NATURAL HEALTH LLC
853 NE 68th St Seattle, WA 98115 206-524-6250

Dr. William Mitchell's Fruit Anthocyanins Are Now Available!

An Organic Blend Of Powerful Dark Berries and Fruits:
Red Grape, Aronia Berry, Elderberry, Blueberry, Red Raspberry, Pomegranate

Dr. William Mitchell used his Fruit Anthocyanins product for thousands of patients. This is a summary of some of the scientific research that has been published which demonstrates the effects of the different berries included in Dr. Mitchell's blend.

Anthocyanins

- Anthocyanins: Are the largest water-soluble pigments in the plant kingdom. They are responsible for the red, purple, and blue colors in fruits and vegetables. Anthocyanins have a wide range of biological activities including: antioxidant, anti-inflammatory, antimicrobial, anti-carcinogenic, fostering eye health, neuroprotective, prevention of LDL oxidation, improvement of capillary stability, inhibition of destruction of collagen, increasing intercellular levels of vitamin C, and normalizing mucopolysaccharide synthesis in the ground substance between cells. (1,2,3) Studies have shown that dietary anthocyanins are bioavailable to humans. (17, 70, 78, 126, 141, 149)

Antioxidant

- Anthocyanins are potent oxygen radical scavengers. (11, 37, 138) The anthocyanins from blueberry, aronia berry, and pomegranate are especially potent. (81, 138) Fruits and vegetables rich in anthocyanins demonstrate the highest antioxidant activities. Apple, tomato, pear, and peach consistently have lower antioxidant activities. (143)
- Pomegranate juice has 2-3 times the antioxidant capacity of either red wine or green tea. (17) Anthocyanins from pomegranate scavenged oxygen free radicals and hydroxide ions, and inhibited a fenton reagent OH generating system, (132) decreased macrophage oxidative stress and quenched free radicals in animal studies and humans. (17) Pomegranate specifically increases hepatic enzymes such as catalase, super oxide dismutase, glutathione peroxidase, which lowered lipid peroxidation by 54%. (17, 116) In rats it protects against free radical destruction of nitric oxide, and also enhances nitric oxides antiproliferative action on the rat's aortic smooth muscle cells. (17)
- Red Grape juice increased plasma antioxidant activity more than red wine. Intestinal absorption of the anthocyanins of red grape juice seemed to be improved compared to red wine, suggesting synergistic effect of the glucose content of the juice. Plasmatic bioactivity was also improved. (157)
- Blueberry keeps production of PGE2 produced by human epithelial cells to normal level, having an anti-inflammatory and anti-oxidative effect. (49) It provides protection of membranes against peroxyl radicals by increasing the induction time of oxidation. (57) Blueberry anthocyanins significantly reduced red blood cell resistance to radical oxygen species, such as hydrogen peroxide in vitro and in vivo. (83) Blueberry is associated with diet-induced increase in ex vivo antioxidant status. (75) Blueberry reduced risk of many chronic degenerative diseases through increasing the antioxidant status of serum. (77)
- Aronia Berry juice prevents the formation of free radicals. Aronia berry has an antioxidant capacity of 161 micromol of TE/g of FW. (38)

Anti-inflammatory

- Pomegranate is anti-inflammatory, inhibiting lipozygenase and cyclooxygenase, thereby decreasing metabolism of arachidonic acid to leukotrieese and prostaglandins respectively. (17)
- The anthocyanins in the *Vaccinium spp* such as blueberry are very useful in treating a wide variety of inflammatory conditions, including rheumatoid arthritis, chronic progressive polyarthritis, and gout (due to reduction of uric acid levels and tissue destruction.) (8)
- Quercitin is bioavailable in serum after a single ingestion of red grape juice. (43)
- In a study investigating the effect of aronia berry extract on endotoxin-induced uveitis (EIU) in rats, the anti-inflammatory effect of 100 mg of aronia extract was as strong as that of 10mg prednisolone. The anti-inflammatory action of aronia extract was stronger than that of either quercetin or anthocyanin administered alone. Aronia has a dose dependent ocular anti-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, PGE2, and TNF-alpha (25)

Anti-Bacterial

- Pomegranate's antimicrobial action has been demonstrated in vitro, inhibiting growth of the following organisms: Staphyloccocus aureus, methicillin-resistant Staphylococcus aureus (MRSA), Streptococcus pyogenes, Diplococcus pneumoniae, Escherichia coli 0157:H7, and Candida albicans. (17) This was by direct antibacterial and antifungal action. A study of pomegranate methanolic extract and antibiotics against 30 clinical isolates of MRSA and methicillin-sensitive Staphylococcus aureus showed synergistic activity between the pomegranate extract and the antibiotics. The pomegranate extract did not interfere with any of the antibiotics tested, and in fact dramatically enhanced the activity of all of the antibiotics used. (109)
- Raspberry, elderberry, and blueberry all showed in vitro inhibition of H. pylori, and increased the susceptibility of H. pylori to clarithromycin. (144)
- Raspberry has been shown in vitro to selectively inhibit harmful bacteria and pathogens in human intestines, while not harming the beneficial bacteria. *Salmonella* and *Staphylococcus* strains were especially sensitive, and *Campylobacter jejuni* and *Candida albicans* were also inhibited by phenolic extracts of raspberry. (14) Polyphenolic compounds from red raspberry exhibit anti-bacterial activity against opportunistic pathogens such as *B. cereus, E. coli, P. aeruginosa,* and *S. aureus strains*. (162)
- Gram-Positive and Gram-negative pathogenic bacterial strains were selectively inhibited by bioactive berry compounds…raspberry along with cloudberry were the best inhibitors. The most sensitive bacteria to berry phenolics tested were Heliobacter pylori and Bacillus cereus. (86, 88, 122)

Anti-Viral

- Elderberry inhibited all strains of flu virus tested in this study. It seems to stop the replication of the virus and to result in higher levels of antibodies against the virus (1). It inactivates neuraminidase which eats through the cell walls of intact healthy cells when it is released by hemaglutinins that are formed by flu viruses. (1) 90% of flu infections resolved in only 3 days in the elderberry group, versus 6 days in placebo, (7) and elderberry relieved influenza A and B symptoms 4 days earlier than in the control group. (145) (151)
- Blueberry extracts almost completely inactivated tick-borne encephalitis virus (6).

Cancer

- Prostate Cancer: Pomegranate extracts have been shown to inhibit prostate cancer cell lines including DU-145, LNCaP, and PC-3 (a highly aggressive prostate cancer cell line), and to inhibit prostate cancer cells invasiveness and proliferation. (96, 125) It also can cause induction of apoptosis, cell cycle disruption for cancer cells, and inhibition of tumor growth. (17) In athymic nude mice implanted with androgen-sensitive CWR22Rnu1 cells, pomegranate fruit extract led to a significant inhibition of tumor growth , and a reduction in PSA in the serum. (96, 108) Use of 8 ounces of pomegranate juice in men with prostate cancer led to decreased serum prostate specific antigen (PSA) levels by an average of 27%. (17, 91) These men also showed a 12% decrease in cell proliferation and a 17% increase in apoptosis of cancer cells. (91) The doubling time for PSA levels went from 15 months to 54 months post treatment. (91) Clinical trials done on men who had recurrent prostate cancer and rising PSA levels found that when given pomegranate supplementation there was a 35% reduction seen in PSA levels and a 40% reduction in lipid peroxidation. (17) Several studies have shown that the effects of multiple biochemicals of pomegranate together are more effective against cancer cells than isolated compounds. (117,121) Blueberry proanthocyanins have an effect on inhibiting androgen-dependent growth of prostate cancer cells. (48)
- Colon Cancer: In HT-29 colon cancer cells, treatment with pomegranate juice resulted in significant decrease in COX-2 expression (which is an inflammatory signaling process that may cause cancer initiation and progression). The whole juice was much more powerful (79% suppression) than any single constituent. (97) Pomegranate juice showed higher antioxidant and antiproliferative activity than isolated pomegranate constituents when studying HT-29 and HCT 116 colon cancer cell lines. (113) Pomegranate ellagitannins, which in the colon release ellagic acid that is metabolized by human microflora were shown to induce apoptosis of Caco-2 colon cancers cells via the mitochondrial pathway. They did not induce apoptosis in healthy cells. (98) Elderberry and aronia berry anthocyanins have demonstrated suppression of human colon cancer growth. These anthocyanin-rich extracts afforded chemoprotection and exerted an additive interaction with the other phenolics present. (146) Anthocyanin fractions from blueberry demonstrated >50% inhibition of cell growth of HT-29 and Caci-2 colon cancer lines, and resulted in 2-7 times increases in DNA fragmentation, indicating induction of apoptosis. (55) Aronia berry fed to rats decreased colonic cellular proliferation, and therefore may play a protective roll against colon carcinogenesis. (84) In vitro studies also suggest that aronia berry may play a protective role in colon carcinogenesis and indicate multiple mechanisms of action. (28)

- Oral cancer: Suppression of oral cancer cell lines KB and CAL-27 by pomegranate juice were higher than using isolated constituents. (17) Again, the synergistic aspect of the whole fruit seems best.
- Breast Cancer: Components of pomegranate inhibit blood vessel formation in breast cancer cell lines by downregulating vascular endothelial growth factor in MCF-7 breast cancer and human umbilical vein endothelial cell lines. (17) This can help deprive the cancer of the blood supply it needs to thrive. In breast cancer cell lines MCF-7 and MB-MDA-231 pomegranate constituents inhibited angiogenesis, tumor growth, proliferation, and invasiveness, and induced apoptosis. (131, 17) This was seen in vitro with both pomegranate alone and in combination with genistein. The combination of the two was more helpful than either alone. (102) Pomegranate fermented juice, pericarp and oil all exhibit the ability to effect a blockade of endogenous active estrogen biosynthesis, by inhibiting aromatase activity by 60-80% and inhibiting 17-beta-hyproxysteroid dehydrogenase type 1 from 34-79% depending on concentrations. (131) In a study of mouse mammary organ culture exposed to carcinogen 7,12-dimethylbenz(a)anthracene (DMBA) 10 day treatment with pomegranate seed oil resulted in a 87% reduction in the number of tumors compared to controls. (120).
- Cervical and Breast Cancer: Ethanol extracts of blueberry and aqueous extracts of raspberry showed anticancer activity on cervical and breast cancer cell lines. They also inhibited both direct-acting and metabolically activated carcinogens. (73)
- Lung and Skin Cancer: In mice, both lung and skin cancers showed inhibition of tumorigenesis by pomegranate fruit extract. Lung tumor growth was significantly less in mice fed a quantity of pomegranate fruit extract that was equivalent to a dose that humans could reasonably consume compared to those not fed any pomegranate extract. (17) Pomegranate fruit extract inhibited human A549 lung carcinoma cells, while having little effect on normal human bronchial epithelial cells. (90) In mice exposed to skin cancer causing 12-O-tetradecanoylphorbol-13-acetate (TPA) only 30% of the mice who were treated with topical pomegranate fruit extract 30 minutes before exposure developed skin tumors, compared to 100% of the group not given topical treatment. This was due to decreased inflammation and decreased tumor proliferation marker ornithine decarbozylase. (123, 17)
- Berry extracts (including blueberry, elderberry, raspberry) inhibited H2O2 as well as TNF alpha induced VEGF espression by the human keratinocytes. (76)
- Leukemia: In HL-60 human leukemia cells treated with fermented pomegranate juice and pericarp extracts led to increased cell differentiation and inhibited proliferation of the cancer cells. (128)
- The growth of cancer cell lines, including those of stomach, intestine, prostate and breast are strongly inhibited by raspberry when used in conjunction with black currant, white currant, gooseberry, velvet leaf blueberry, low-bush blueberry, sea buckthorn and cranberry juice. The study illustrated 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. (153)
- Brain Cancer: Aronia extracts introduced to highly malignant brain tumor lines slowed down regulation of MMP-9 activity, and killed cancer cells within 24 hours. Other studies have also shown remarkable apoptosis in various cancer cell lines, without harming healthy cells. (10)
- Flavonoids from Blueberry possess the ability to effectively decrease Matrix metalloproteinase (MMP) activity, which may decrease overall extra cellular matrix degradation. This ability may be important in controlling metastasis formation. (52) The proanthocyanidin fraction of blueberry exhibits potential anticarcinogenic activity in vitro by inducing the phase II xenobiotic detoxification enzyme quinine reductase and inhibiting the induction of ornithine decarboxylase (the rate-limiting enzyme in polyamine synthesis, by the tumor promoter phorbol 12-myristate 13-acetate). (89) Blueberry anthocyanins have shown antiproliferation and antiadhesion properties in vitro. (67) For cancers cells to thrive they need to feed on protein degradation products called polyamines. The anthocyanins of blueberries inhibit a specific enzyme called ornithine decarboxylase needed to create these polyamines, thereby limiting the food supply of cancer cells. (4)
- Juice from blueberry and raspberry both significantly inhibited mutagenesis caused by mutagen methyl methanesulfonate and the metabolically activated carcinogen benzo[a]pyrene. (64)
- Anthocyanins isolated from fruits of aronia melanocarpa markedly inhibit the mutagenic activity of benzo[a]pyrene and 2-amino fluorine in the Ames test (23)
- Resveratrol in red grapes and other berries has demonstrated ability to interfere with cell-signaling pathways involved in cancer. (94) Red grape juice compounds that inhibit iron availability are also linked to anticancer benefits. (72)

Cardiovascular Conditions

- Anthocyanins strengthen capillaries while decreasing capillary permeability and fragility by about twice the extent of rutin, and increasing vitamin C levels inside of cells. Dark berry extracts have been used for capillary fragility, venous insufficiency, varicose veins, microscopic hematuria due to kidney capillary disorders, blood purpuras, and circulation disorders to brain tissue. Anthocyanins stabilize the phospholipid membrane of the blood vessels and increase mucopolysaccharides that help restore the peri-capillary sheath. Anthocyanins also help decrease blood brain barrier permeability, protecting the brain from drugs, pollutants, naturally occurring degradation products, etc. (8)
- New research has shown that aronia berries are very potent in helping relax the arteries, aiding blood flow, protecting the coronary arteries from oxidant injury, and inhibiting the development of blood clots and the early processes of atherosclerosis. (11) Aronia also helps to keep the blood pressure from becoming dangerously high, prevents spasms in blood vessels, and is thought to be useful in combating oxidative stress. (11)
- Aronia's rich polyphenal content reduces platelet adhesion better than pure resveratrol. (22) Red grape juice also exhibits platelet inhibition in vitro (44), and is more effective than red wine or dealoholized red wine at the same polyphenol dose in inhibiting atherosclerosis and improving lipids and antioxidant parameters. (105)
- Regular ingestion of concentrated red grape juice by hemodialysis patients reduces neutrophil NADPH-oxidase activity and plasma concentrations of oxidized LDL and inflammatory biomarkers to a greater extent than does Vitamin E. (148)
- Red grape skin polyphenolic extracts enriched in anthocyanins prevented hypertension, cardiac hypertrophy, and production of reactive oxygen species in rats. (159)
- Anthocyanins also have been shown to reduce serum cholesterol and triglyceride levels in primary dyslipidemia, and reduced calcium and lipid deposition in the aorta. (8)
- Tests conducted investigating the putative antioxidant and anti-inflammatory effects of blueberry and cranberry anthocyanins and hydroxycinnamic acids against H(2)O(2) and TNFalpha induced damage to human microvascular endothelial cells concluded that polyphenols from both berries were able to localize into endothelial cells, subsequently reducing endothelial cells vulnerability to increased oxidative stress at both the membrane and cytosol level. It was concluded that polyphenols isolated from both blueberry and cranberry were able to afford protection to endothelial cells against stressor induced upregulation of oxidative and inflammatory insults. (79)
- Pomegranate protects LDL oxidation by direct interaction of the polyphenols with the lipoprotein and/or an indirect effect through accumulation of polyphenols in arterial macrophages. It reduces the capacity of macrophages to oxidatively modify LDL and scavenges reactive oxygen and nitrogen species. Pomegranate increases serum paraoxonase activity, resulting in the hydrolysis of lipid peroxides in oxidized lipoproteins and in atherosclerotic lesions. (130) Pomegranate extracts inhibited atherogenesis (134), and reduced the size of atherosclerotic lesions in apolipoprotein E-deficient mice by 44%. And in humans pomegranate juice consumption decreased LDL susceptibility to aggregation and retention. (135) Studies of mice show that pomegranate juice supplementation resulted in 27% lower macrophage peroxide levels, 42% decreased cellular lipid peroxide levels, and 19% decrease in peritoneal macrophage uptake of oxidized LDL. (17)
- In patients with Carotid artery stenosis after 1 year of 50ml pomegranate juice consumption per day this group was compared to controls who received no pomegranate juice. The control group had a mean 9% increase in intima-media thickness of both left and right carotid arteries. The pomegranate juice group had a mean reduction in intima-media thickness of 35%. The pomegranate group also showed reduced lipid peroxidation by 59% and LDL-associated lipid peroxides decreased by 90% after only 6 months. In addition systolic blood pressure decreased by 16% on average over 3 years. (127, 17)
- Pomegranate juice helped to lower blood pressure in hypertensive patients (133), and in separately conducted tests, improved perfusion of the myocardium (heart muscle blood flow), decreased ischemia to the myocardial tissue, and resulted in a 50% reduction in angina episodes, as well as decreased stress-induced ischemia. (110)
- Pomegranate juice has been shown to lower cholesterol in type 2 diabetic patients via several mechanisms: decreased cholesterol absorption, increased fecal excretion of cholesterol, and by effecting the enzymes involved in cholesterol metabolism. Both total and LDL cholesterol were lowered. (17) In a study of 22 type II diabetic patients, consumption of pomegranate juice concentrate for 8 weeks resulted in significant reductions in total and LDL cholesterol. No changes were seen in HDL or triglycerides. (124) In vitro pomegranate juice in macrophages led to lowered cholesterol biosynthesis and suppression of oxidized-LDL degradation, which can result in reduced cellular cholesterol accumulation and foam cell formation. (111)

- Pomegranate juice's great antioxidant ability resulted in significant protection of Nitric Oxide against oxidative destruction and thereby resulted in increased biological activity of Nitric Oxide on the vascular smooth muscle cells in rat aorta's. (92) (50) Pomegranate juice also was shown to revert the potent down-regulation of the expression of endothelial nitric-oxide synthase that is induced by oxidized low-density lipoprotein in human coronary endothelial cells. Therefore pomegranate can be beneficial in conditions such as coronary artery disease, atherogenesis, and other vascular complications. (100)

Connective Tissue Health

- Anthocyanosides have significant collagen-stabilizing action, helping to maintain the integrity of tendons, ligaments, and cartilage. (8) Collagen can be destroyed by inflammatory processes like arthritis, and anthocyanins prevent collagen destruction in multiple ways: a) cross-linking collagen fibers, thereby forming the collagen matrix of connective tissue; b) preventing free radical damage; c) inhibiting enzymatic cleavage of collagen, by enzymes that leukocytes secrete during inflammation; d) preventing the release and synthesis of inflammatory molecules such as histamine, prostaglandins, leukotrienes, and serine proteases; and d) promoting collagen synthesis. (8)

Dental Health

- Pomegranate juice has applications for dental conditions including plaque, oral inflammation, and periodontal disease. A study comparing oral rinsing with distilled water, pomegranate fruit extract, or chlorhexidine (which is a standard antiplaque mouth wash) showed that both pomegranate fruit extract and chlorhexidine decreased plaque after a one minute rinse much more than distilled water alone (84%, 79%, and only 11% respectively). (17) In periodontal disease, patients were compared using biodegradable chips impregnated with Centella asiatica and P. granatum (pomegranate) versus controls. All started with 5-8mm gum pockets. After 3 and 6 months there was a trend toward decreased plaque and significant improvement in pocket depth and attachment level in the treatment group compared to controls. Inflammatory markers interleukin-1beta and interleukin-6 both decreased significantly following treatment (17). Pomegranate gel was used topically to treat candidosis associated with denture estomatitis with good results after 15 days of use. Pomegranate performed similarly to use of miconazole. (129)

Diabetes

- During his use of the Fruit Anthocyanins, Dr. William Mitchell observed stabilization of blood sugar levels in hypoglycemics and lowered levels in diabetics (W. Mitchell)
- Blueberry has been used in folk medicine for many years to treat diabetes. Research has shown that giving blueberry orally reduced hyperglycemia in normal dogs as well as dogs who have had their pancreas removed. This was true even when glucose was given IV at the same time. The anthocyanin myrtillin (3-glucoside of delphinidin) seems to be the most active blood sugar lowering anthocyanin in the V. myrtillus species (blueberry, bilberry). A single injection of myrtillin lowers blood sugar for several hours. It is somewhat weaker than insulin, but is also less toxic. Anthocyanins improve the integrity of collagen and reduce capillary permeability. In addition they inhibit sorbitol accumulation, which protects against serious vascular and neurological symptoms in diabetes. (8)
- A 3 month study of 10 type 2 diabetic patients supplemented with 50ml/day pomegranate juice showed C-peptide (a proinsulin metabolite marker for endogenously secreted insulin) was lowered by 23% and lipid peroxides were reduced by 56% compared to baseline. And the uptake of oxidized LDL by human monocyte-derived macrophages (which are an early development in foam cell formation and atherogenesis) decreased by 39% compared to baseline. No significant changes were seen in triglycerides, HDL, HbA1C, glucose or insulin values. These results suggest that pomegranate juice consumption in diabetics can significantly reduce oxidative stress and the atherogenesis it causes without having a negative impact on other diabetic parameters such as blood sugar levels. (17, 106)
- Daily doses of 200 ml of aronia extract over a period of 3 months effectively lowered 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. (34) Aronia melanocarpa reduced changes in rat liver and inhibited the increase of plasma AST and ALT activities induced by CC14 (0.2ml kg(-1). It also prevented the CC14-induced elevation of MDA formation and depletion of GSH content in rat liver. Other studies have shown plasma glucose reduction in diabetic rats by as much as 44%, and TB by as much as 39% (26, 21, 19)

- Analysis of changes occurring 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), found that aronia may act as a promising supplementary therapeutic option in the prevention and treatment of disorders occurring in metabolic syndrome, as well as their complications (24)

Erectile Dysfunction/Infertility

- Rabbit studies showed increased intracavernous blood flow and smooth muscle relaxation after 8 weeks of pomegranate juice. This was probably due to antioxidant effect on enhanced nitric oxide preservation and bioavailability. (112) Pomegranate juice prevented erectile tissue fibrosis in rabbit ED group, and shows high capacity to decrease low density lipoprotein oxidation and inhibit cellular stress in macrophages. Antioxidant therapy may be a useful prophylactic tool for preventing smooth muscle dysfunction and fibrosis in ED. (59)
- In a human trial after 4 weeks, men said that they experienced some improvement in erectile dysfunction with pomegranate juice versus placebo. However, no statistically significant changes were seen. (17)
- In a study of male infertility in rats, pomegranate juice consumption resulted in higher antioxidant enzyme activity in both plasma and sperm, increased sperm motility, a decreased number of abnormal sperm, improved epididymal sperm concentration, spermatogenic cell density and diameter of seminiferous tubules. (17)

Eye Conditions

- Many eye conditions may benefit from anthocyanin intake, including macular degeneration, retinal degeneration, diabetic retinopathy, glaucoma, cataracts, and night vision. Vaccinium myrtillus (bilberry, blueberry) have shown such benefits. (8) Blueberry decreased the number of OXYS rats to form cataracts. (69) Progression of macular degeneration seems to stop with use of the Fruit Anthocyanins product (W. Mitchell). Also, this product seems to be protective against diabetic retinopathy (W. Mitchell).

Gastrointestinal Conditions:

- Aronia has been effective in treating acute gastric hemorrhagic lesions in rats, suggesting it might be an effective treatment for severe stomach problems in humans, including ulcers. (Matsumoto et al) (11) Pretreatment with aronia berry juice decreased gastric lesions in rats caused by indomethacin, probably due to the increased mucus production and interference with oxidative stress development as evidenced by the decreased plasma and gastric mucosal MDA (27)
- Elderberry inhibits neuraminidase, helping to minimize the disruption of the mucosal barrier and resultant conditions such as leaky guy, inflammation, adverse reactions of dietary lectins, and microbial translocation. (1)

Nerve Conditions:

- Studies done on pregnant mice fed pomegranate juice versus a control beverage showed that pomegranate juice offered antioxidant-based neuroprotection to the offspring. This was tested by exposing the newborns to hypoxic-ischemic brain injury in both the pomegranate and control groups. In the pomegranate group, the offspring showed 60% decrease in brain tissue loss, and decrease in caspase-3 activity by 84% in the hippocampus and 64% in the cortex. (115)
- In mice with Alzheimer's-like pathology, those treated with pomegranate juice showed 50% less soluble amyloid-beta and less hippocampal amyloid deposition than the controls who consumed sugar water. The treatment mice also did better in water maze tasks and swam faster than the control mice. (17)
- Blueberry improves neuronal communication by altering neuronal signaling. Blueberry can offset negative consequences of amyloid beta deposition on behavior in mice by increasing extracellular signal regulated kinase (ERK) and protein kinase C (PKC) which are both important to learning and memory. In rats, blueberry supplementation seems to enhance endogenous antioxidant and neuronal signaling capabilities. In addition it increases neurogenesis associated with increased ERK and insulin growth factor-1 (IGF-1). Blueberry also reduced stress signaling triggered by oxidative or inflammatory stress (e.g., Nuclear factor kappa B, and cyclic AMP response to element binding protein, CREB, and cytokines). Blueberry supplementation has been shown to enhance signaling and prevent behavioral deficits in mice with Alzheimer's disease. (120) Blueberry was beneficial in reversing age-related declines in neuronal signal transduction, cognitive, and motor behavioral deficits in rats. (87)

- Aged rats fed blueberry supplemented diets did much better in terms of object recognition memory than aged control diet rats. And aged rats fed blueberry supplemented diets did similarly to young rats. (68) Blueberry extract may protect against oxidative stress and inflammation that contributes to functional declines in neuronal aging. Reduced activation of the involved receptors results from Blueberry acting as an antagonist to effects of dopamine. (45)
- Diets enriched in antioxidants and anti-inflammatory phytochemicals from blueberry and spirulina modulate neuro-inflammation in animals with brain injury and neurodegenerative diseases. Enhanced striatal dopamine recovery coincided with an early, transient increase in OX-6-positive microglia. (54)
- A 10 week blueberry supplemented diet completely restored the HSP70 response to LPS (in vitro) inflammatory challenge in old rats at 90 and 240 min. time points in the trial. Blueberry intervention may result in improved HSP70 mediated protection against a number of neurodegenerative processes in the brain. (60)
- Chronic treatment with blueberry, spinach, or spirulina reduces ischemia/reperfusion-induced apoptosis and cerebral infarction and increases post-stroke locomotor activity. (61)
- Hippocampal neuronal plasticity is increased in blueberry supplemented animals. Proliferation, extracellular receptor kinase activation, and IGF-1 and IGF-1R levels correlate with improvements in spatial memory. (63) Polyphenols found in blueberries can reverse age-related declines in neuronal signal transduction as well as cognitive and motor deficits. (53)
- Dietary supplementation using blueberry can decrease the brain's vulnerability to oxidative stress as assessed in vivo by examining reductions in neuronal signaling and behavioral deficits and in vitro via H202-induced decrements in striatal synaptosomal calcium buffering. (80)
- Lyophilized berries significantly enhanced short-term memory, but not long-term memory in the inhibitory avoidance task, and may be beneficial in prevention of memory deficits. (58)

Obesity

- Anthocyanins significantly suppress the development of obesity, normalized hypertrophy of adipocytes (fat cells), and relieved hyperglycemia induced by high-fat diets in mice. (16) Anthocyanins increase the expression of adipocytokine (adiponectin and leptin), RPAR and adipocyte specific genes in rats without the stimulation of RPAR ligand activity. (16) Dysregulation of adipokinase plays an important role in the development of metabolic syndrome, so anthocyanins may be helpful in its prevention. (16)
- Raspberry ketone (4-(4-hydroxyphenyl) butan-2-one; RK) is a major aromatic compound of red raspberry (Rubus idaeus). The structure of RK is similar to the structures of capsaicin and synephrine, compounds known to exert anti-obese actions and alter lipid metabolism by increasing norepinephrine-induced lipolysis in white adipocytes. It is also possible that RK activates sensory neurons thereby increasing skin elasticity and promoting hair growth by increasing dermal IGF-I production. This possibility was examined in both mice and humans, and strongly suggests RK indeed increases dermal IGF-I production. (65, 155, 161)
- In Mice, blueberry anthocyanins extracts fed in a high fat diet decreased weight gain and fat deposition. (15)

Pulmonary Conditions

- Cases of pulmonary fibrosis, asbestosis, and emphysema have all benefited from use of the fruit anthocyanins (W. Mitchell)

Skin Health

- Pomegranate fruit extract has been studied in the lab on normal human epidermal keratinocytes and the extract has resulted in reduced cell damage from ultraviolet A and B radiation. (93, 17) In a trial of healthy women, the group given pomegranate pulp extract versus placebo, reported less UV-induced damage following exposure to 1.5 minimum erythema dose of UV radiation. The skin measurements in terms of luminance, melanin, and erythema were not significantly different. (17)

Urinary Conditions

- Blueberry has similar anti-adhesion properties as cranberry, blocking the ability of E. coli to adhere to the bladder and urinary tract cells, helping to prevent and treat urinary tract infections (5). Blueberry anthocyanins also reduce microscopic hematuria (blood in the urine). Because the kidneys and skin are both very rich in collagen and mucopolysaccharides, the anthocyanins have a good affinity for these tissues. (8).
- Aronia berry has 10 times more quinic acid than cranberry, which prevents urinary infection. (11)

Citations/Bibliography:

1) Zakay-Jones Z., Versano N. Zlotnik M, et al. Inhibition of several strains of influenza virus in vitro and reduction of symptoms by an elderberry extract (Sambucus nigra L.) during an outbreak of influenza B Panama. Journal of Alternative and Complementary Medicine. 1995; 1:361-369.
2) Mazza, G. *Anthocyanins and Heart Health.* Berry Health Berry Symposium. Corvallis, OR. June 2007.
3) Erdman, J. W. Jr. et al. Flavonoids and Heart Health. Journal of Nutrition. 137: 718S-737S.
4) Bomser J. et al. In vitro anticancer activity of fruit extracts from Vaccinium species. Planta Med. 1996; 62: 212-216.
5) Ofek, I et al. Anti-Escherichia coli adhesion activity of cranberry and blueberry juices. New England Journal of Medicine. 1991; 324: 1599.
6) Fokina GI, et al. Experimental phytotherapy of tick-borne encephalitis. Vopr Virusol. 1991; 36: 18-21.
7) www.vitaminstuff.com/herbs-elderberry
8) Pizzorno and Murray. *Vaccinium myrtillus.* 1987.
9) Howard, L.R. et al. *Processing Effects on Berry Polyphenolics.* Berry Health Benefits Symposium, 2007.
10) www.antioxidant-fruits.com Learn More about how the Aronia Berry/Chokeberry has Been Successful in Battling Cancer.
11) www.antioxidant-fruits.com Learn More About the Uses of the Aronia Berry or Chokeberry.
12) Joseph, J.A. et al. *The beneficial properties of berrryfruit polyphenolics in brain aging involves reductions in oxidative and inflammatory signaling cascades.* Berry Health Benefits Symposium, 2007.
13) Kalt, W. *Distribution of anthocyanins in pig tissues after long-term blueberry feeding.* Berry Health Benefits Symposium, 2007.
14) Puupponin-Pimia, R. *Therapeutically Active Berry Compounds – In Vitro and In Vivo Effects on Human Health.* Berry Health Benefits Symposium, 2007.
15) Prior, R.L. *Berries and Berrry Anthocyanins: Interactions with Dietary Fat Levels in a Mouse Model of Obesity.* Berry Health Benefits Symposium, 2007.
16) Tsuda, T. *Regulation of Adipocyte Function by Anthocyanins; Possibility of Preventing the Metabolic Syndrome.* Berry Health Benefits Symposium, 2007.
17) Jurenka, J. *Therapeutic Applications of Pomegranate (Punica granatum L.): A Review.* Alternative Medicine Review: A Journal of Clinical Therapeutics. Vol 13, No 2. June 2008.
18)Valcheva-Kuzmanova SV and A Belcheva. *Current knowledge of Aronia melanocarpa as a medicinal plant.* Folia Med (Plovidiv). 2006; 48(2):11-7.
19)Valcheva-Kuzmanova S et al. *Hypoglycemic and hypolipidemic effects of Aronia melanocarpa fruit juice in streptozotocin-induced diabetic rats.* Methods Find Exp Clin Pharmacol. 2007 Mar; 29(2):101-5.
20) Matsumoto M et al. *Gastroprotective effect of red pigments in black chokeberry fruit (Aronia melanocarpa Elliot) on acute gastric hemorrhagic lesions in rats.* J Agric Food Chem. 2004 Apr 21; 52(8):2226-9.
21) Valcheva-Kuzmanova SV et al. *Protective effect of Aronia melanocarpa fruit juice pretreatment in a model of carbon tetrachloride-induced hepatotoxicity in rats.* Folia Med (Plovdiv); 2006; 48(2): 57-62.
22) Olas B et al. *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 Feb; 19(1): 70-7.
23) Gasiorowski K et al. *Antimutegenic activity of anthocyanins isolated from Aronia melanocarpa fruits.* Cancer Lett. 1997 Oct 28; 119(1):37-46.
24) Jurgonski A et al. *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 Aug 23.
25) Ohgami K et al. *Anti-inflammatory effects of aronia extract on rat endotoxin-induced uveitis.* Invest Opthalmol Vis Sci. 2005 Jan; 46(1): 275-81.
26) Valcheva-Kuzmanova S. et al. *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.
27) Valcheva-Kuzmanova S. et al. *Effects of Aronia melanocarpa fruit juice on indomethacin-induced gastric mucosal damage and oxidative stress in rats.* Exp Toxicol Pathol. 2005 Apr; 56(6): 385-92.
28) Lala G et al. *Anthocyanin-rich extracts inhibit multiple biomarkers of colon cancer in rats.* Nutr Cancer. 2006; 54(1): 84-93.
29) Valcheva-Kuzmanova S. et al. *Antihyperlipidemic effect of Aronia melanocarpa fruit juice in rats fed a high-cholesterol diet.* Plant Foods Hum Nutr. 2007 Mar; 62(1): 19-24.
30) Pool-Zobel BL et al. *Anthocyanins are potent antioxidants in model systems but do not reduce endogenous oxidative DNA damage in human colon cells.* Eur J Nutr. 1999 Oct; 38(5): 227-34.
31) Kahkonen MP et al. *Berry phenolics and their antioxidant activity.* J Agric Food Chem. 2001 Aug; 49(8): 4076-82.
32) Kmiecik W et al. *Effect of aronia berry honey syrup used for sweetening jams on their quality.* Nahrung. 2001 Aug; 45(4): 273-9.
33) Zheng W. and SY Wang. *Oxygen radical absorbing capacity of phenolics in blueberries, cranberries, chokeberries, and lingonberries.* J Agric Food Chem. 2003 Jan 15; 51(2): 502-9.
34) Simeonov SB et al. *Effects of Aronia melanocarpa juice as part of the dietary regimen in patients with diabetes mellitus.* Folia Med (Plovdiv). 2002; 44(3): 20-3.
35) Kasparaviciene G and V Briedis. *Stability and antioxidant activity of black currant and black aronia berry juices.* Medicina (Kaunas). 2003; 39 Suppl 2:65-9.
36) Matsumoto M et al. *Gastroprotective effect of red pigments in black chokeberry fruit (Aronia melanocarpa Elliot) on acute gastric hemorrhagic lesions in rats.* J Agric Food Chem. 2004 Apr 21; 52(8): 2226-9.
37) Nakajima JI et al. *LC/PDA/ESI-MS Profiling and Radical scavenging activity of anthocyanins in various berries.* J Biomed Biotechnol. 2004; 2004 (5): 241-247.
38) Wu X et al. *Characterization of anthocyanins and proanthocyanidins in some cultivars of Ribes, Aronia, and Sumbucus and their antioxidant capacity.* J Agric Food Chem. 2004 Dec 29; 52(26): 7846-56.
39) Zhao C et al. *Effects of commercial anthocyanin-rich extracts on colonic cancer and nontumorigenic colonic cell growth.* J Agric Food Chem. 2004 Oct 6; 52(20): 6122-8.
40) Atanosova-Goranova VK et al. *Effect of food products on endogenous generation of N-nitrosamines in rats.* Br J Nutr. 1997 Aug; 78(2): 335-45.
41) *Aronia berry, 'the healthiest fruit in the world,' hits the High Street.* www.dailymail.co.uk/health/article-1050077/Aronia-berry-health.
42) Sahalian R. *Aronia berry by Ray Sahelian, M.D. Health Benefit of Aronia Berry.* www.raysahelian.com/aronia.
43) Davalos A et al. *Quercitin is bioavailable from a single ingestion of grape juice.* Int J Food Sci Nutr. 2006 Aug-Sep; 57(5-6): 391-8.
44) Demrow HS et al. *Administration of wine and grape juice inhibits in vivo platelet activity and thrombosis in stenosed canine coronary arteries.* Circulation. 1995 Feb 15; 91(4): 1182-8.
45) Joseph JA et al. *Blueberry extract alters oxidative stress-mediated signaling in COS-7cells transfected with selectively vulnerable muscarinic receptor subtypes.* J Alzheimers Dis. 2006 Mar;9(1):35-42.
46) Chrubasik C et al. *An observational study and quantification of the actives in a supplement with Sambucus nigra and Asparagus officinalis used for weight reduction.* Phytother Res. 2008 Jul;22(7):913-8.
47) Dunlap KL et al. *Total antioxidant power in sled dogs supplemented with blueberries and the comparison of blood parameters associated with exercise.* Comp Biochem Physiol A Mol Integr Physiol. 2006 Apr;143(4):429-34. Epub 2006 Mar 6.
48) Schmidt BM et al. *Differential effects of blueberry proanthocyanidins on androgen sensitive and insensitive human prostate cancer cell lines.* Cancer Lett. 2006 Jan 18;231(2):240-6.
49) Han GL et al. *Effect of anthocyanin rich fruit extract on PGE2 produced by endothelial cells.* Wei sheng Yan Jiu. 2005 Sep;34(5):581-4.
50) Ignarro LJ, et al. *Pomegranate juice protects nitric oxide against oxidative destruction and enhances the biological actions of nitric oxide.* Nitric Oxide. 2006 Sep;15(2):93-102. Epub 2006 Apr 19.
51) McAnulty SR et al. *Effect of daily fruit ingestion on angiotensin converting enzyme activity, blood pressure, and oxidative stress in chronic smokers.* Free Radic Res. 2005 Nov;39(11):1241-8.

52) Matchett MD et al. *Blueberry flavonoids inhibit matrix metalloproteinase activity in DU145 human prostate cancer cells.* Biochem Cell Bio. 2005 Oct;83(5):637-43.
53) Lau FC et al. *The beneficial effects of fruit polyphenols on brain aging.* Neurobiol Aging. 2005 Dec;26 Suppl 1:128-32. Epub 2005 Sep 27.
54) Stromberg I et al. *Blueberry- and spirulina-enriched diets enhance striatal dopamine recovery and induce a rapid, transient microglea activation after injury of the rat nigrostriatal dopamine system.* Exp. Neurol. 2005 Dec'196(2):298-307. Epub 2005 Sep 19.
55) Yi W et al. *Phenolic compounds from blueberries can inhibit colon cancer cell proliferation and induce apoptosis.* J Agric Food Chem. 2005 Sep 7;53(18):7320-9.
56) Matchett MD et al. *Inhibition of matrix metalloproteinase activity in DU145 human prostate cancer cells by flavonoids from lowbush blueberry (Vaccinium angutifolium): possible roles for protein kinase C and mitogen-activated protein-kinase-mediated events.* J Nutr Biochem. 2006 Feb;17(2):117-25. Epub 2005 Jun 20.
57) Faria A et al. *Antioxidant properties of prepared blueberry (Vaccinium myrtillus) extracts.* J Agric Food Chem. 2005 Aug 24;53(17):6896-902.
58) Ramirez MR et al. *Effect of lyophilized Vaccinium berries on memory, anxiety and locomotion in adult rats.* Pharmacol Res. 2005 Dec; 52(6):457-62. Epub 2005 Aug 10.
59) Azadzoi KM et al. *Oxidative stress in arteriogenic erectile dysfunction: prophylactic role of antioxidants.* J Urol. 2006 Mar;175(3Pt 1): 1175-6.
60) Galli RL et al. *Blueberry supplemented diet reverses age-related decline in hippocampal HSP70 neuroprotection.* Neurobiol Aging. 2006 Feb;27(2):344-50.
61) Wang Y et al. *Dietary supplementation with blueberries, spinach or spirulina reduces ischemic brain damage.* Exp Neurol. 2005 May;193(1):75-84.
62) Lekakis J et al. *Polyphenolic compounds from red grapes acutely improves endothelial function in patients with coronary heart disease.* Eur J Cardiovasc Prev Rehabil. 2005 Dec; 12(6): 596-600.
63) Casadesus G et al. *Modulation of hippocampal plasticity and cognitive behavior by short-term blueberry supplementation in aged rats.* Nutr. Neurosci. 2004 Oct-Dec;7(5-6):309-16.
64) Hope Smith S et al. *Antimutagenic activity of berry extracts.* J Med Food. 2004 Winter; 7(4): 450-5.
65) Harada N et al. *Effect of topical application of raspberry ketone on dermal production of insulin-like growth factor-1 in mice and on hair growth and skin elasticity in humans.* Growth Horm IGF Res. 2008 Aug; 18(4): 335-44.
66) Davalos A et al. *Red grape juice polyphenols alter cholesterol homeostasis and increase LDL-receptor activity in human cells in vitro.* J Nutr. 2006 Jul; 136(7): 1766-73.
67) Schmidt BM et al. *Effective separation of potent antiproliferation and antiadhesion components from wild blueberry (Vaccinium angustifolium Ait.) fruits.* J Agric Food Chem. 2004 Oct 20; 52(21): 6433-42.
68) Govarzu P et al. *Blueberry supplemented diet: effects on object recognition memory and nuclear factor-kappa B levels in aged rats.* Nutr Neurosci. 2004 Apr; 7(2): 75-83.
69) Kolosova NG et al. *Comparison of antioxidants in the ability to prevent cataract in prematurely aging OXYS rats.* Bull Exp Biol Med. 2004 Mar; 137(3): 249-51.
70) Kay CD et al. *Anthocyanin metabolites in human urine and serum.* Br J Nutr. 2004 Jun; 91(6): 933-42.
71) Boata F et al. *Red Grape juice inhibits iron availability: application of an in vitro digestion/caco-2 cell model.* J Agric Food Chem. 2002 Nov 6; 50(23): 6935-8.
72) Joseph JA et al. *Blueberry supplementation enhances signaling and prevents behavioral deficits in an Alzheimer disease model.* Nutr Neurosci. 2003 Jun; 6(3): 153-62.
73) Wedge DE et al. *Anticarcinogenic activity of strawberry, blueberry, and raspberry extracts to breast and cervical cancer.* J Med Food. 2001 Spring; 4(1): 49-51.
74) Zheng W and SY Wang. *Oxygen radical absorbing capacity of phenolics in blueberries, cranberries, chokeberries, and lingonberries.* J Agric Food Chem. 2003 Jan 15; 51(2): 502-9.
75)Mazza G et al. *Absorption of anthocyanins from blueberries and serum antioxidant status in human subjects.* J Agric Food Chem. 2002 Dec 18;50(26):7731-7.
76) Roy S et al. *Anti-angiogenic property of edible berries.* Free Radic Res. 2002 Sep;36(9):1023-31.
77) Kay CD et al. *The effect of wild blueberry (Vaccinium angutifolium) consumption on postprandial serum antioxidant status in human subjects.* Br J Nutr. 2002 Oct;88(4):389-98.
78) Wu X. et al. *Absorption and metabolism of anthocyanins in elderly women after consumption of elderberry or blueberry.* J Nutr. 2002 Jul; 132(7): 1865-71.
79) Youdim KA et al. *Potential role of dietary flavonoids in reducing microvascular endothelium vulnerability to oxidative and inflammatory insults (small star, filled).* J Nutr Biochem. 2002 May; 13(5): 282-288.
80) Galli RL et al. *Fruit polyphenolics and brain aging: nutritional interventions targeting age-related neuronal and behavioral deficits.* Ann N Y Acad Sci. 2002 Apr; 959: 128-32.
81) Halvorsen BL et al. *A systematic screening of total antioxidants in dietary plants.* J Nutr. 2002 Mar;132(3):461-71.
82) Papanikolaou N. *MR cholangiopancreatography before and after oral blueberry juice administration.* J Comput Assist Tomogr. 2000. Mar-Apr; 24(2): 229-34.
83) Youdim KA et al. *Polyphenolics enhance red blood cell resistance to oxidative stress: in vitro and in vivo.* Biochim Biophys Acta. 2000 Sep 1; 1523(1): 117-22.
84) Lala G et al. *Anthocyanin-rich extracts inhibit multiple biomarkers of colon cancer in rats.* Nutr Cancer. 2006; 54(1): 84-93.
85) Matsumoto M et al. *Gastroprotective effect of red pigments in black chokeberry fruit (Aronia melanocarpa Elliot) on acute gastric hemorrhagic lesions in rats.* J Agric Food Chem. 2004 Apr 21; 52(8): 2226-9.
86) Puupponen-Pimia R et al. *Berry phenolics selectively inhibit the growth of intestinal pathogens.* J Appl Microbiol. 2005; 98(4): 991-1000.
87) Joseph, JA et al. *Resersals of age-related declines in neuronal signal transduction, cognitive, and motor behavioral deficits with blueberry, spinach and strawberry dietary supplementation.* J Neurosci. 1999 Sep 15; 19(18): 8114-21.
88) Nohynek LJ et al. *Berry phenolics: antimicrobial properties and mechanisms of action against severe human pathogens.* Nutr Cancer. 2006; 54(1): 18-32.
89) Bomser, et al. *In vitro anticancer activity of fruit extracts from Vaccinium species.* Planta Med. 1996 Jun; 62(3): 212-6.
90) Khan N et al. *Pomegranate fruit extract inhibits prosurvival pathways in human A549 lung carcinoma cells and tumor growth in athymic nude mice.* Carcinogenesis. 2006 Aug 18.
91) Pantuck, AJ et al. *Phase II study of pomegranate juice for men with rising prostate-specific antigen following surgery or radiation for prostate cancer.* Department of Urology, David Geffen School of Medicine. University of California at Los Angeles, Los Angeles, California. Clinical Cancer Research, Jul 2006. 1;12(13): 4018-26.
92) Ignarro, LJ et al. *Pomegranate juice protects nitric oxide against oxidative destruction and enhances the biological actions of nitric oxide.* Dept of Molecular and medical Pharmacology, David Geffen Scholl of Medicine at UClA. LA, California. Nitric Oxide. Sep 2006; 15(2): 93-102.
93) Syed, DN et al. *Photochemopreventive effect of pomegranate fruit extract on UVA-mediated activation of cellular pathways in normal human epidermal keratinocytes.* Photochem Photobio. Mar-Apr, 2006; 82(2): 398-405.
94) Aggarwal, BB and S Shishodia. *Molecular targets of dietary agents for prevention and therapy of cancer.* Biochem Pharmacol, 20006 May 14; 71(10): 1397-421. Epub 2006 Feb 23.
95) Rosenblat, M. et al. *Pomegranate byproduct administration to apolipoprotein e-deficient mice attenuates atherosclerosis development as a result of decreased macrophage oxidative stress and reduced cellular uptake of oxidized low-density lipoprotein.* J Agric Food Chem,. 2006 Mar 8; 54(5): 1928-35.
96) Malik, A and H Mukhtar. *Prostate cancer prevention through pomegranate fruit.* Cell Cycle. 2006 Feb; 5(4): 371-3.
97) Adams, LS et al. *Pomegranate juice, total pomegranate ellagitannins, and punicalagin suppress inflammatory cell signaling in colon cancer cells.* J Agric Food Chem. 2006 Feb 8; 54(3): 980-5.
98) Larrosa, M et al. *The dietary hydrolysable tannin punicalagin releases ellagic acid that induces apoptosis in human colon adenocarcinoma Caco-2 cells by using the mitochondrial pathway.* J Nutr Biochem. 2006 Sep; 17(9): 611025.
99) Day AP et al. *Effect of concentrated red grape juice consumption on serum antioxidant capacity and low-density lipoprotein oxidation.* Ann Nutr Metab. 1997;41(6):363-7.

100) deNigris, F et al. *Pomegranate juice reduces oxidized low-density lipoprotein downregulation of endothelial nitric oxide synthase in human coronary endothelial cells.* Nitric Oxide. 2006 Jan 11.
101) Neurath, AR et al. *Punica granatum (Pomegranate) Juice Provides an HIV-1 Entry inhibitor and Candidate Topical Microbicide.* Ann NY Acad Sci. 2005 Nov; 1056: 311-27.
102) Jeune, MA et al. *Anticancer activities of pomegranate extracts and genistein in human breast cancer cells.* J Med Food. 2005 Winter; 8(4): 469-75.
103) Yoshimura, M. et al. *Inhibitory effect of an ellagic acid-rich pomegranate extract on tyrosinase activity and ultraviotlet-induced pigmentation.* Biosci Biotechnol Biochem. 2005 Dec; 69(12): 2368-73.
104) Roxenberg O et al. *Pomegranate juice sugar fraction reduces macrophage oxidative state, whereas white grape juice sugar fraction increases it.* Atherosclerosis. 2006 Sep; 188(1): 68-76.
105) Vinson JA et al. *Red wine, dealcoholized red wine, and especially grape juice, inhibit atherosclerosis in a hamster model.* Atherosclerosis. 2001 May; 156(1): 67-72.
106) Rosenblat M et al *Anti-oxidative effects of pomegranate juice (PJ) consumption by diabetic patients on serum and on macrophages*. Atherosclerosis. 2006 Aug; 187(2): 363-71.
107) Asiam MN et al. *Pomegranate as a cosmeceutical source: pomegranate fractions promote proliferation and procollagen synthesis and inhibit matrix metallopproteinase-1 in human skin cells.* J Ethnopharmacol. 2006 Feb 20; 103(3): 311-8.
108) Malik A et al. *Pomegranate fruit juice for chemoprevention and chemotherapy of prostate cancer.* Proc Natl Acad Sci U.S.A. 2005 Oct 11; 102(41); 14813-8.
109) Braga LC et al. *Synergic interaction between promegranate extract and antibiotics against Stephylococcus aureus.* Can J Microbiol. 2005 Jul; 51(7); 541-7.
110) Sumner MD et al. *Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease.* Am J Cardio. 2005 Sep 15; 96(6): 810-4.
111) Fuhrman B et al. *Pomegranate juice inhibits oxidized LDL uptake and cholesterol biosynthesis in macrophages.* J Nutr Biochem. 2005 Sep; 16(9): 570-6.
112) Azadzoi KM et al. *Oxidative stress in arteriogenic erectile dysfunction: prophylactic role of antioxidants.* J Urol. 2005 Jul; 174(1):386-93.
113) Seeram NP et al. *In vitro antiproliferative, apoptotic and antioxidant activities of punicalagin, ellagic acid and a total pomegranate tannin extract are enhanced in combination with other polyphenols as found in pomegranate juice.* J Nutr Biochem. 2005 Jun; 16(6):360-7.
114) Voravuthikunchai SP and L Kitpipit. *Activity of medicinal plant extracts against hospital isolates of methicillin-resistant Staphylococcus aureus.* Clin Microbiol Infect. 2005 Jul;11(6):510-2.
115) Loren DJ et al. *Maternal dietary supplementation with pomegranate juice is neuroprotective in an animal model of neonatal hypoxic-ischemic brain injury.* Pediatr Res. 2005 Jun; 57(6):858-64.
116) Sudheesh S and NR Vijayalakshmi. *Flavonoids from Punica granatum – potential antiperoxidative agents.* Fitoterapia. 2005 Mar; 76(2): 181-6.
117) Lansky EP et al. *Pomegranate (Punica granatum) pure chemicals show possible synergistic inhibition of human PC-3 prostate cancer cell invasion across Matrigel.* Invest New Drus. 2005 Mar; 23(2):121-2.
118) Hidaka M et al. *Effects of pomegranate juice on human cytochrome p450 3A (CYP3A) and carbamazepine pharmacokinetics in rats.* Drug Metab Dispos. 2005 May; 33(5); 644-8.
119) Braga LC et al. *Pomegranate extract inhibits Staphylococcus aureus growth and subsequent enterotoxin production.* J Ethnopharmacol. 2005 Jan 4; 96(1-2):335-9.
120) Mehta R and EP Lansky. *Breast cancer chemopreventive properties of pomegranate (Punica granatum) fruit extracts in a mouse.* Eur J Cancer Prev. 2004 Aug; 13(4): 345-8.
121) Lansky EP et al. *Possible synergistic prostate cancer suppression by anatomically discrete pomegranate fractions.* Invest New Drugs. 2005 Jan; 23(1): 11-20.
122) Puupponen-Pimia R et al. *Bioactive berry compounds-novel tools against human pathogens.* Appl Microbiol Biotechnol. 2005 Apr; 67(1):8-18.
123) Afag F et al. *Anthocyanin- and hydrolysable tannin-rich pomegranate fruit extract modulates MAPK and NF-kappaB pathways and inhibits skin tumorigenesis in CD-1 mice.* Int J Cancer. 2005 Jan 20; 113(3): 423-33.
124) Esmaillzadeh A et al. *Concentrated pomegranate juice improves lipid profiles in diabetic patients with hyperlipidemia.* J Med Food. 2004 Fall; 7(3):305-8.
125) Albrecht M et al. *Pomegranate extracts potently suppress proliferation, xenograft growth ,and invasion of human prostate cancer cells.* J Med Food. 2004 Fall; 7(3): 274-83.
126) Seeram NP et al. *Bioavailability of ellagic acid in human plasma after consumption of ellagitannins from pomegranate (Punica granatum L.) juice.* Clin Chim Acta. 2004 Oct; 348(1-2): 63-8.
127) Aviram M et al. *Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation.* Clin Nutr. 2004 Jun; 23(3): 423-33.
128) Kawaii S and EP Lansky. *Differentiation-promoting activity of pomegranate (Punica granatum) fruit extracts in HL-60 human promyelocytic leukemia cells.* J Med Food. 2004 Spring; 7(1): 13-8.
129) Vasconcelos LC et al. *Use of Punica grnatum as an antifungal agent against candidosis associated with denture estomatitis.* Mycoses. 2003 Jun; 46(5-6); 192-6.
130) Aviram M et al. *Pomegranate juice flavonoids inhibit low-density lipoprotein oxidation oand cardiovascular diseases; studies in atherosclerotic mice and in humans.* Drugs Exp Clin Res. 2002; 28(2-3): 49-62.
131) Kim ND et al. *Chemopreventive and adjuvant therapeutic potential of pomegranate (Punica granatum) for human breast cancer.* Breast Cancer Res Treat. 2002 Feb; 71(3): 203-17.
132) Noda Y et al. *Antioxidant activities of pomegranate fruit extract and its anthocyanidins: delphinidin, cyanidin, and pelargonidin.* J Agric Food Chem. 2002 Jan 2; 50(1): 166-71.
133) Aviram M and L Dornfeld. *Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure.* Atherosclerosis. 2001 Sep; 158 (1): 195-8.
134) Kaplan M et al. *Pomegranate juice supplementation to atherosclerotic mice reduces macrophage lipid peroxidation, cellular cholesterol accumulation and development of atherosclerosis.* J Nutr. 2001 Aug; 1318): 2082-9.
135) Aviram M et al. *Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation; studies in human and in atherosclerotic apolipoprotein E-deficient mice.* Am J Clin Nutr. 2000 May; 71(5);: 1062-76.
136) Gaig P et al. *Allergy to pomegranate (Punica granatum).* J Investig Allergol Clin Immunol. 1992 Jul-Aug; 2(4): 216-8.
137) Igea JM et al. *Adverse reaction to pomegranate ingestion.* Allergy. 1991 Aug; 46(6): 472-4.
138) Bell DR and K Gochenaur. *Direct vasoactive and vasoprotective properties of anthocyanin-rich extracts.* J Appl Physiol. 2006 Apr; 100(4): 1164-70.
139) Bagchi D et al. *Safety and whole-body antioxidant potential of a novel anthocyanin-rich formulation of edible berries.* Mol Cell Biochem. 2006 Jan; 28(1-2): 197-209.
140) Morillas-Ruiz J et al. *The effects of an antioxidant-supplemented beverage on exercise-induced oxidative stress: results from a blacebo-controlled double-blind study in cyclists.* Eur J Appl Physiol. 2005 Dec; 95 (5-6): 543-9.
141) McGhie TK et al. *Anthocyanin glycosides from berry fruit are absorbed and excreted unmetabolized by both humans and rats.* J Agric Food Chem. 2003 Jul 30;51(16): 4539-48.
142) Parry J et al. *Fatty acid composition and antioxidant properties of cold-pressed marionberry, boysenberry, red raspberry, and blueberry seed oils.* J Agric Food Chem. 2005 Feb 9; 53(3): 566-73.
143) Proteggente AR et al. *The antioxidant activity of regularly consumed fruit and vegetables reflects their phenolic and vitamin C composition.* Free Redic Res. 2002 Feb; 36(2): 217-33.

144) Chattarjee A et al. *Inhibition of Helicobacter pylori in vitro by various berry extracts, with enhanced susceptibility to clarithromycin.* Mol Cell Biochem. 2004 Oct; 265(1-2): 19-26.

145) Zakay-Rones Z et al. *Randomized study of the efficacy and safety of oral elderberry extract in the treatment of influenza A and B virus infections.* J Int Med Res. 2004 Mar-Apr; 32(2): 132-140.
146) Jing P et al. *Structure-function relationships of anthocyanins from various anthocyanin-rich extracts on the inhibition of colon cancer cell growth.* J Agric Food Chem. 2008 Oct 22; 56(20): 9391-8.
147) Murkovic M et al. *Effects of elderberry juice on fasting and postprandial serum lipids and low density lipoprotein oxidation in healthy volunteers: a randomized, double-blind, placebo-controlled study.* Eur J Clin nutr. 2004 Feb;58 (2): 244-9.
148) Castilla P et al. *Comparative effects of dietary supplementation with red grape juice and vitamin E on production of superoxide by circulating neutrophil NADPH oxidase in hemodialysis patients. Am J Clin Nutr. 2008 Apr;87(4):1053-61.*
149) Milbury PE, et al. *Bioavailability of Elderberry anthocyanins.* Mech Ageing Dev. 2002 Apr 30; 123(8): 997-1006.
150) Youdim KA et al. *Incorporation of the elderberry anthocyanins by endothelial cells increases protection against oxidative stress.* Free Radic Biol. Med. 2000 Jul 1; 29(1) 51-60.
151) Zakay-Rones Z et al. *Inhibition of several strains of influenza virus in vitro and reduction of symptoms by an elderberry extract (Sambucus nigra L.) during outbreak of influenza B in Panama.* J Altern Complement. Med. 1995 Winter; 1 (4):361:9.
152) Kahkonen MP et al. *Berry phenolics and their antioxidant activity.* J Agric Food Chem. 2001 Aug; 49(8): 4076-82.
153) Biovin D et al. *Inhibition of cancer cell proliferation and suppression of TNF-induced activation of NFkappaB by edible berry juice.* Anticancer Res. 2007 Mar-Apr; 27(2): 937-48.
154) http://www.armeniapedia.org/index.php?title=Rubus_idaeus
155) Morimoto C et al. *Anti-obese action of raspberry ketone.* Life Sce. 2005 May 27l 77(2):194-204. Epub 2005 Feb 25
156) Zafrilla P et al. *Effects of processing and storage on the antioxidant ellagic acid derivatives and flavonoids of red raspberry.* J Agric food Chem. 2001 Aug; 49(8): 3651-5.
157) Bitsch R et al. *Bioavailability and Biokinetics of Anthocyanins from Red Grape Juice and Red Wine.* J Biomed Biotechnol. 2004; 2004(5): 293-298.
158) Passamonti S et al. *Fast access of some grape pigments to the brain.* J Agric Food Chem. 2005 Sep 7; 53(18):7029-34.
159) Al-Awwadi NA et al. *Extracts enriched in different polyphenolic families normalize increased cardiac NADPH oxidase expression while having differential effects on insulin resistance, hypertension, and cardiac hypertrophy in high-fructose fed rats.* J. Agric Food Chem. 2005 Jsn 12;53 (1):151-7.
160) Beekwilder J et al. *Indentification and dietary relevance of antioxidants from raspberry.* Biofactors. 2005; 23(4): 197-205.
161) Morimoto C et al. *Anti-obese action of raspberry ketone.* Life Sci. 2005 May 27; 77(2): 194-204.
162) Nikitina VS et al. *Antibacterial activity of polyphenolic compounds isolated from plants of Geraniaceae and Rosaceae families.* Prikl Biokhim Mikrobiol. 2007 Nov-Dec; 43 (6): 705-12.