

Berry Research Breakthroughs: Top 10 Medical Studies of 2006

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After review of more than 300 research reports on berries in 2006, here are The Berry Doctor's choices of the top 10 medical science studies over the past year.

Format of the presentation is to give the report title, authors' names, research institution and published reference followed by a synopsis of main research findings. To conclude each review, a "note to consumers" provides a single message having potential interest to the general public.

This presentation reveals 3 significant trends in berry research:

1. sophisticated biological models are being applied to demonstrate properties of berry constituents, particularly antioxidant phytochemicals (evident in papers 6,9,10);
2. there is increasing focus on identifying potential health benefits of berries against major diseases such as cardiovascular disorders, diabetes, viral infections and particularly cancer (papers 1,3-5,7,8); and
3. exotic, nutrient- and antioxidant-dense berries (sometimes called "superfruits"), such as açai, are increasingly under systematic investigation to more completely define their properties (paper 2)

10. Direct vasoactive and vasoprotective properties of anthocyanin-rich extracts.

Bell DR, Gochenaur K. Department of Cellular and Integrative Physiology, Indiana University School of Medicine, 2101 Coliseum Blvd. East, Fort Wayne, IN 46805-1499.

J Appl Physiol. 2006 Apr;100(4):1164-70.

Synopsis.

Although nitric oxide is a reactive oxygen specie (ROS), it is, under normal conditions, an important universal transmitter in the human body, having a role in numerous physiological processes. It is particularly important for regulation of blood flow and blood pressure by dilation of small arteries whose smooth muscle layers are under control by nitric oxide as the endothelium-dependent relaxation factor. Nitric oxide, however, can be attacked by other ROS and its normal functions deterred. This study examined the effect of anthocyanin phenolics from chokeberries (*Aronia melanocarpa*), bilberries (*Vaccinium myrtillus*) and elderberries (*Sambucus nigra*) on protection of nitric oxide regulation of vascular tone in pig coronary (heart) artery rings in vitro (a model for human heart artery function). The berry anthocyanins themselves caused the heart arteries to relax (dilate) and also protected normal nitric oxide-mediated dilation in the presence of other ROS.

Note to consumers: This study concluded that berry anthocyanins, either through the diet or as therapeutic agents, may be important for protection of blood flow in coronary artery disease. Such results indicate that colorful berries could be valuable as dietary preventative agents for general health of the heart and vascular system.

9. Neuroprotective effects of *Lycium barbarum* Lynn on protecting retinal ganglion cells in an ocular hypertension model of glaucoma.

Chan HC, Chuen-Chung Chang R, Koon-Ching Ip A, Chiu K, Yuen WH, Zee SY, So KF. Department of Anatomy, Faculty of Medicine, The University of Hong Kong, Pokfulam, Hong Kong.

Exp Neurol. Epub 2006 Oct 11; 203(1):269-73.

Synopsis.

The high intraocular pressure of glaucoma is a threat to vision quality in many aging seniors. Goji ("wolfberry"), well-known for its rich antioxidant content of vitamin C and carotenoids, beta-carotene, zeaxanthin and lycopene, may be a valuable food choice for maintenance of eye health. Zeaxanthin particularly is necessary as a pigment filter and antioxidant in the retina. In rats surgically prepared to have high intraocular pressure characteristic of glaucoma, this study found treatment with an extract of goji berries preserved retinal ganglion cells in this model of glaucoma.

Note to consumers: The results are evidence that components of the goji berry – likely its vitamin C and carotenoids – created a protective effect on retinal ganglion cells in this experimental model of glaucoma. Goji berries may be valuable either as a whole food in the diet or from its extracts to create a therapeutic agent against the effects of glaucoma.

8. Induction of cell death in Caco-2 human colon carcinoma cells by ellagic acid rich fractions from muscadine grapes (*Vitis rotundifolia*).

Mertens-Talcott SU, Lee JH, Percival SS, Talcott ST. Department of Pharmaceutics, University of Florida, P. O. Box 110494, Gainesville, FL 32610-0494.

J Agric Food Chem. 2006 Jul 26;54(15):5336-43.

Synopsis.

Muscadine grapes (*Vitis rotundifolia*) contain some of the richest pigmentation and phenolic concentrations known among berry fruits. This study examined the effect of ellagic acid and other flavonoids from muscadine grapes on parameters of colon cancer cells in vitro. Cancer cells were prevented from proliferating and had increased rates of apoptosis (higher natural self-induced death rates) resulting from exposure to ellagic acid from muscadine grapes.

Note to consumers: An indigenous specie of the southeast USA, muscadine grapes are exceptional sources of ellagic acid and other phenolics that may reduce cancer cell numbers and stimulate cancer cell death.

7. Blackberry, black raspberry, blueberry, cranberry, red raspberry, and strawberry extracts inhibit growth and stimulate apoptosis of human cancer cells in vitro.

Seeram NP, Adams LS, Zhang Y, Lee R, Sand D, Scheuller HS, Heber D. Center for Human Nutrition, David Geffen School of Medicine, University of California, Los Angeles, CA 90095.

J Agric Food Chem. 2006 Dec 13;54(25):9329-9339.

Synopsis.

Six species of common berries – blackberry, black raspberry, blueberry, cranberry, red raspberry and strawberry – were studied for their phenolic antioxidant contents by high-performance liquid chromatography and mass spectrometry. Anthocyanins, flavonols, flavanols, tannins, ellagic acid, proanthocyanidins and other phenolics were found in high concentrations. Tested in vitro for their effects on cell numbers in four different types of cancer – breast, colon, prostate and oral cancer - - the berry phenolics proved effective for inhibiting cancer cell proliferation and stimulating apoptosis (increased rate of cell death, a desirable anti-cancer effect).

Note to consumers: Phenolic antioxidants from common berries proved effective in vitro against four different kinds of cancer.

6. Blueberry polyphenols increase lifespan and thermotolerance in *Caenorhabditis elegans*

Wilson MA, Shukitt-Hale B, Kalt W, Ingram DK, Joseph JA, Wolkow CA. Laboratory of Neurosciences, National Institute on Aging, Intramural Research Program, Baltimore, MD 21224.

Aging Cell. 2006 Feb;5(1):59-68.

Synopsis.

As an experimental model in medical research, the roundworm nematode called *C.elegans* has provided a wealth of scientific information in studies of genetic composition and disease resistance, drug discovery and aging. In this interesting series of experiments using blueberry extracts on *C. elegans*, the authors found that blueberry phenolic proanthocyanidins increased lifespan and tolerance to heat. The effect was mediated through a genetic pathway that regulates osmotic stress.

Note to consumers: blueberry proanthocyanidins have antioxidant and other regulatory effects that may improve resistance to disease and aging.

5. Anti-diabetic properties of the Canadian lowbush blueberry *Vaccinium angustifolium* Ait.

Martineau LC, Couture A, Spoor D, Benhaddou-Andaloussi A, Harris C, Meddah B, Leduc C, Burt A, Vuong T, Mai Le P, Prentki M, Bennett SA, Arnason JT, Haddad PS. Department of Pharmacology and Membrane Protein Study Group, Universite de Montreal, P.O. Box 6128, Downtown Station, Montreal, QC, Canada H3C 3J7; Institut des Nutraceutiques et des Aliments Fonctionnels, Universite Laval, Quebec City, QC, Canada.

Phytomedicine. 2006 Nov;13(9-10):612-23.

Synopsis.

Extracts of blueberry fruit plus other plant components (leaves, roots, stems) improved glucose transport and the insulin response of muscle and pancreas cells in vitro while protecting these cells against glucose toxicity commonly seen in diabetes. Pancreatic beta cells were increased in number by treatment with blueberry extracts.

Note to consumers: blueberry fruit and other plant components contain phenolic antioxidants with properties that favorably improve the response of muscle and pancreas cells to diabetic stimuli, and so have promise as anti-diabetic agents.

4. Antiviral effects on bacteriophages and rotavirus by cranberry juice.

Lipson SM, Sethi L, Cohen P, Gordon RE, Tan IP, Burdowski A, Stotzky G.
Biology Department, St. Francis College, 180 Remsen Street, Brooklyn Heights, NY 11201.

Phytomedicine. 2006 Nov 28; [Epub ahead of print]

Synopsis.

In a study comparing the antiviral effects of juices from cranberries, oranges and grapefruit, the authors found cranberry juice to be 100% effective against monkey viruses called rotavirus SA-11 and bacteriophage T4. Cranberry juice was more effective against these viruses than orange or grapefruit juice.

Note to consumers: commercial cranberry juice has significant antiviral effects under the conditions of these experiments.

3. 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.

Bermudez-Soto MJ, Larrosa M, Garcia-Cantalejo JM, Espin JC,
Tomas-Barberan FA, Garcia-Conesa MT. Grupo de Investigacion en Calidad, Seguridad y Bioactividad de Alimentos Vegetales; Ciencia y Tecnologia de los Alimentos, CEBAS-CSIC, 30100 Murcia, Spain.

J Nutr Biochem. 2006 Jul 21; [Epub ahead of print]

Synopsis.

Chokeberry (*Aronia melanocarpa*) is well-known for its intense sourness, a reflection of strong phenolic acids serving the fruit as antioxidant pigments. In this study of chokeberry juice containing mixed phenolics, several regulatory mechanisms of colon cancer cell function were affected. Chokeberry juice inhibited genes involved in cancer cell growth, reduced cell proliferation and upregulated suppressor genes involved in growth of adenomas and carcinomas.

Note to consumers: Chokeberry juice, normally so bitterly sour that it cannot be taken as a native juice, provided strong anti-cancer effects in vitro. This experiment indicates that phenolic-rich plants like dark berries have promising potential as anti-cancer agents. The study also suggests that modification of chokeberry juice to make it palatable, or use of its extracts, could have significant potential as an anti-cancer tool.

2. Antioxidant capacity and other bioactivities of the freeze-dried amazonian palm berry, *Euterpe oleraceae* mart. (açai).

Schauss AG, Wu X, Prior RL, Ou B, Huang D, Owens J, Agarwal A, Jensen GS, Hart AN, Shanbrom E. Natural and Medicinal Products Research, AIMBR Life Sciences, 4117 South Meridian, Puyallup, WA 98373.

J Agric Food Chem. 2006 Nov 1;54(22):8604-10.

Synopsis.

One of nature's most color-intense fruits, açai is attracting interest for its future use in functional foods where it could supply rich concentration of phenolic antioxidants and value as a deep violet colorant. In studies to characterize the antioxidant strength of açai, these authors measured freeze-dried açai powder against several assays of antioxidant capacity, finding the highest scores yet measured for a fruit against the superoxide radical and for total antioxidant strength. Anthocyanins were only partly responsible for this effect, as other, yet unidentified phenolics were present. Using human neutrophil cells as a model, the authors also showed that açai phenolics remain intact and effective in low doses in exerting their antioxidant effect. This finding indicates that small amounts of açai added to foods or beverages could provide significant antioxidant protection.

Note to consumers: açai fruit from the South American tropics has the strongest antioxidant properties yet observed and has high promise for entering first-world markets as a functional food ingredient and colorant. As its effects are evident at low doses, it may become an ingredient of numerous foods, drugs and other consumer products where antioxidant protection is needed.

1. Transitioning from preclinical to clinical chemopreventive assessments of lyophilized black raspberries: interim results show berries modulate markers of oxidative stress in Barrett's esophagus patients.

Kresty LA, Frankel WL, Hammond CD, Baird ME, Mele JM, Stoner GD, Fromkes JJ.
Division of Hematology and Oncology, Department of Internal Medicine, The Ohio State University College of Medicine and Public Health, Columbus 43210, USA.

Nutr Cancer. 2006;54(1):148-56.

Synopsis.

Over the past five years, research from this group at Ohio State University has been establishing experimental evidence for how phenolics from black raspberries in the diet have preventative effects against several types of cancer (oral, esophageal or throat, breast, colon). The research has progressed sufficiently now to be carried to the next landmark stage – a preliminary investigation of anti-cancer activity in patients with Barrett's esophageal cancer. The research is significant as it directly examines the role of dietary berries on anti-cancer activity in patients with an aggressive cancer.

Note to consumers: preliminary laboratory evidence is significant showing that black raspberries in the diet provides anti-cancer activity against oral, esophageal, breast and colon cancers. Research on humans begun in Autumn 2006 is examining potential benefits of dietary black raspberries on Barrett's esophageal cancer. This is the first human clinical trial of dietary berries as a preventative dietary agent against cancer.

About the Author. Paul M. Gross, Ph.D., received his doctorate in physiology from the University of Glasgow, Scotland and was a post-doctoral fellow in neuroscience at the Laboratory of Cerebral Metabolism, National Institutes of Health, Bethesda, MD. A former Research Scholar for the Heart and Stroke Foundation of Ontario, he published 85 peer-reviewed journal reports and book chapters over a 25 year career in medical science, and was recipient of the Karger Memorial Award, Switzerland, for publications on brain capillaries. Dr. Gross is on the Steering Committee of the International Berry Health Association. He is senior author of a 2006 book on the goji berry entitled *Wolfberry: Nature's Bounty of Nutrition and Health* (Booksurge Publishing, Amazon.com, <http://wolfberry.org>) and is publisher of *The Berry Doctor's Journal*, <http://berrydoctor.com> where the public can obtain free information on berry science and nutrition.