rich extracts from black chokeberry and grape seeds. *Journal of Phytotherapy*

*Fitoterapia*. 2011 Sep; 82(6): 811-7. doi: 10.1016/j.fitote.2011.04.017. Epub 2011 May 6.

Blood coagulation consists of a series of zymogens that can be converted by limited proteolysis to active enzymes leading to the generation of thrombin. Fresh plasma and human thrombin was incubated with extracts from berries of *Aronia melanocarpa* or seeds of *Vitis vinifera* (0.5; 5; 50 µg/ml). The in vitro experiments showed that both extracts prolonged clotting time and decreased the maximal velocity of fibrin polymerization in human plasma. Moreover thrombin incubation with both extracts results in the inhibition of amidolytic activity of this enzyme. It gives hopes for development of diet supplements, which may be preventing thrombosis in pathological states.

<http://www.ncbi.nlm.nih.gov/pubmed/21596108>

60

Cardiovascular (anthocyanin extracts, vascular disease, vasoactive, vasoprotective, in vitro)

Bell DR, Gochenaur K

Direct vasoactive and vasoprotective properties of anthocyanin-rich extracts

*J Appl Physiol*. 2006 Apr; 100(4):1164-70. Epub 2005 Dec 8.

“These results suggest that such extracts could have significant beneficial effects in vascular disease.”

Reactive oxygen species (ROS) play a critical role in the impairment of nitric oxide-mediated vascular functions and overall pathogenesis associated with cardiovascular disease. Plant pigment anthocyanins are exceptionally potent oxygen radical scavengers that produce beneficial effects in diseases outside the cardiovascular system. We examined for the first time the potential coronary vasoactive and vasoprotective properties of three anthocyanin enhanced extracts prepared from

chokeberry (Ck), bilberry (B), or elderberry (E). Coronary arterial rings were isolated from 64 pigs and incubated in sterile tissue culture media overnight for use in one of four separate in vitro isometric force recording studies. Ck and B, but not E, produced dose- and endothelium-dependent vasorelaxation. (%maximal relaxation at 5 mg total anthocyanins per liter: Ck = 68 +/- 11, B = 59 +/- 10). Coronary vascular tone, endothelium-dependent vasorelaxation to A23187, and vasorelaxation to DEA NONOate were not affected by exposure of rings to any extract at 0.05 mg total anthocyanins per liter for 5 or 30 min. Ck extract at 0.05 mg total anthocyanins per liter showed the greatest protection against loss of A23187 relaxation following exposure to ROS from pyrogallol (Ck, % maximal relaxation and -logED50 to A23187, respectively, means +/- SE: Ck alone, 93 +/- 5%, 7.91 +/- 0.1; pyrogallol alone, 76 +/- 7%, 7.46 +/- 0.06; pyrogallol + Ck, 98 +/- 1%, 7.82 +/- 0.06; control: 99 +/- 1%, 7.86 +/- 0.07; P < 0.05 control vs. pyrogallol alone). Neither the extracts nor pyrogallol affected responses to DEA NONOate. Thus anthocyanin-enhanced extracts produce endothelium-dependent relaxation in porcine coronary arteries. Extract concentrations too low to directly alter coronary vascular tone protect coronary arteries from ROS without altering vasorelaxation to endogenous or exogenous NO. These results suggest that such extracts could have significant beneficial effects in vascular disease.

<http://www.ncbi.nlm.nih.gov/pubmed/16339348>

<http://jap.physiology.org/content/100/4/1164.full.pdf>

61

Cardiovascular (myocardial infarction, reduced risk, women)

Aedín Cassidy, PhD; Kenneth J. Mukamal, MD; Lydia Liu, MSc; Mary Franz, MSc; A. Heather Eliassen, ScD; Eric B. Rimm, ScD

High Anthocyanin Intake Is Associated With a Reduced Risk of Myocardial Infarction in Young and Middle-Aged Women

Circulation. 2013; 127: 188-196. doi: 10.1161/CIRCULATIONAHA.112.122408

Background—Our current knowledge of modifiable risk factors to prevent myocardial infarction (MI) in young and middle-aged women is limited, and the impact of diet is largely unknown. Dietary flavonoids exert potential beneficial effects on endothelial function in short-term trials; however, the relationship between habitual intake and risk of MI in women is unknown. Methods and Results—We followed up 93 600 women 25 to 42 years of age from the Nurses' Health Study (NHS) II who were healthy at baseline (1989) to examine the relationship between anthocyanins and other flavonoids and the risk of MI. Intake of flavonoid subclasses was calculated from validated food-frequency questionnaires collected every 4 years using an updated and extended US Department of Agriculture database. During 18 years of follow-up, 405 cases of MI were reported. An inverse association between higher intake of

anthocyanins and risk of MI was observed (hazard ratio, 0.68; 95% confidence interval, 0.49–0.96;  $P=0.03$ , highest versus lowest quintiles) after multivariate adjustment. The addition of intermediate conditions, including history of hypertension, did not significantly attenuate the relationship (hazard ratio, 0.70; 95% confidence interval, 0.50–0.97;  $P=0.03$ ). Combined intake of 2 anthocyanin-rich foods, blueberries and strawberries, tended to be associated with a decreased risk of MI (hazard ratio, 0.66; 95% confidence interval, 0.40–1.08) in a comparison of those consuming >3 servings a week and those with lower intake. Intakes of other flavonoid subclasses were not significantly associated with MI risk. Conclusions—A high intake of anthocyanins may reduce MI risk in predominantly young women. Intervention trials are needed to further examine the health impact of increasing intakes of commonly consumed anthocyanin-rich foods.

<http://circ.ahajournals.org/content/127/2/188>

62

Cardiovascular (reduced cardiovascular disease risk, women)

Amy Jennings, Ailsa A Welch, Sue J Fairweather-Tait, Colin Kay, Anne-Marie Minihane, Phil Chowienczyk, Benyu Jiang, Marina Cecelja, Tim Spector, Alex Macgregor, Aedín Cassidy

Higher anthocyanin intake is associated with lower arterial stiffness and central blood pressure in women

Am J Clin Nutr 10/2012, 96(4): 781-788. doi: 10.3945/ajcn.112.042036

Background: Although a high intake of some flavonoid subclasses may reduce cardiovascular disease mortality, data regarding the *in vivo* mechanisms of action are limited. Objective: We examined associations between habitual flavonoid intakes and direct measures of arterial stiffness, central blood pressure, and atherosclerosis.

Design: In a cross-sectional study of 1898 women aged 18–75 y from the Twins UK registry, intakes of total flavonoids and their subclasses (flavanones, anthocyanins, flavan-3-ols, polymers, flavonols, and flavones) were calculated from validated food-frequency questionnaires by using an updated and extended USDA database. Direct measures of arterial stiffness and atherosclerosis included central systolic blood pressure (cSBP), central diastolic blood pressure, mean arterial pressure (MAP), augmentation index, pulse wave velocity (PWV), and intima-media thickness.

Results: In multivariate analyses, a higher anthocyanin intake was associated with significantly lower cSBP (mean  $\pm$  SE:  $-3.0 \pm 1.4$  mm Hg for quintile 5 compared with quintile 1;  $P$ -trend = 0.02), MAP ( $-2.3 \pm 1.2$  mm Hg for quintile 5 compared with quintile 1;  $P$ -trend = 0.04), and PWV ( $-0.4 \pm 0.2$  m/s for quintile 5 compared with quintile 1;  $P$ -trend = 0.04), whereas a higher flavone intake was associated with a lower PWV ( $-0.4 \pm 0.2$  m/s for quintile 5 compared with quintile 1;  $P$ -trend = 0.04). Although a higher wine and berry intake was associated with a lower PWV, no associations were observed for total and other flavonoid subclasses. Conclusions:

These data, which include direct measures of arterial stiffness and thickness, suggest that higher intake of anthocyanins and flavones are inversely associated with lower arterial stiffness. The intakes of anthocyanins associated with these findings could be incorporated into the diet by the consumption of 1–2 portions of berries daily and are, therefore, relevant for public health strategies to reduce cardiovascular disease risk.

<http://ajcn.nutrition.org/content/96/4/781.abstract>

63

Cardiovascular (arterial hypertension, reduce oxidative stress, prophylactic agent, nutritional supplement)

Manuela Ciocoiu, Laurentiu Badescu, Anca Miron, Magda Badescu

The Involvement of a Polyphenol-Rich Extract of Black Chokeberry in Oxidative Stress on Experimental Arterial Hypertension

Evidence-Based Complementary and Alternative Medicine, vol. 2013, Article ID 912769, 8 pages, 2013. doi:10.1155/2013/912769

The aim of this study is to characterize the content of Aronia melanocarpa Elliott (black chokeberry) extract and also to estimate the influence of polyphenolic compounds contained in chokeberries on oxidative stress, on an L-NAME-induced experimental model of arterial hypertension. The rat blood pressure values were recorded using a CODA Noninvasive Blood Pressure System. HPLC/DAD coupled with ElectroSpray Ionization-Mass Spectrometry allowed identification of five phenolic compounds in berries ethanolic extract as follows: chlorogenic acid, kuromanin, rutin, hyperoside, and quercetin. The serous activity of glutathione-peroxidase (GSH-Px) has significantly lower values in the hypertensive (AHT) group as compared to the group protected by polyphenols (AHT + P). The total antioxidant capacity (TAC) values are lower in the AHT group and they are significantly higher in the AHT + P group. All the measured blood pressure components revealed a biostatistically significant blood pressure drop between the AHT group and the AHT + P group. The results reveal the normalization of the reduced glutathion (GSH) concentration as well as a considerable reduction in the malondialdehyde (MDA) serum concentration in the AHT + P group. Ethanolic extract of black chokeberry fruits not only has a potential value as a prophylactic agent but also may function as a nutritional supplement in the management of arterial hypertension. Ethanolic extract of black chokeberry fruits has a potential value as prophylactic agent, but also may function as a nutritional supplement in the therapy of arterial hypertension. The role of the polyphenolic extract of Aronia melanocarpa is to prevent the total antioxidant capacity decrease and also to reduce the oxidative stress. Knowing the cellular and molecular mechanisms through which each compound of the Aronia melanocarpa extract acts in arterial hypertension requires further studies.

<http://www.hindawi.com/journals/ecam/2013/912769/>

64

Cardiovascular (coronary arteries, vasorelaxation, porcine)

Bell D R, Burt T D

Phenolic acids contained in anthocyanin enriched extracts from elderberry, bilberry and chokeberry possess endothelium dependent and independent vasorelaxation properties in porcine coronary arteries

Faseb J. 2007; 21: A366

We have reported previously that anthocyanin-enriched extracts from Elderberry, Bilberry and Chokeberry differ in their vasodilator and vasoprotective effects in coronary arteries. These differences appear to be related more to differences in the total phenolic content of the extracts than to differences in their anthocyanin profiles. Therefore we examined in vitro dose-response relationships to 6 phenolic acids (1nM-3uM) in isolated, precontracted porcine coronary arterial rings, +/- endothelium, from 18 female pigs to determine the vasoactive profile of phenolic acids believed to be present in our berry extracts. Arteries relaxed to cumulative log additions of coumaric, caffeic, ferulic, or chlorogenic acid, but were unresponsive to gallic or ellagic acid. Vasorelaxation and its endothelium contribution were least for chlorogenic acid (max relaxation = 69±5%, +endothelium; 43±16%, -endothelium) and greatest for coumaric acid (max relaxation = 89±11%, +endothelium; 14±4% -endothelium) with half maximal doses for coumaric acid less than 30 nM. We conclude that phenolic acids produce vasorelaxation in coronary arteries with varying degrees of efficacy and dependence on the vascular endothelium. It is likely that these acids contribute significantly to the endothelium dependent vasorelaxation properties of anthocyanin-enriched extracts from chokeberry, bilberry and elderberry.

[http://www.fasebj.org/cgi/content/meeting\\_abstract/21/5/A366-c](http://www.fasebj.org/cgi/content/meeting_abstract/21/5/A366-c)

65

Cardiovascular (hypercholesterolemia, endothelial function, men)

Poreba R, Skoczynska A, Gac P, Poreba M, Jedrychowska I, Affelska-Jercha A, Turczyn B, Wojakowska A, Oszmianski J, Andrzejak R

Drinking of chokeberry juice from the ecological farm Dzieciolowo and distensibility of brachial artery in men with mild hypercholesterolemia

Ann Agric Environ Med. 2009 Dec; 16(2): 305-8.

“This study showed that regularly drinking aronia juice had a statistically significant increase in serum nitric oxide (NO) concentration and in the flow mediated dilatation

(FMD). 35 of 35 patients with moderately high cholesterol had a  $\geq 7\%$  increase in FMD after consumption of aronia juice.”

The aim of the study was to estimate the influence of drinking chokeberry juice on the endothelial function in men with mild hypercholesterolemia. It was shown that chronic treatment with flavonoids improves vascular function and reduces cardiovascular remodelling by increasing NO release from endothelial cells. A group of 35 men diagnosed with mild hypercholesterolemia (mean age: 53.9  $\pm$  5.8 years), with no earlier pharmacological treatment, were enrolled to the study. In all men, assessment of endothelial function, and serum lipids level were carried out at four time points: at the beginning of the studies, after 6 weeks of regular drinking of chokeberry juice, after 6 weeks without drinking the juice, then after repeated 6 weeks of drinking chokeberry juice. During the study, significant decreases in serum total cholesterol, LDL cholesterol and triglycerides levels were observed. A statistically significant increase in serum nitric oxide (NO) concentration and in the flow mediated dilatation (FMD) were observed. At the beginning, FMD  $\geq 7\%$  was present in 13 of 35 subjects (37.1 %). After 6 weeks of regular chokeberry juice drinking, FMD  $\geq 7\%$  was present in 29 of 35 subjects (82.9 %). However, after 6 weeks abstaining from drinking the juice and repeated exposure to 6 weeks drinking of chokeberry juice, FMD  $\geq 7\%$  was present in all studied subjects. Regular drinking of chokeberry juice has a beneficial effect on endothelial function and lipid metabolism in men with mild hypercholesterolemia. This study showed that regularly drinking aronia juice had a statistically significant increase in serum nitric oxide (NO) concentration and in the flow mediated dilatation (FMD). 35 of 35 patients with moderately high cholesterol had a  $\geq 7\%$  increase in FMD after consumption of aronia juice.

<http://www.ncbi.nlm.nih.gov/pubmed/20047267>

66

Cardiovascular (cholesterol, antihyperlipidemic, rats)

Valcheva-Kuzmanova S, Kuzmanov K, Mihova V, Krasnaliev I, Borisova P, Belcheva A

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

Plant Foods Hum Nutr. 2007 Mar;62(1):19-24. Epub 2006 Nov 29.

Rats fed a high cholesterol diet along with aronia berries showed no increase in LDL and total cholesterol concentrations, vs control. 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.

<http://www.ncbi.nlm.nih.gov/m/pubmed/17136466/>

67

Diabetes (prediabetes, hyperlipidemia, metabolic syndrome, supplementary therapeutic option, rats)

Adam Jurgoński, Jerzy Juśkiewicz, Zenon Zduńczyk

Ingestion of black chokeberry fruit extracts leads to intestinal and systemic changes in a rat model of prediabetes and hyperlipidemia

Plant Food Hum Nutr 2008; 4: 176–182

This report presents a complex analysis of changes proceeding in the gut, blood and internal organs of rats with induced oxidative stress, glucose intolerance and hyperlipidemia after dietary supplementation with an extract from black chokeberry (*Aronia melanocarpa*) fruit, that is a condensed source of polyphenols (714 mg/g), especially anthocyanin glycosides (56.6%). The disturbances mimicking those observed in metabolic syndrome were induced by a high-fructose diet and simultaneous single injection of streptozotocin (20 mg/kg). Dietary supplementation with the chokeberry fruit extract (0.2%) decreased activity of maltase and sucrase as well as increased activity of lactase in the mucosa of the small intestine. Its ingestion led also to the improvement of antioxidant status, especially, the concentration of a lipid peroxidation indicator (TBARS) in organ tissues (liver, kidney and lung) was normalized; some cholesterol-lowering and distinct hypoglycemic actions were also observed. The mechanism of glucose reduction is likely to be multifactorial, and we suggest the factors related with the decreased activity of mucosal disaccharidases important for further investigation. In conclusion, chokeberry fruit derivatives may act as a promising supplementary therapeutic option in the prevention and treatment of disorders occurring in metabolic syndrome, as well as their complications.

<http://link.springer.com/article/10.1007%2Fs11130-008-0087-7>

68

Diabetes (prevention, diabetes complications, pentosidine, flavonoids, oral intake)

Urios P, Grigorova-Borsos A M, Peyroux J, Sternberg M

Inhibition of advanced glycation by flavonoids. A nutritional implication for preventing diabetes complications

J Soc Biol 2007; 201: 189-98

Advanced glycation of collagens contributes to development of micro- and macrovascular complications in diabetes. Since flavonoids are potent natural antioxidants, it was interesting to examine their effect on the formation of a cross-linking advanced glycation endproduct, pentosidine, in collagen incubated with glucose. Monomeric flavonoids (25 and 250 microM) markedly reduced pentosidine/hydroxyproline values in a concentration- and structure-dependent manner. Procyanidin oligomers from grape seed were more active than pine bark procyanidin oligomers. Oligomers are known to be cleaved into monomers in the gastric milieu and monomeric flavonoids to be absorbed and recovered at micromolar concentrations (with a long plasmatic half-life) in extracellular fluids, in contact with collagens. In conclusion, flavonoids are very potent inhibitors of pentosidine formation in collagens, active at micromolar concentrations; these concentrations might be achieved in plasma of diabetic patients after oral intake of flavonoids.

<http://europepmc.org/abstract/MED/17978753>

69

Diabetes (prevention, diabetes mellitus, complications, hypoglycemic effects, rats)

Valcheva-Kuzmanova S, Kuzmanov K, Tancheva S, Belcheva A

Hypoglycemic effects of Aronia melanocarpa fruit juice in streptozotocin-induced diabetic rats

Methods Find Exp Clin 2007; 29: 101–105.

AMFJ was applied by gavage at doses of 10 and 20 ml/kg for 6 weeks to normal and diabetic rats. Streptozotocin caused a significant elevation of plasma glucose by 141% and of plasma triglycerides (TG) by 64% in comparison with normal control rats and induced statistically insignificant elevations of total cholesterol and LDL-cholesterol and a reduction of HDL-cholesterol. Applied to normal rats, AMFJ did not influence plasma glucose and lipid levels. Applied to diabetic rats, AMFJ (10 and 20 ml/kg) significantly reduced plasma glucose by 44% and 42% and TG by 35% and 39%, respectively, to levels that did not significantly differ from those of the normal control rats and counter- acted the influence of streptozotocin on total cholesterol, LDL-

cholesterol and HDL-cholesterol. In conclusion, AMFJ significantly decreased the streptozotocin-induced abnormalities in blood glucose and TG in diabetic rats and might be useful in prevention and control of diabetes mellitus and diabetes-associated complications.

[http://journals.prous.com/journals/servlet/xmlxsl/pk\\_journals.xml\\_summary\\_pr?p\\_JournalId=6&p\\_RefId=1075349&p\\_IsPs=N](http://journals.prous.com/journals/servlet/xmlxsl/pk_journals.xml_summary_pr?p_JournalId=6&p_RefId=1075349&p_IsPs=N)

<http://www.aronslim.pl/data/Hypoglycemic%20and%20Hypolipidemic%20Effects%20of%20Aronia%20melanocarpa.pdf>

70

Diabetes (diabetes mellitus, hypoglycemic, dietary treatment)

Simeonov S B, Botushanov N P, Karahanian E B, Pavlova M B, Husianitis H K, Troev D M

Effects of Aronia melanocarpa juice as part of the dietary regimen in patients with diabetes mellitus

Folia Med (Plovdiv) 2002; 44: 20-3

The low calorie juice Aronia melanocarpa (sugar free, with artificial sweeteners) could be a valuable adjunct to the complex therapy of patients with diabetes mellitus. In this study no increased blood glucose levels were established 60 min. following ingestion of 200 ml Aronia juice. On the contrary, lower fasting blood glucose concentrations were measured in 16 patients with insulin dependent diabetes and in 25 patients with non-insulin dependent diabetes (25 women and 16 men, 3 to 62 years of age, median age 38.8 +/- 4.7) with duration of the disease from 1 month to 13 years. Serial blood glucose measurements showed: 14.23 +/- 1.32 mmol/l at baseline and 11.4 +/- 0.89 mmol/l blood glucose level after 60 min., the difference being statistically significant ( $p < 0.05$ ). The ingestion of 200 ml Aronia juice combined with a standard breakfast produced similar results (the basal concentration of glucose was 13.43 +/- 1.12 mmol/l; it decreased to 11.94 +/- 1.02 mmol/l at 60 min., the difference did not reach statistical significance. The daily intake of 200 ml Aronia juice over a period of 3 months was effective in lowering fasting blood glucose levels from 13.28 +/- 4.55 mmol/l to 9.10 +/- 3.05 mmol/l ( $p < 0.001$ ) in 21 patients with non-insulin dependent diabetes – 13 women and 8 men aged from 42 to 62 (median age 53.6 +/- 3.65) with disease duration from 6 to 17 years. Aronia had a beneficial effect on HbA1c, total cholesterol and lipid levels. They dropped from 9.39 +/- 2.16% to 7.49 +/- 1.33% ( $p < 0.001$ ), from 6.45 +/- 1.59 mmol/l to 5.05 +/- 0.96 mmol/l ( $p < 0.001$ ) and from 2.92 +/- 2.15 mmol/l to 1.7 +/- 1.07 mmol/l ( $p < 0.001$ ), respectively. Results were compared with those obtained in 23 patients with non-insulin dependent diabetes (15 women and 8 men aged from 48 to 67 years, median age 54.9 +/- 3.34) with disease duration from 6 to 17 years. The above mentioned parameters remained unchanged in these patients. Accumulated data illustrated the hypoglycemic potential

of Aronia juice. The precise mechanism of its action is unknown but its beneficial effects and good taste make it a valuable adjunct to the dietary treatment of patients with diabetes mellitus.

<http://europepmc.org/abstract/MED/12580526>

71

Diabetes (hypolipemic, plasma glucose reduction, plasma triglyceride reduction, prevention, control)

Valcheva-Kuzmanova, S., Kuzmanov, K., Tancheva, S., Belcheva, A

Hypoglycemic effects of Aronia melanocarpa fruit juice in streptozotocin-induced diabetic rats.

Methods Find Exp Clin Pharmacol 2007, 29(2): 101. DOI:  
10.1358/mf.2007.29.2.1075349

Aronia melanocarpa fruit juice (AMFJ) is rich in phenolic antioxidants, especially flavonoids from the anthocyanin subclass. The aim of the present study was to investigate the influence of AMFJ on plasma glucose and lipids in diabetic rats. Diabetes was induced by an intraperitoneal injection of streptozotocin (50 mg/kg). AMFJ was applied by gavage at doses of 10 and 20 ml/kg for 6 weeks to normal and diabetic rats. Streptozotocin caused a significant elevation of plasma glucose by 141% and of plasma triglycerides (TG) by 64% in comparison with normal control rats and induced statistically insignificant elevations of total cholesterol and LDL-cholesterol and a reduction of HDL-cholesterol. Applied to normal rats, AMFJ did not influence plasma glucose and lipid levels. Applied to diabetic rats, AMFJ (10 and 20 ml/kg) significantly reduced plasma glucose by 44% and 42% and TG by 35% and 39%, respectively, to levels that did not significantly differ from those of the normal control rats and counteracted the influence of streptozotocin on total cholesterol, LDL-cholesterol and HDL-cholesterol. In conclusion, AMFJ significantly decreased the streptozotocin-induced abnormalities in blood glucose and TG in diabetic rats and might be useful in prevention and control of diabetes mellitus and diabetes-associated complications.

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<http://www.aronslim.pl/data/Hypoglycemic%20and%20Hypolipidemic%20Effects%20of%20Aronia%20melanocarpa.pdf>

72

Diabetes (idem 66)

Valcheva-Kuzmanova S, Kuzmanov K, Mihova V, Krasnaliev I, Borisova P, Belcheva A

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

Plant Foods Hum Nutr 2007; 62: 19-24

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.

<http://www.ncbi.nlm.nih.gov/pubmed/17136466>

73

Gastrointestinal (antioxidative, gastric mucosa, hemorrhage, in vivo, rats)

Matsumoto M, Hara H, Chiji H, Kasai T

Gastroprotective effect of red pigments in black chokeberry fruit (Aronia melanocarpa Elliot) on acute gastric hemorrhagic lesions in rats

J Agric Food Chem 2004; 52: 2226-9.

It has been reported that the fruits and leaves of berries such as the blackberry, raspberry, and strawberry contain a high level of scavenging activity for chemically generated active oxygen species. This study investigated the antioxidative activities of black chokeberry fruit (Aronia melanocarpa Elliot) both in vitro and in vivo using the DPPH stable radical and rats with ethanol-induced gastric injury, respectively. The red pigment fraction of the black chokeberry contained three main components, one of which was identified as cyanidin 3-O-beta-glucoside by HPLC analysis and <sup>1</sup>H NMR. The black chokeberry red pigment fraction scavenged >44% of DPPH radicals at a concentration of 25 µg/mL compared to the control solution. The black

chokeberry extract and its hydrolysate administered at 2 g/kg of body weight each had nearly the same protective effect as quercetin administered at 100 mg/kg of body weight in suppressing the area of gastric mucosal damage caused by the subsequent application of ethanol to <30% compared to the control group. The black chokeberry red pigment fraction had a similarly significant protective effect on gastric mucosa in a dose-dependent manner when administered at 30-300 mg/kg of body weight, and the administration of 30 mg/kg of body weight could suppress ethanol-induced gastric mucosal damage by approximately 50% (ID<sub>50</sub>=30 mg/kg of body weight).

<http://www.ncbi.nlm.nih.gov/pubmed/15080625>

74

Gastrointestinal (gut, colonic microflora, in vitro)

Scalbert A, Deprez S, Mila I, Albrecht A M

Proanthocyanidins and human health: Systemic effects and local effects in the gut

Biofactors 2000; 13: 115-20

Proanthocyanidins share common properties with other polyphenols, in particular their reducing capacity and ability to chelate metal ions. However, their polymeric nature clearly makes them different. They have a high affinity for proteins and their absorption through the gut barrier is likely limited to the molecules of low polymerization degree and to the metabolites formed by the colonic microflora, as suggested by in vitro experiments. The nutritional significance of proanthocyanidins is discussed in relation to their physico-chemical properties and bioavailability.

<http://www.ncbi.nlm.nih.gov/pubmed/11237169>

75

Hemorrhoids (hemorrhoids, varicose veins, non-surgical)

MacKay D

Hemorrhoids and varicose veins: a review of treatment options

Altern Med Rev 2001; 6: 126–140

Hemorrhoids and varicose veins are common conditions seen by general practitioners. Both conditions have several treatment modalities for the physician to choose from. Varicose veins are treated with mechanical compression stockings. There are several over-the-counter topical agents available for hemorrhoids. Conservative therapies for both conditions include diet, lifestyle changes, and hydrotherapy which require a high degree of patient compliance to be effective. When conservative hemorrhoid therapy

is ineffective, many physicians may choose other non-surgical modalities: injection sclerotherapy, cryotherapy, manual dilation of the anus, infrared photocoagulation, bipolar diathermy, direct current electrocoagulation, or rubber band ligation. Injection sclerotherapy is the non-surgical treatment for primary varicose veins. Non-surgical modalities require physicians to be specially trained, own specialized equipment, and assume associated risks. If a non-surgical approach fails, the patient is often referred to a surgeon. The costly and uncomfortable nature of treatment options often lead a patient to postpone evaluation until aggressive intervention is necessary. Oral dietary supplementation is an attractive addition to the traditional treatment of hemorrhoids and varicose veins. The loss of vascular integrity is associated with the pathogenesis of both hemorrhoids and varicose veins. Several botanical extracts have been shown to improve microcirculation, capillary flow, and vascular tone, and to strengthen the connective tissue of the perivascular amorphous substrate. Oral supplementation with *Aesculus hippocastanum*, *Ruscus aculeatus*, *Centella asiatica*, *Hamamelis virginiana*, and bioflavonoids may prevent time-consuming, painful, and expensive complications of varicose veins and hemorrhoids.

<http://www.ncbi.nlm.nih.gov/pubmed/11302778>

76

Lead poisoning (lead poisoning, reduced oxidative stress)

Kowalczyk E, Jankowski A, Niedworok J, Smigielski J, Jankowska B

The effect of *Aronia melanocarpa* and acetylcysteine on selected after-effects of lead acetate poisoning [in Polish]

Pol Merkur Lekarski 2002; 12: 221–223.

In recent years we have widely examined the results of protracted exposures on lead. Lead mostly shows that it accumulates in bones in an insoluble phosphate form. In much of the experimental research we observed that lead can cause reactive forms of oxygen and oxidative stress. The examination was carried out on 40 female and male Wistar rats weighing 200-250 g. They lived in the animal quarters with a stable temperature and humidity. They were fed with standard fodder (Murigan) and water ad libitum. In the work carried out the effect of anthocyanins of *Aronia Melanocarpa* Elliot and acetylcysteine on the selected parameters of oxidative stress of experimental animals with chronic lead acetate poisoning were examined. After administration anthocyanins substantially decreased the concentration of unsaturated fatty acid peroxidation and carbonyls in blood serum. At the same time we observed a significant decrease of 8-hydroxy-2'-deoxyguanosine in urine. Antocyanins from *Aronia Melanocarpa* appear to be a good substance for the diminishing of oxidative stress, these results caused with long-term administration of lead acetate.

<http://europepmc.org/abstract/MED/12053593>

77

Liver (hepatoprotective, rats)

Kowalczyk E, Kopff A, Niedworok J, Kopff M, Jankowski A

Hepatoprotective effect of the natural fruit juice from *Aronia melanocarpa* on carbon tetrachloride-induced acute liver damage in rats

Exp Toxicol Pathol. 2004 Dec; 56(3): 195-201.

Anthocyanins are one of the most important water-soluble plant pigments. They belong to flavonoids and are derivatives of 2-phenyl-benzo-gamma pyren. They have antioxidant and anti-inflammatory properties and, therefore, may be potentially used to combat oxidative stress, frequently present in cardiovascular diseases. AIM: To assess the effects of anthocyanins from chokeberry (*Aronia Melanocarpa*) on some parameters of oxidation-reduction balance in an animal model. METHODS: Of 20 male Wistar rats, 10 received for 3 months pure water, and the other rats 10-100 mg/l of anthocyanins from *Aronia melanocarpa*. Afterwards, blood samples were collected for assessment of the (1) content of substances reacting with thiobarbituric acid – TBARS, (2) antioxidant status and glutathione peroxidase activity, (3) concentration of sulphhydryl groups, and (4) nitrite concentration.

RESULTS: Anthocyanins significantly reduced the content of TBARS and thiol protein groups and non-significantly increased glutathione peroxidase activity, total content of antioxidants and nitrite concentration. CONCLUSIONS: Anthocyanins from chokeberry decrease lipid peroxidation which may be potentially used to combat oxidative stress.

<http://www.ncbi.nlm.nih.gov/pubmed/12917728>

78

Liver (idem 77)

Valcheva-Kuzmanova S, Borisova P, Galunska B, Krasnaliev I, Belcheva A

Hepatoprotective effect of the natural fruit juice from *Aronia melanocarpa* on carbon tetrachloride-induced acute liver damage in rats

Exp Toxicol Pathol 2004; 56: 195-201

The fruits of *Aronia melanocarpa* are rich in anthocyanins — plant pigments with anti-inflammatory and anti-oxidant activity. We studied the effect of the natural fruit juice from *A. melanocarpa* (NFJAM) on carbon tetrachloride (CCl<sub>4</sub>)-induced acute liver damage in rats. Histopathological changes such as necrosis, fatty change, ballooning degeneration and inflammatory infiltration of lymphocytes around the central veins occurred in rats following acute exposure to CCl<sub>4</sub> (0.2 ml kg<sup>-1</sup>, 2 days).

The administration of CCl<sub>4</sub> increased plasma aspartate transaminase (AST) and alanine transaminase (ALT) activities, induced lipid peroxidation (as measured by malondialdehyde (MDA) content in rat liver and plasma) and caused a depletion of liver reduced glutathione (GSH). NFJAM (5, 10 and 20 ml kg<sup>-1</sup>, 4 days) dose-dependently reduced the necrotic changes in rat liver and inhibited the increase of plasma AST and ALT activities, induced by CCl<sub>4</sub> (0.2 ml kg<sup>-1</sup>, 3rd and 4th days). NFJAM also prevented the CCl<sub>4</sub>-induced elevation of MDA formation and depletion of GSH content in rat live

<http://www.sciencedirect.com/science/article/pii/S0940299304000181>

79

Liver (anticarcinogen, rats)

Krajka-Kuźniak V, Szafer H, Ignatowicz E, Adamska T, Oszmiański J, Baer-Dubowska W

Effect of Chokeberry (*Aronia melanocarpa*) juice on the metabolic activation and detoxication of carcinogenic N-nitrosodiethylamine in rat liver

J Agric Food Chem. 2009 Jun 10; 57(11): 5071-7. doi: 10.1021/jf803973y.

Chokeberry is a rich source of polyphenols, which may counteract the action of chemical carcinogens. The aim of this study was to examine the effect of chokeberry juice alone or in combination with N-nitrosodiethylamine (NDEA) on phase I and phase II enzymes and DNA damage in rat liver. The forced feeding with chokeberry juice alone decreased the activities of enzymatic markers of cytochrome P450, CYP1A1 and 1A2. NDEA treatment also decreased the activity of CYP2E1 but enhanced the activity of CYP2B. Pretreatment with chokeberry juice further reduced the activity of these enzymes. Modulation of P450 enzyme activities was accompanied by the changes in the relevant proteins levels. Phase II enzymes were increased in all groups of animals tested. Chokeberry juice augmented DNA damage and aggravated the effect of NDEA. These results indicate that chokeberry may protect against liver damage; however, in combination with chemical carcinogens it might enhance their effect.

<http://www.ncbi.nlm.nih.gov/pubmed/19378944>

80

Liver (hepatoprotection, apoptosis, rats)

Keskin N, Mammadov R, Ili P

The effects of *Crataegus aronia* var. *dentata* Browicz extract on biochemical indices and apoptosis in partially hepatectomized liver in rats.

Bosn J Basic Med Sci. 2012 Aug; 12(3): 177-81.

*Crataegus* species have been widely used in herbal medicine, especially for the heart diseases. In the present study, the effect of *Crataegus aronia* var. *dentata* Browicz extract on partially hepatectomized rats was investigated with biochemical and TUNEL apoptosis assays. The extracts of the plant at the concentrations of 0.5 and 1 ml/100 g body weight/day were administered orally to the two experimental groups including partially hepatectomized rats for 42 days. At the end of the experimental period, animals were sacrificed, blood was collected for the assessment of serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma-glutamyltransferase (GGT), and the liver tissue was used for TUNEL assay. In biochemical assay, it was found a significant decrease in the levels of serum ALT and AST in the experimental groups. On the other hand, the plant extract did not cause any significant changes in the level of GGT in these groups. In apoptosis assay, TUNEL positive hepatocytes could not be detected in both experimental groups. The present findings can suggest that *Crataegus aronia* var. *dentata* Browicz extract can decrease the levels of serum ALT and AST and play a role in apoptosis of hepatocytes in the liver of partially hepatectomized rats. However, further studies are required to confirm the effects of the plant extract on hepatoprotection and apoptosis in the regenerating liver after partial hepatectomy in animal models.

<http://www.ncbi.nlm.nih.gov/pubmed/22938545>

81

Metabolism (thermogenesis, temperature, women)

Sonoda K, Aoi W, Iwata T, Li Y

Anthocyanin-rich *Aronia melanocarpa* extract improves body temperature maintenance in healthy women with a cold constitution

Springerplus. 2013; 2: 626. doi: <http://dx.doi.org/10.1186%2F2193-1801-2-626>

**PURPOSE:** Specific anthocyanin-rich dietary factors have been shown to improve metabolic functions associated with thermogenesis in animal studies. *Aronia melanocarpa*, commonly known as wild chokeberry, contains a high level of anthocyanin that would be expected to maintain body temperature through thermogenesis. We here investigated the effects of *Aronia melanocarpa* extracts on body temperature and peripheral blood flow in healthy women with a cold constitution. **METHODS:** A pre/post comparison trial was performed in 11 women with a cold constitution, who were taking *Aronia melanocarpa* extracts (150 mg/day) for 4 weeks. Physiological and biochemical parameters, along with psychological tests were examined. **RESULTS:** The subjects' body surface temperature was significantly higher in the post-trial than in the pre-trial. In psychological tests, factors related to cold were significantly improved by *Aronia* intake. On the other hand,

peripheral blood flow was not affected by Aronia supplementation. Plasma noradrenalin level was significantly elevated by Aronia intake, and subjects with a higher level of 8-hydroxy-2'-deoxyguanosine in the pre-trial showed decreased levels in the post-trial. CONCLUSIONS: These data suggest that dietary Aronia melanocarpa extract improves the maintenance of body temperature in healthy women with a cold constitution, which may be mediated by noradrenalin and oxidative stress levels.

<http://www.ncbi.nlm.nih.gov/pubmed/24303339>

82

Metabolism (metabolic syndrome, blood pressure, endothelin, lipids, antioxidant)

Broncel M, Kozirog M, Duchnowicz P, Koter-Michalak M, Sikora J, Chojnowska-Jeziarska J

Aronia melanocarpa extract reduces blood pressure, serum endothelin, lipid, and oxidative stress marker levels in patients with metabolic syndrome

Med Sci Monit 2010;16(1): CR28-34

Background: Experimental studies have shown that anthocyanins may exert pleiotropic effects. The aim of the study was to determine the influence of Aronia melanocarpa extract on blood pressure and serum concentration of endothelin-1 (ET-1), lipids, glucose, uric acid, C-reactive protein (CRP), fibrinogen, the antioxidant enzymes catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GSH-Px), and lipid peroxidation (thiobarbituric acid-reacting substrates, TBARS) in erythrocytes of patients with metabolic syndrome (MS). Material and Method: The study comprised 22 healthy volunteers and 25 patients with MS. Patients with MS were treated with aronia extract (3\*100 mg/day) for two months. The above parameters were measured. Results: After two months of therapy, statistically significant decreases were observed in SBP (143.40±7.87 vs. 131.83±12.24 mmHg, p<0.001), DBP (87.20±9.9 vs. 82.13±10.33 mmHg, p<0.05), ET-1 (2.44±0.51 vs. 1.74±0.42 pg/ml, p<0.001), TC (242.80±34.48 vs. 227.96±33.07 mg/dl, p<0.001), LDL-C (158.71±35.78 vs. 146.21±34.63 mg/dl, p<0.01), TG (215.92±63.61 vs. 187.58±90 mg/dl, p<0.05), TBARS (0.0712±0.0191 vs. 0.0362±0.0135 micromol/g-Hb, p<0.001), and CAT (261.30±59.78 vs. 213.34±47.36 U/mg-Hb) and significant increases in SOD (2380.63±419.91 vs. 3066.53±542.24 U/g-Hb, p<0.001), GSH-Px (12.60±5.97 vs. 19.18±9.09 U/g-Hb, p<0.01), and fibrinogen levels (249.20±27.17 vs. 276.67±57.41 mg/dl, p<0.05) compared with the baseline values. Conclusions: Aronia extract may be of benefit to patients with MS. This seems to result from the influence of anthocyanins and possibly other flavonoids on blood pressure, serum level of ET-1, lipids, and oxidative status (GSH-Px, SOD, TBARS).

<http://www.medscimonit.com/download/index/idArt/878315>

<http://www.aronslim.pl/data/aronia%20reduces%20blood%20pressure,...lipid%20in%20patients%20with%20metabolic%20syndrome.pdf>

83

Metabolism (idem 67)

Jurgoński A, Juśkiewicz J, Zduńczyk Z

Ingestion of black chokeberry fruit extract leads to intestinal and systemic changes in a rat model of prediabetes and hyperlipidemia

Plant Foods Hum Nutr. 2008 Dec; 63(4): 176-82. Epub 2008 Aug 23.

This report presents a complex analysis of changes proceeding in the gut, blood and internal organs of rats with induced oxidative stress, glucose intolerance and hyperlipidemia after dietary supplementation with an extract from black chokeberry (*Aronia melanocarpa*) fruit, that is a condensed source of polyphenols (714 mg/g), especially anthocyanin glycosides (56.6%). The disturbances mimicking those observed in metabolic syndrome were induced by a high-fructose diet and simultaneous single injection of streptozotocin (20 mg/kg). Dietary supplementation with the chokeberry fruit extract (0.2%) decreased activity of maltase and sucrase as well as increased activity of lactase in the mucosa of the small intestine. Its ingestion led also to the improvement of antioxidant status, especially, the concentration of a lipid peroxidation indicator (TBARS) in organ tissues (liver, kidney and lung) was normalized; some cholesterol-lowering and distinct hypoglycemic actions were also observed. The mechanism of glucose reduction is likely to be multifactorial, and we suggest the factors related with the decreased activity of mucosal disaccharidases important for further investigation. In conclusion, chokeberry fruit derivatives may act as a promising supplementary therapeutic option in the prevention and treatment of disorders occurring in metabolic syndrome, as well as their complications.

<http://www.ncbi.nlm.nih.gov/pubmed/18726160>

84

Muscle Recovery (idem 14)

Lucja Pilaczynska-Szczesniak, A. Skarpanska-Steinborn, E. Deskur, P. Basta, and M. Horoszkiewicz-Hassan

The Influence of Chokeberry Juice Supplementation on the Reduction of Oxidative Stress Resulting from an Incremental Rowing Ergometer Exercise

International Journal of Sport Nutrition and Exercise Metabolism, 03/2005, 15(1): 45-58

The aim of the study was to investigate the influence of an increased intake of anthocyanins, contained in chokeberry juice, on the redox parameters in rowers performing a physical exercise during a 1-month training camp. The athletes were randomly assigned to receive 150 mL of chokeberry juice daily, containing 23 mg/100 mL of anthocyanins (supplemented group), or placebo (control group). Before and after the supplementation period, the subjects performed an incremental rowing exercise test. Blood samples were taken from the antecubital vein before each exercise test, 1 min after the test, and following a 24-h recovery period. After the supplementation period, TBARS concentrations in the samples collected 1 min after the exercise test and following a 24-h recovery period were significantly lower in the subjects receiving chokeberry juice than in the control group. In the supplemented group, glutathione peroxidase activity was lower in the samples collected 1 min after the exercise test, and superoxide dismutase activity was lower in the samples taken following a 24-h recovery, as compared to the subjects receiving placebo. These findings indicate that an increased intake of anthocyanins limits the exercise-induced oxidative damage to red blood cells, most probably by enhancing the endogenous antioxidant defense system.

<http://www.researchgate.net/publication/7838609> The influence of chokeberry juice supplementation on the reduction of oxidative stress resulting from an incremental rowing ergometer exercise

85

ORAC

Measured in ORAC (Oxygen Radical Absorbance Capacity – by the USDA), the high concentration of anthocyanins and polyphenols make it more superior and better than any other product in the nature. According to [oracvalues.com](http://oracvalues.com), the Aronia Berry (Black Chokeberry) has the highest anthocyanin and proanthocyanidin content in any fruit ever! The Black Chokeberry has attracted scientific interest due to its deep purple, almost black pigmentation that arises from dense contents of phenolic phytochemicals, especially anthocyanins. Total anthocyanin content in chokeberries is 1480 mg per 100 g of fresh berries, and proanthocyanidin concentration is 664 mg per 100 g (Wu et al. 2004, 2006). Both values are among the highest measured in plants to date. The ORAC value is expressed in micromoles of Trolox Equivalents per 100 grams of sample (this is the laboratory measure of ORAC).

<http://www.oracvalues.com/chokeberry-raw>

86

Pancreatitis (pancreatitis, rats)

Jankowski A, Jankowska B, Niedworok J

The influence of Aronia melanocarpa in experimental pancreatitis

Pol Merkur Lekarski. 2000 Jun; 8(48): 395-8.

The administration of anthocyanin dyes from *Aronia melanocarpa* in the rats before the intraperitoneal injections of PAF and ceruleine have a beneficial effect on the development of the acute experimental pancreatitis. It was revealed the reduction of pancreas swelling and decreasing of lipid peroxidation and adenosine deaminase activity. The examination was carried out on 149, weighing 200-250 g, female and male Wistar rats. They lived in the animal quarters with a stable temperature and humidity being fed with standard fodder (Murigan) and water ad libitum.

<http://www.ncbi.nlm.nih.gov/pubmed/10967916>

87

Respiratory (bacterial, viral, upper respiratory tract)

A Pampura, N Beuscher, M Smirnova, M Horoszkiewicz-Hassan, K Schönknecht

Clinical evaluation of the efficacy and safety of Bioaron C® in children with recurrent bacterial and viral infections of the upper respiratory tract

Planta Med 2007; 73-P\_034. DOI: 10.1055/s-2007-986816

Bioaron C® syrup is a popular herbal product having an immunostimulant effect. The product has been used in Poland for the treatment of upper respiratory tract infections and in the prevention of recurrent bacterial and viral infections of the upper respiratory tract. Bioaron C® syrup contains water extract of aloe leaf (*Aloe arborescens* Mill.), chokeberry fruit juice (*Aronia melanocarpa* Elliot.) and vitamin C. Pharmacological studies in Balb/c mice have shown a stimulant effect on the B-cell and T-cell responses, a post marketing clinical study good tolerability (1,2). Clinical evaluation of the efficacy of Bioaron C®, in terms of the frequency and duration of infection in children with recurrent upper respiratory tract infections, was performed in a clinical hospital in Moscow. The study was completed by 60 children. The group comprised 21 children aged from 3 to 6 years and 39 children aged from 6 to 12 years. The total disease duration within 6 months after medicinal product administration was reduced from 35.64±1.18 to 31.33±1.84 days (p=0.045) compared to the same individual calendar period in the previous year. In the T-cell immunity test, an increase in the relative and total T-cell counts (CD3+, CD4+, CD8) was seen; there was a statistically significant increase in the relative number of CD3+ and CD4+ and total T-cell count (CD4+, CD8) as well. A statistically significant reduction in the relative number of CD16+ cells was seen. In the drug safety tests, no biochemical abnormalities in blood parameters have been seen.

<https://www.thieme-connect.de/products/ejournals/abstract/10.1055/s-2007-986816>

88

Weight (skin morphology, cellulite)

Savikin K, Menković N, Zdunić G, Pljevljakušić D, Spasić S, Kardum N, Konić-Ristić A

Dietary Supplementation with Polyphenol-Rich Chokeberry Juice Improves Skin Morphology in Cellulite

J Med Food. 2014 May; 17(5): 582-7. doi: 10.1089/jmf.2013.0102. Epub 2014 Jan 16.

The aim of our study was to investigate possible beneficial effects of organic chokeberry juice (OCJ) consumption in the treatment of cellulite. Twenty-nine women aged 25–48 with a cellulite grade 2 according to the Nurnberger–Muller scale were included. Anthropometric and biochemical parameters were measured. Skin structure was analyzed by ultrasonography. All subjects consumed 100 mL of OCJ per day, during 90 days. Measurements of investigated parameters were performed at 0, 45, and 90 days of the study. A marked reduction in the subcutaneous tissue thickness was observed in all subjects, with the average reduction of 1.9 mm. The length of subcutaneous tissue fascicles (ScTFL) was reduced in 97% (28 out of 29) of subjects, with the average value of 1.18 mm. After 45 days of chokeberry juice consumption, reduction of edema was observed in 55.2% of the subjects with edema at the baseline, while at the endpoint of the study, edemas were not observed in any of the subjects involved in the study. OCJ could have beneficial effects on the cellulite condition, including the length of ScTFL, subcutaneous tissue, and dermis thickness as well as on edema reduction.

<http://online.liebertpub.com/doi/abs/10.1089/jmf.2013.0102>

89

Weight (modulation, insulin signaling, adipogenesis, inflammation, rats)

Bolin Qin and Richard A. Anderson

An extract of chokeberry attenuates weight gain and modulates insulin, adipogenic and inflammatory signalling pathways in epididymal adipose tissue of rats fed a fructose-rich diet

Br J Nutr. 2012 Aug; 108(4): 581-7. doi: 10.1017/S000711451100599X. Epub 2011 Dec 6.

The aim of the present study was to determine if an extract from chokeberries would reduce weight gain in rats fed a fructose-rich diet (FRD) and to explore the potential mechanisms related to insulin signalling, adipogenesis and inflammatory-related pathways. Wistar rats were fed a FRD for 6 weeks to induce insulin resistance, with or without chokeberry extract (CBE) added to the drinking-water (100 and 200 mg/kg

body weight, daily: CBE100 and CBE200). Both doses of CBE consumption lowered epididymal fat, blood glucose, TAG, cholesterol and LDL-cholesterol. CBE consumption also elevated plasma adiponectin levels and inhibited plasma TNF- $\alpha$  and IL6, compared with the control group. There were increases in the mRNA expression for Irs1, Irs2, Pi3k, Glut1, Glut4 and Gys1, and decreases in mRNA levels of Gsk3 $\beta$ . The protein and gene expression of adiponectin and Pparg mRNA levels were up-regulated and Fabp4, Fas and Lpl mRNA levels were inhibited. The levels of gene expression of inflammatory cytokines, such as Il1 $\beta$ , Il6 and Tnfa were lowered, and protein and gene expression of ZFP36 (zinc finger protein) were enhanced in the epididymal adipose tissue of the rats that consumed the CBE200 extract. In summary, these results suggest that the CBE decreased risk factors related to insulin resistance by modulating multiple pathways associated with insulin signalling, adipogenesis and inflammation.

<http://www.ncbi.nlm.nih.gov/pubmed/22142480>

<http://www.aronslim.pl/data/An%20extract%20of%20chokeberry%20attenuates%20weight%20gain%20and%20modulates%20insulin.pdf>

90

Weight (weight gain inhibition, insulin, gene modulation, rats)

Bolin Qin and Richard A Anderson

Chokeberry extract consumption inhibits weight gain by modulating adipogenesis, insulin signaling, and inflammatory related gene expression in adipose tissue in rats fed a fructose rich diet

FASEB J., April 2010, 24 (Meeting Abstract Supplement) 555.7

"provides evidence that the chokeberry (Aronia) extract inhibits weight gain in insulin-resistant animals and that it modulates multiple genes associated with adipose tissue growth, blood glucose regulation, and inflammatory pathways." (USDA study)

Chokeberries are a rich source of anthocyanins which may contribute to the prevention of weight gain and obesity. The aim of present study was to determine if an extract from chokeberries inhibits weight gain in rats fed a fructose-rich diet (FRD, 60%) and explore the potential molecular mechanisms related to adipogenesis, insulin signaling, and inflammatory related pathways in epididymal adipose tissue (EAT). Chokeberry extract (CB, CellBerry®, 200 mg/kg daily) was added to the drinking water for 6 wks in rats made insulin resistant by feeding a FRD. Chronic CB intake lowered body weight gain, epididymal fat accumulation, blood glucose, triglycerides, cholesterol, and LDL-C in the FRD-induced insulin resistant rats and improved glucose intolerance and elevated plasma adiponectin levels. Gene expression of adiponectin, PPAR $\gamma$ , IRS1, IRS2, PI3K, and glycogen synthesis 1 were all improved by the CB supplement. The levels of adipocyte gene expression of inflammatory

*draft*–Aronia melanocarpa research bibliography  
[bit.ly/aronia-bibl](http://bit.ly/aronia-bibl)



genes such as IL-1b, IL-6 and TNF- were lowered by CB. In summary, these results suggest that the chokeberry extract (CellBerry®) inhibited weight gain in FRD-induced insulin resistant animals, and decreased risk factors related to insulin resistance by modulating multiple genes associated with adipogenesis, insulin signaling, and inflammation. (Funded by USDA/ARS CRADA No.58-3K95-7-1184 with Integrity Nutraceuticals International).

[http://www.fasebj.org/cgi/content/meeting\\_abstract/24/1\\_MeetingAbstracts/555.7](http://www.fasebj.org/cgi/content/meeting_abstract/24/1_MeetingAbstracts/555.7)