Wild Blueberries™

Blueberries & Health:

A Research Update

Donald K. Ingram, PhD

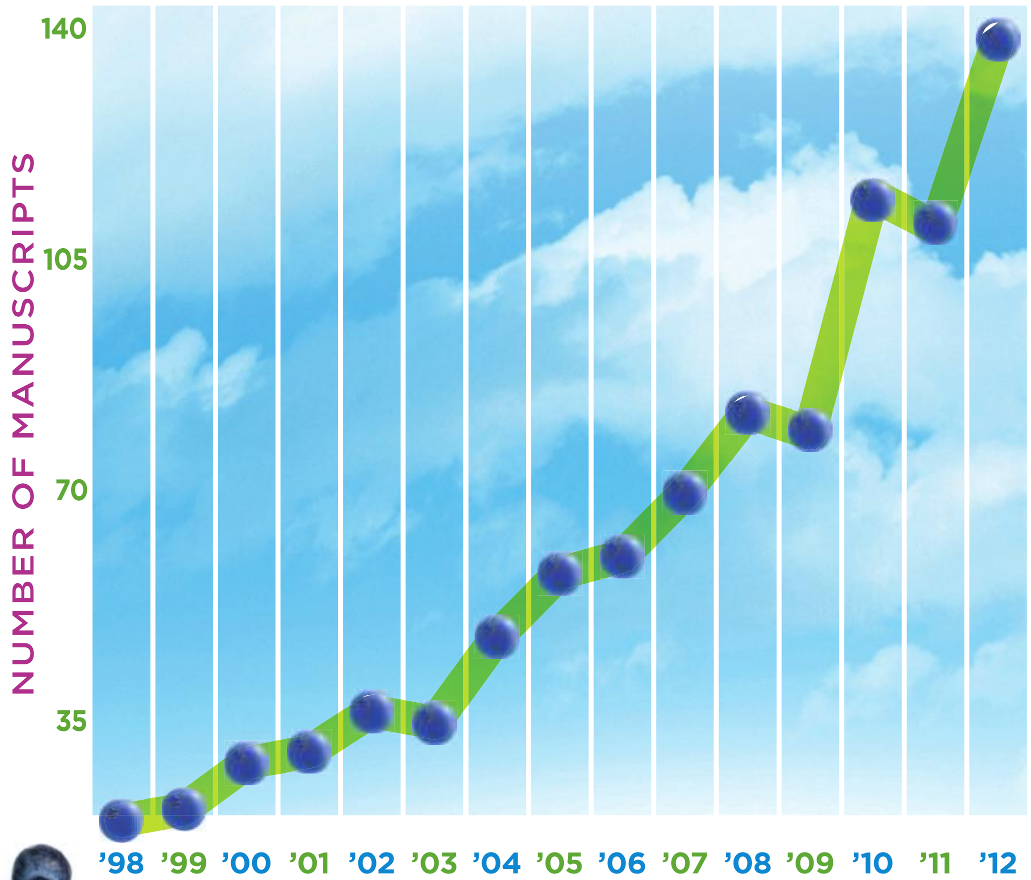
Professor, Pennington Biomedical Research Center
Louisiana State University
Baton Rouge, Louisiana, USA

Genus: *Vaccinium*

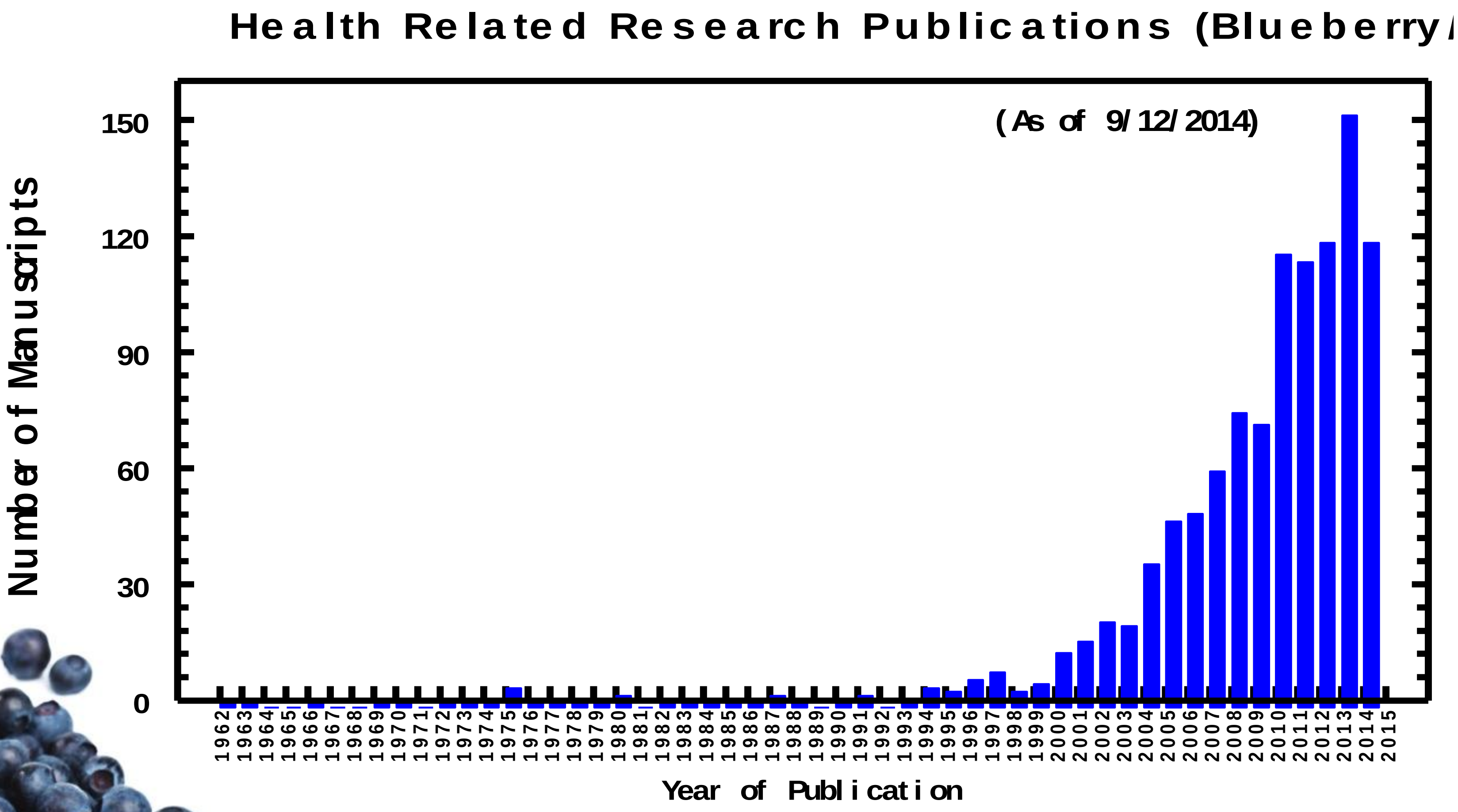
Also includes Bilberry

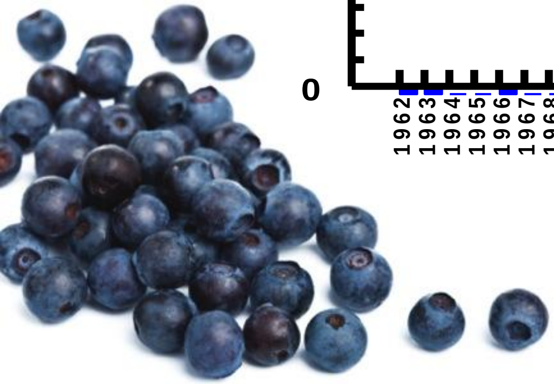
Blueberry Research Gone Wild!

BLUEBERRY/BILBERRY PUBLISHED HEALTH STUDIES



A Focus on Health and Nutrition





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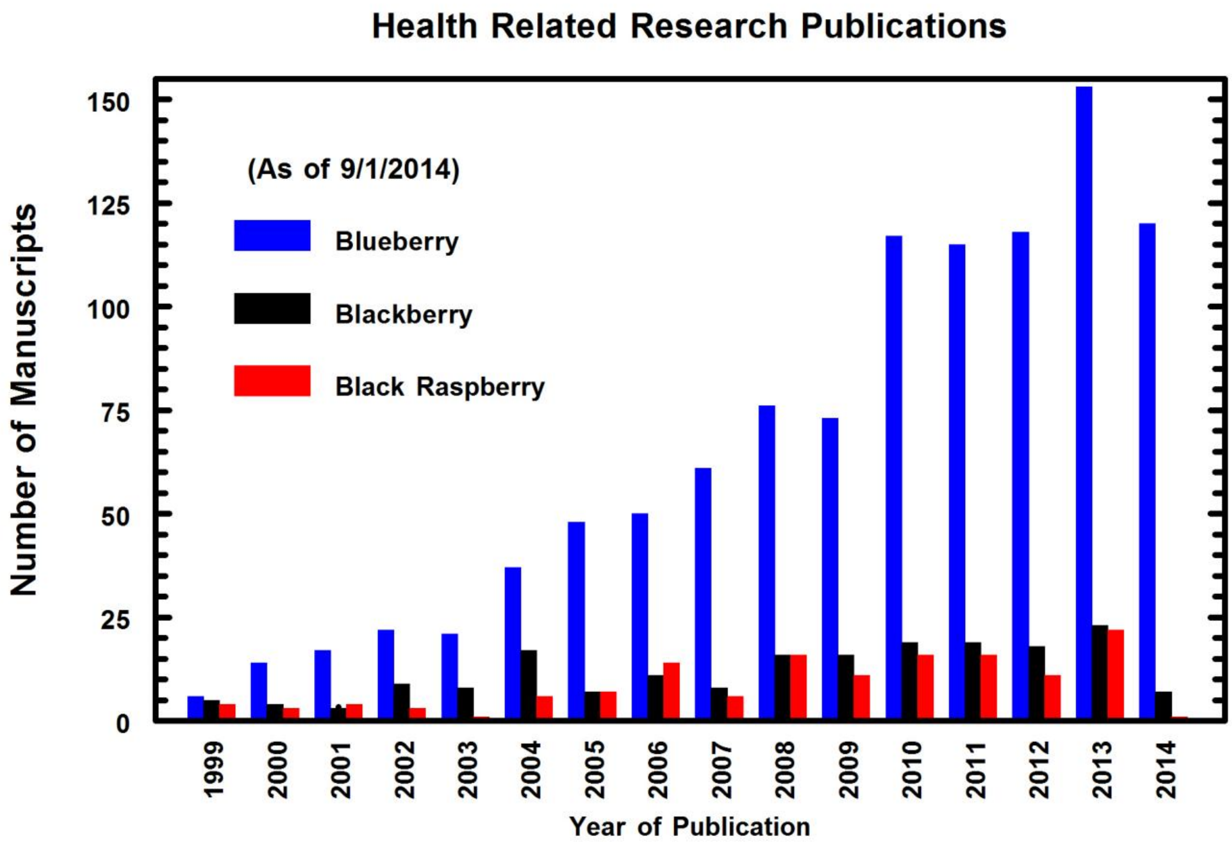
A Focus on Health and Nutrition



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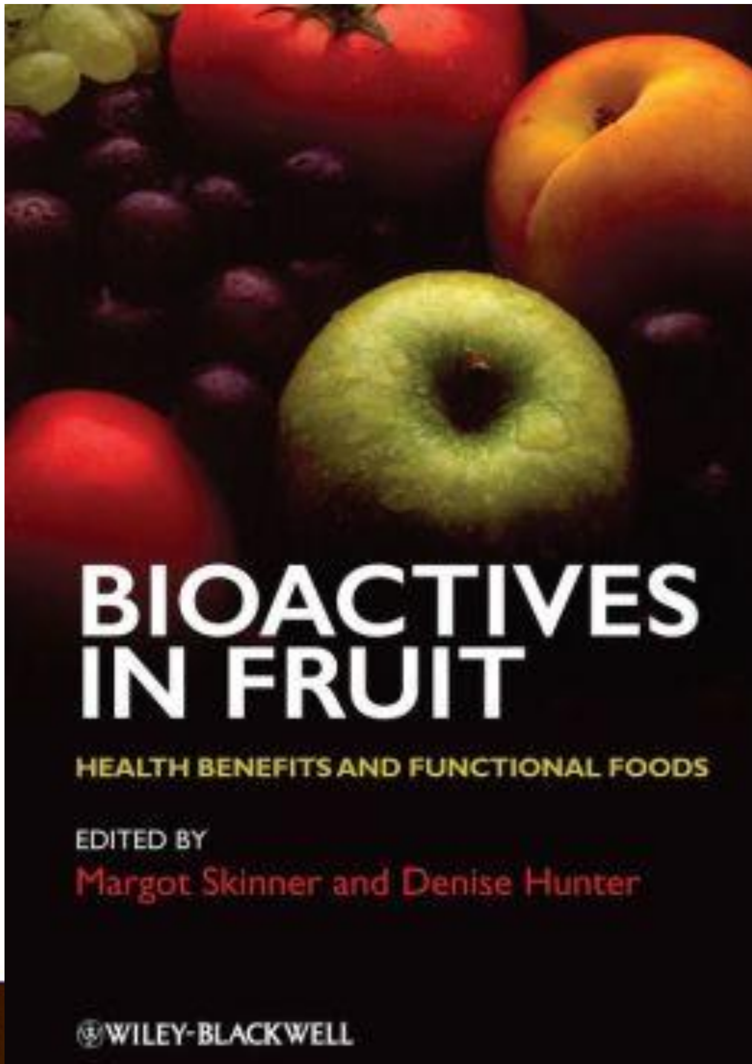
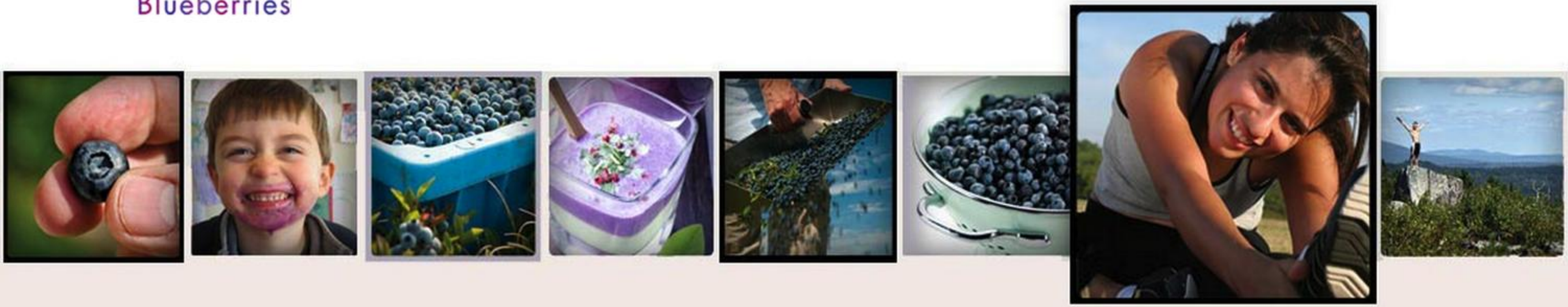


11 Overview of the Health Properties of Blueberries

Carrie M. Elks, Joseph Francis, April J. Stull, William T. Cefalu, Barbara Shukitt-Hale and Donald K. Ingram

2014 Wild Blueberry Health Research Summit



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Jeong, H. R.; Jo, Y. N.; Jeong, J. H.; Kim, H. J.; Kim, M. J.; Heo, H. J.

Blueberry (Vaccinium virgatum) leaf extracts protect against Abeta-induced cytotoxicity and cognitive impairment

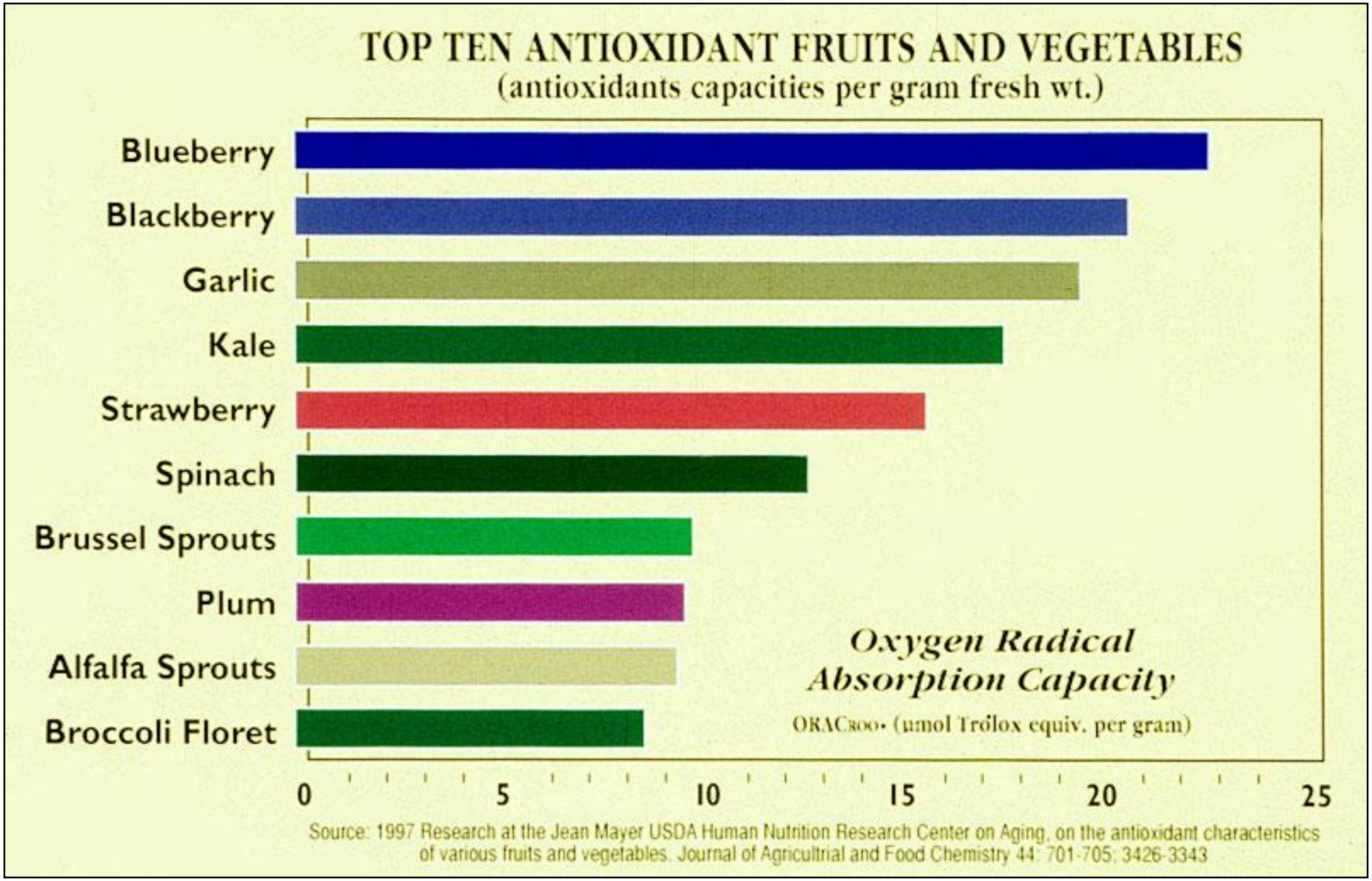
http://dx.doi.org/10.1021/jf400342g

Poulose, Shibu M; Bielinski, Donna F; Gomes, Stacey M; Carrihill-Knoll, Kirsty; Rabin, Bernard M; Shukitt-Hale, Barbara

USDA/ORAC - The Antioxidant Assay

Oxygen Radical Absorbance Capacity

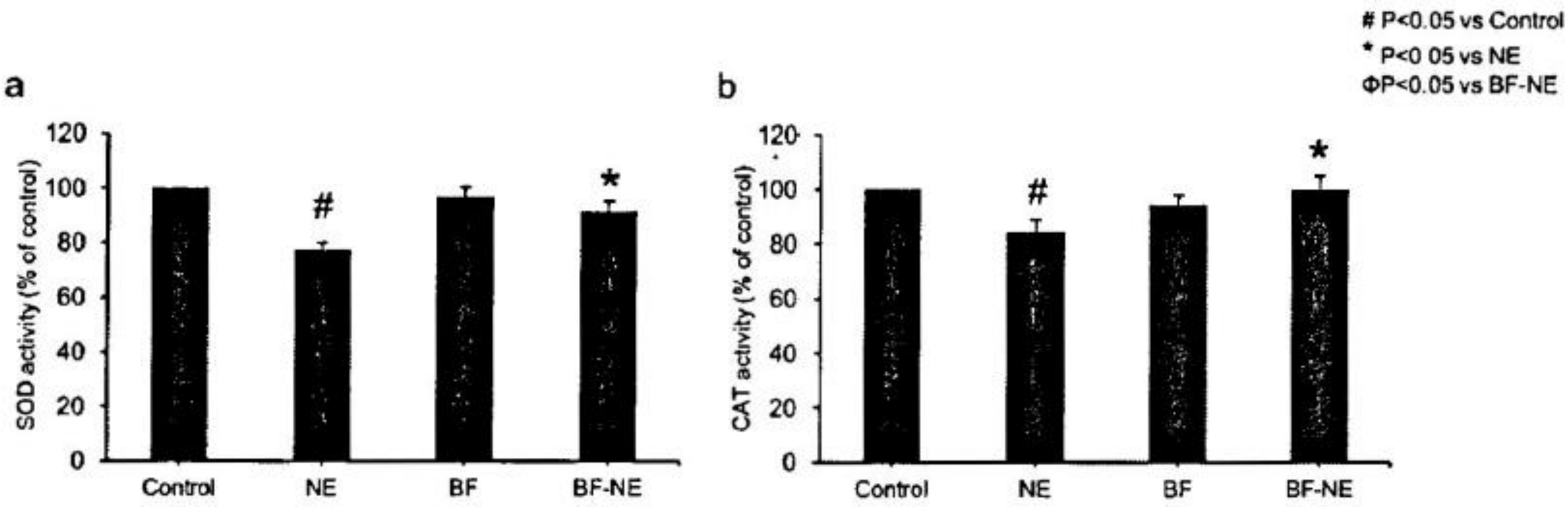
Ron Prior

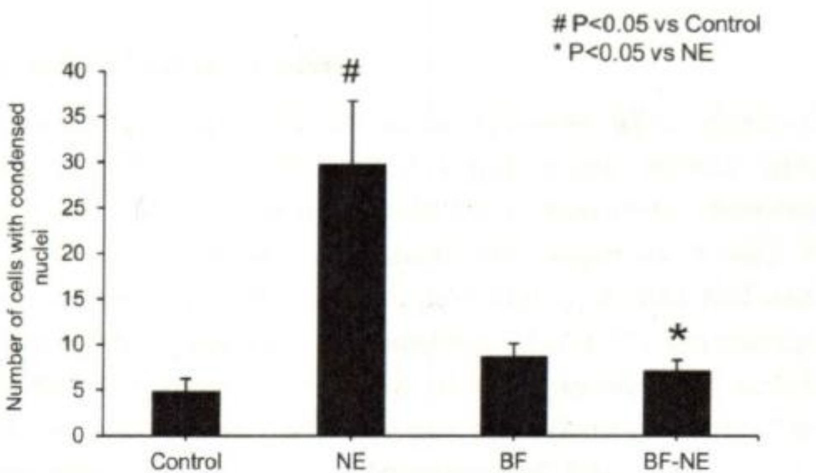


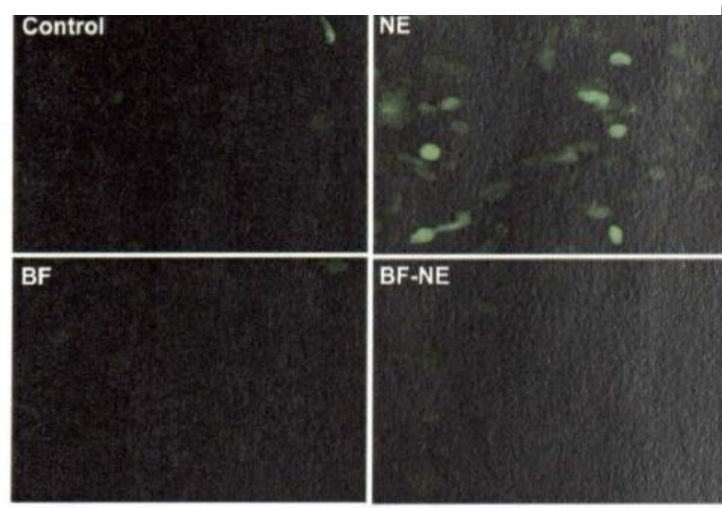
Wang H, Cao, G, Prior, RL. (1996) J. Agric. Food Chem. 44:701-705.

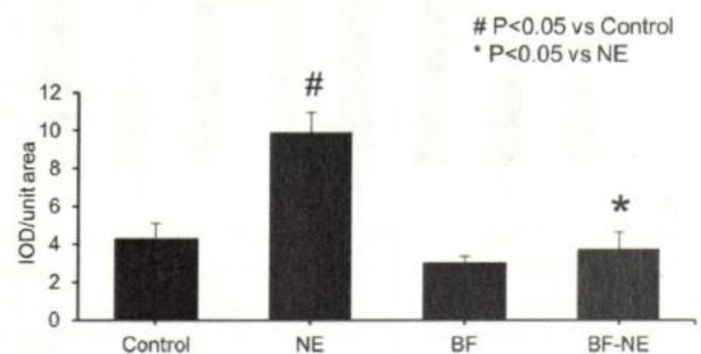
Blueberries Protect Against Toxicity/Stress

Cite tl









Wild BB preparation

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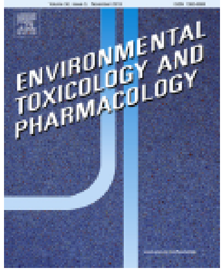

Protective effects of blueberries (*Vaccinium corymbosum* L.) extract against cadmium-induced hepatotoxicity in mice

CrossMark

Pin Gong[a,*], Fu-xin Chen[b], Lan Wang[a], Jing Wang[a], Sai Jin[a], Yang-min Ma[a]

[a] College of Life Science and Technology, College of Chemistry and Chemical Engineering, Shaanxi University of Science and Technology, Xi'an 710021, China

[b] School of Chemistry and Chemical Engineering, Xi'an University of Science and Technology, Xi'an 710054, China

Pharmacogn Mag. 2014 Apr-Jun; 10(Suppl 2): S217–S224.

PMCID: PMC4078330

doi: 10.4103/0973-1296.133234

Vaccinium angustifolium

Chitosan and blueberry treatment induces arginase activity and inhibits nitric oxide production during acetaminophen-induced hepatotoxicity

Eda Ozcelik, Sema Uslu,[1] Dilek Burukoglu,[2] and Ahmet Musmul[3]

J Sci Food Agric (2014) www.soci.org

The protective effects of berry-derived anthocyanins against visible light-induced damage in human retinal pigment epithelial cells

Yon… …ng Ji[a]*

Table 1. High-performan… …ns from different berries

Berry	Reter… time…	…	Purity (%)
Blueberry	3…	…	95.3
Blueberry	2…	…	90.1
Blackberry	2…	…	96.7
Strawberry	2…	…	91.7

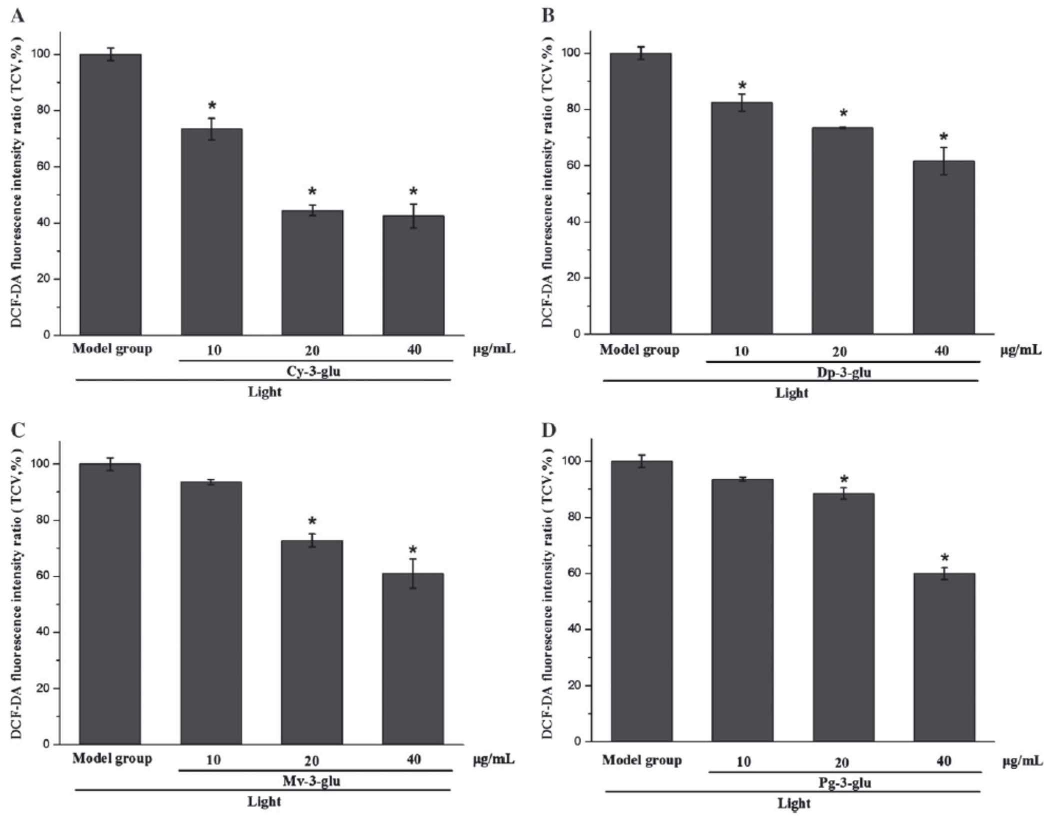

Figure 3. Effects of four anthocyanins (ACNs) on visible light-induced (420–800 nm) increases in intracellular reactive oxygen species (ROS). Confluent cultures were exposed to 2500 lx light for 12 h. The intracellular ROS levels were monitored using 2′,7′-dichlorodihydro-fluorescein diacetate (DCFH-DA). Model group: light exposure, no ACN treatment. DCFH-DA fluorescence intensity ratios [toward the control value (TCV), %] are expressed as means, and standard deviations are represented by vertical bars ($n = 3$). Mean values were significantly different when $^{*}P < 0.05$ (one-way ANOVA). (A) cyanidin-3-glucoside (Cy-3-glu), (B) delphinidin-3-glucoside (Dp-3-glu), (C) malvidin-3-glucoside (Mv-3-glu), and (D) pelargonidin-3-glucoside (Pg-3-glu).

Blueberries Attenuate Tumor Growth

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

dx.doi.org/10.1021/jf403734j | J. Agric. Food Chem. 2014, 62, 3963−3971

Article

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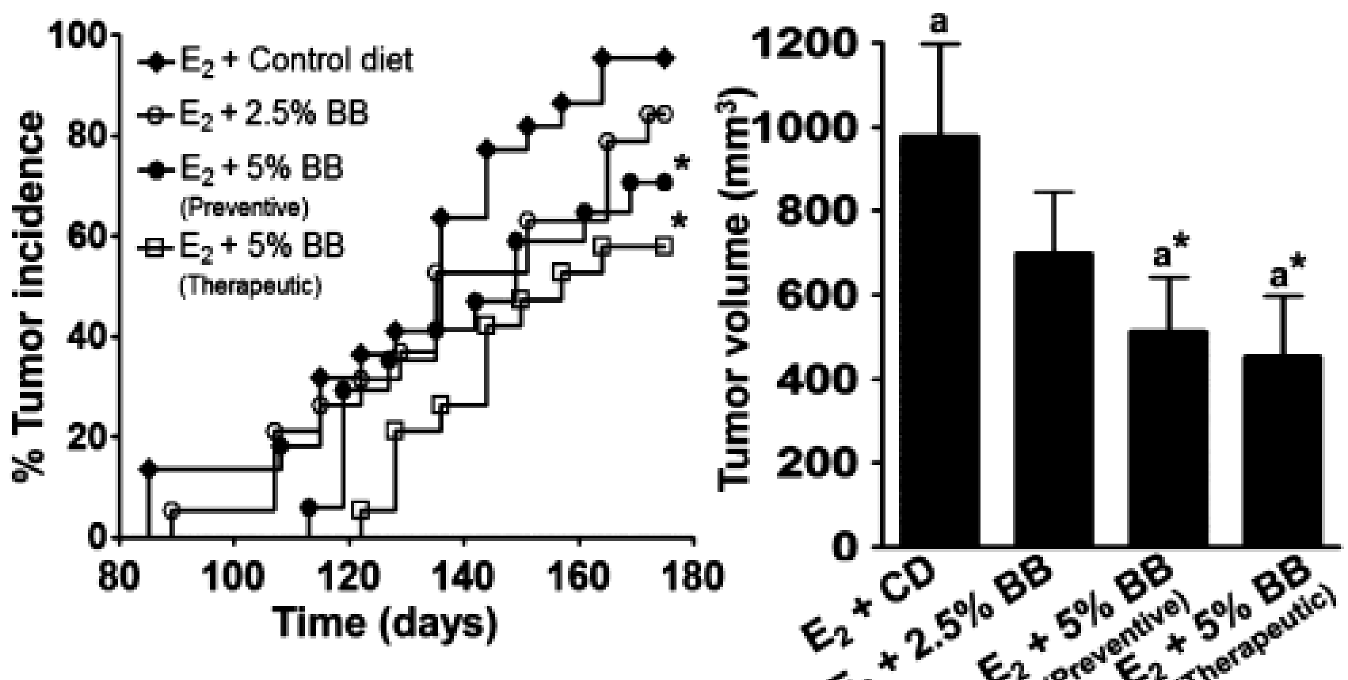
Chemopreventive and Therapeutic Activity of Dietary Blueberry against Estrogen-Mediated Breast Cancer

Jeyaprakash Jeyabalan,[†] Farrukh Aqil,[†,‡] Radha Munagala,[†,‡] Lakshmanan Annamalai,[‡] Manicka V. Vadhanam,[†] and Ramesh C. Gupta*[,†,#]

[†]James Graham Brown Cancer Center, [‡]Department of Medicine, and [#]Department of Pharmacology and Toxicology, University of Louisville, Louisville, Kentucky 40202, United States

9 mg of 17β-estradiol (E2)

High Bush BB for 2 weeks before E2 treatment

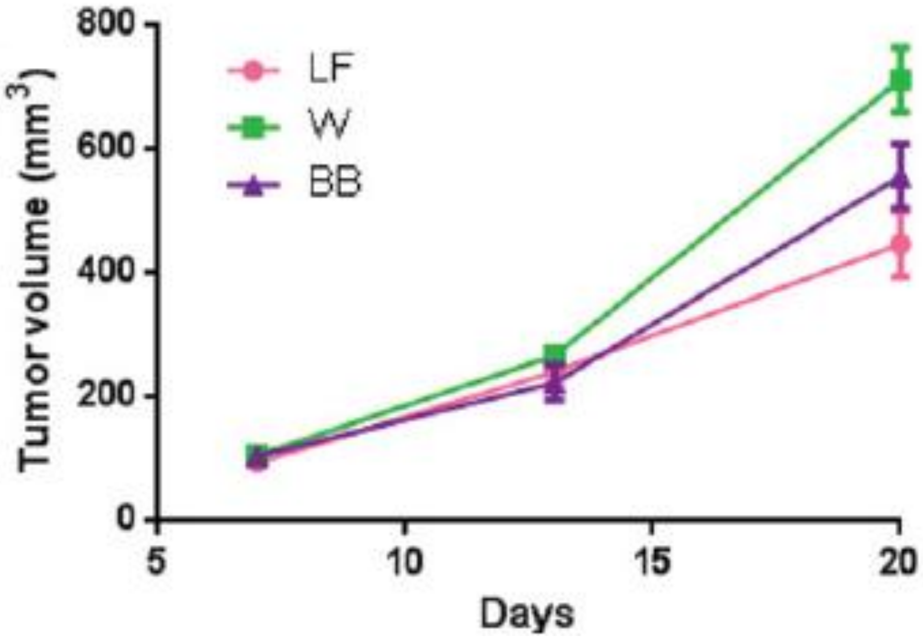


Nutrition and Cancer, 66(2), 242–248

ISSN: 0163-5581 print / 1532-7914 online
DOI: 10.1080/01635581.2014.863366

Whole Blueberry Powder Inhibits Metastasis of Triple Negative Breast Cancer in a Xenograft Mouse Model Through Modulation of Inflammatory Cytokines

Noriko Kanaya, Lynn Adams, Ayano Takasaki, and Shiuan Chen
Department of Cancer Biology, Beckman Research Institute, Duarte, California, USA



5% whole wild BB diet for 2 weeks prior to cancer cell implants

Blueberries Reduce Inflammation

Molecules **2014**, *19*, 12827-12841; doi:10.3390/molecules190812827

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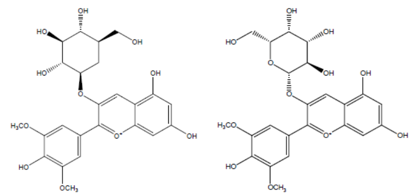


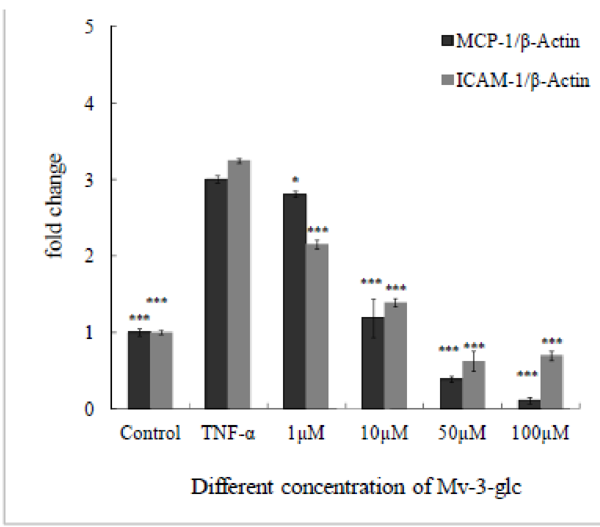
(A) (B)

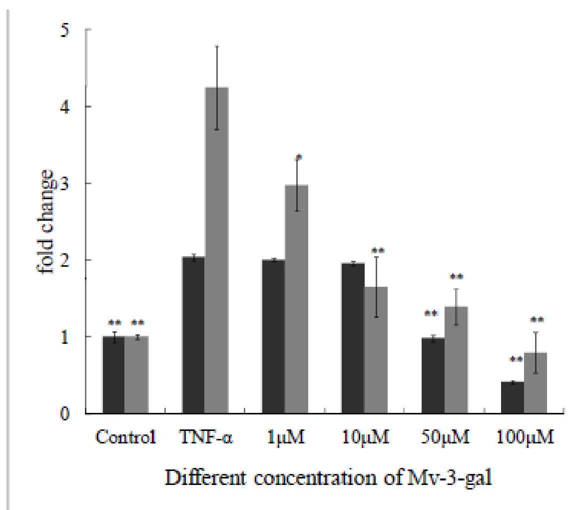
Article

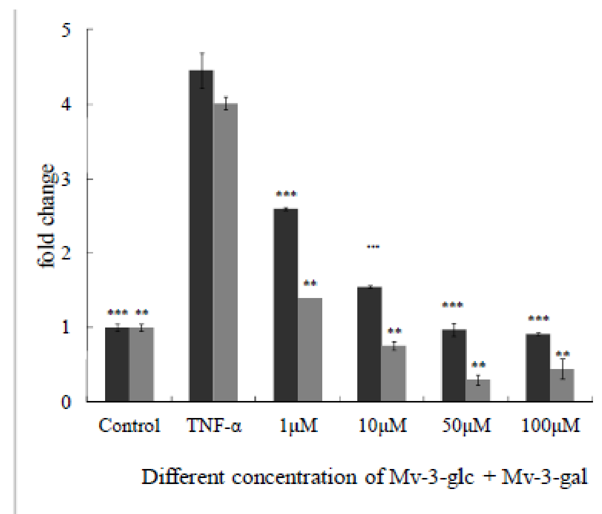
Anti-Inflammatory Effect of the Blueberry Anthocyanins Malvidin-3-Glucoside and Malvidin-3-Galactoside in Endothelial Cells

Wu-Yang Huang [1,†], Ya-Mei Liu [2,†], Jian Wang [1,3], Xing-Na Wang [1] and Chun-Yang Li [1,*]

tumor necrosis factor-alpha (TNF-α); monocyte chemotactic protein-1 (MCP-1); intercellular adhesion molecule-1 (ICAM-1)







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Article
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Immunomodulatory Effect of a Wild Blueberry Anthocyanin-Rich Extract in Human Caco-2 Intestinal Cells

Valentina Taverniti,[†] Daniela Fracassetti,[‡] Cristian Del Bo',[‡] Claudia Lanti,[‡] Mario Minuzzo,[#] Dorothy Klimis-Zacas,[§] Patrizia Riso,[*,‡,∥] and Simone Guglielmetti[†,∥]

[†]Division of Food Microbiology and Bioprocessing and [‡]Division of Human Nutrition, Department of Food, Environmental and Nutritional Sciences (DeFENS), Università degli Studi di Milano, via Celoria 2, 20133 Milan, Italy

[#]Department of Biomolecular Sciences and Biotechnology, Università degli Studi di Milano, via Celoria 20, 20133 Milan, Italy

[§]Department of Food Science and Human Nutrition, University of Maine, Orono, Maine 04469, United States

Table 1. Characterization of the ACN-Rich Fraction

compound	extracted: μg mL^{-1a}	extracted: %
malvidin 3-glc[b]	251 ± 6.3	16.4
malvidin 3-gal[c]	224 ± 8.1	14.3
malvidin 3-ara[d]	65.1 ± 4.1	4.2
delphinidin 3-glc	224 ± 17.2	14.3
delphinidin 3-gal	166 ± 13.1	10.6
delphinidin 3-ara	102 ± 9.8	6.5
cyanidin 3-glc	99.1 ± 8.6	6.3
cyanidin 3-gal	69.1 ± 3.4	4.4
cyanidin 3-ara	124 ± 9.9	7.8
petunidin 3-glc	43.2 ± 2.3	2.8
petunidin 3-gal	107 ± 11.1	6.8
petunidin 3-ara	22.1 ± 3.7	1.4
peonidin 3-glc	28.2 ± 2.2	1.8
peonidin 3-gal	38.2 ± 2.1	2.4
total	1563 ± 102	100

[a]Data are reported as the mean ± standard deviation. [b]glc, glucoside. [c]gal, galactoside. [d]ara, arabinoside.

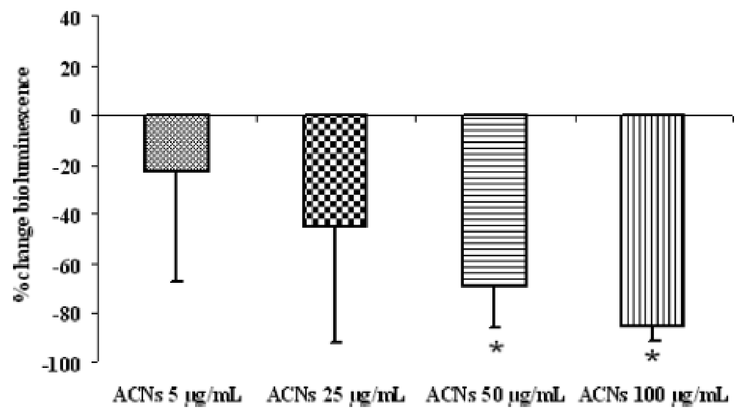
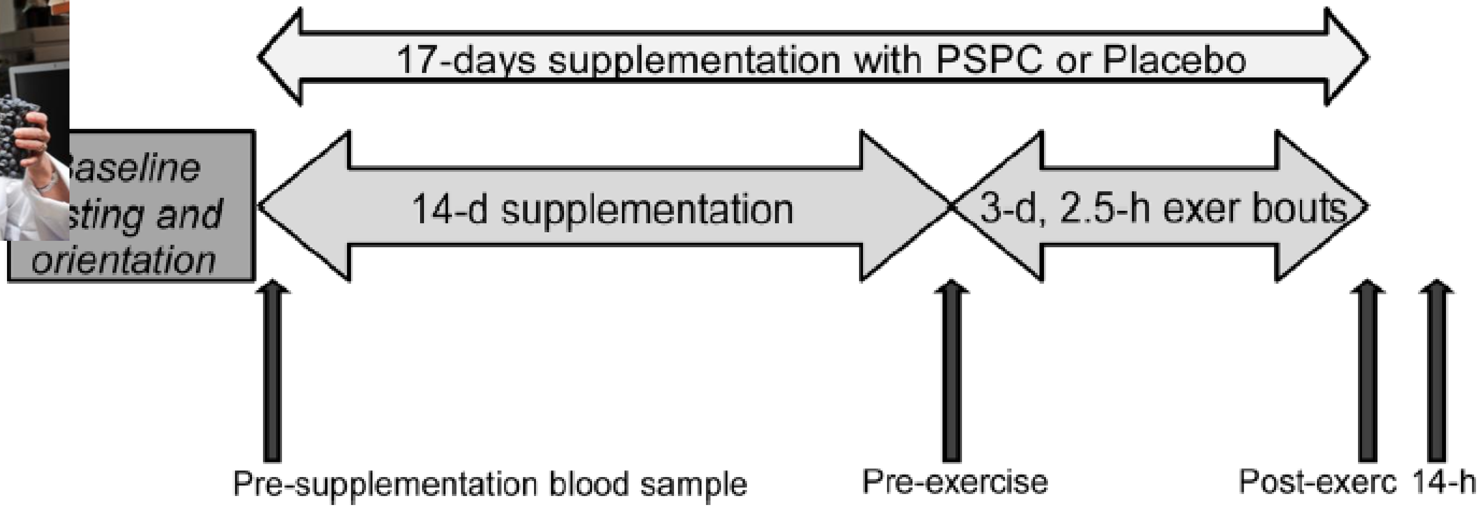


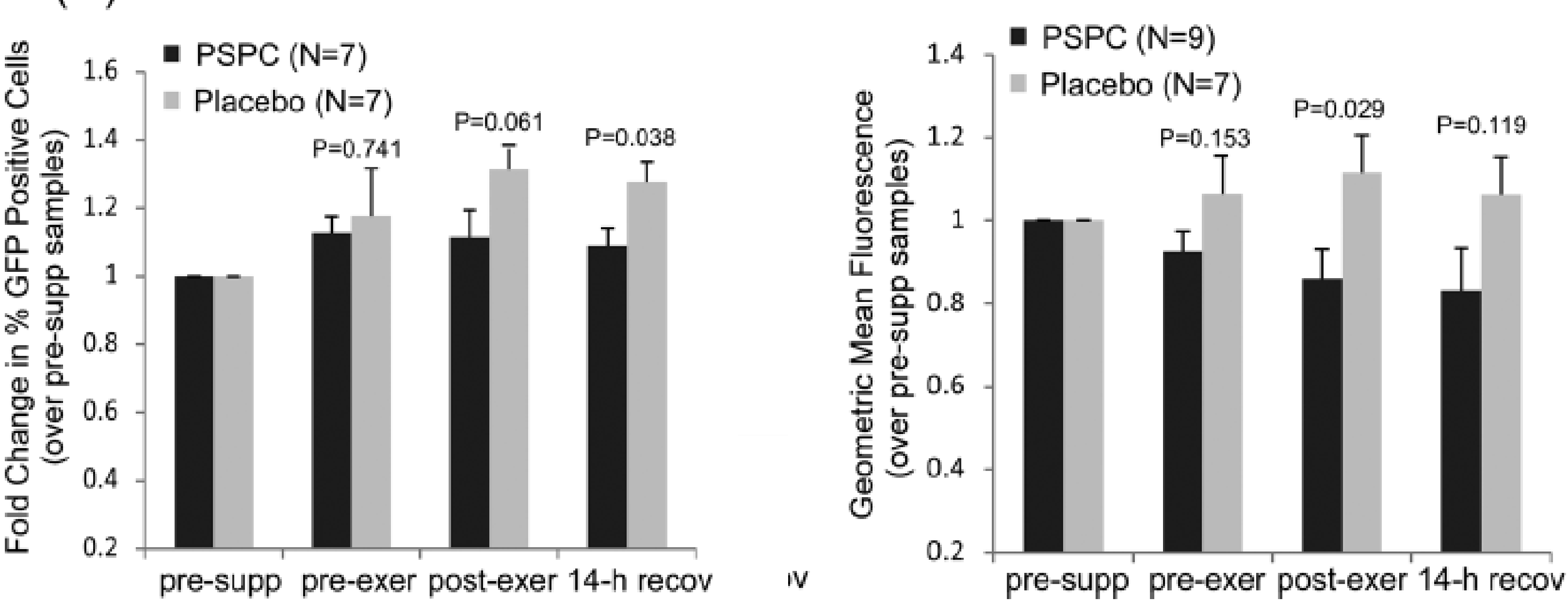
Figure 1. Modulation of light emission expressed by Caco-2 cells transfected with a NF-κB/luciferase reporter vector and incubated in the presence of interleukin-1β with the ACN-rich fraction. Data are reported as percent variation of light emission, referred to the control. Control, Caco-2 cell layers incubated only with media supplemented with MetOH + 0.05 mM HCl. ACNs, anthocyanin-rich fraction. ACN concentrations (5, 25, 50, 100) are referred to μg mL^{-1}. The values are the means (± standard deviations) for eight independent experiments conducted in duplicate. Asterisks indicate statistically significant

Blueberries Improve Immune Function



Replication of vesicular stomatitis virus in HeLa cells

(A.) 6h



Available online at www.sciencedirect.com
ScienceDirect
www.nrjournal.com

Six weeks daily ingestion of whole blueberry powder increases natural killer cell counts and reduces arterial stiffness in sedentary males and females

Lisa S. McAnulty[a,*], Scott R. Collier[b], Michael J. Landram[b], D. Stanton Whittaker[c], Sydeena E. Isaacs[a], Jason M. Klemka[a], Sarah L. Cheek[a], Jennifer C. Arms[b], Steven R. McAnulty[b]

[a] Dept. of Nutrition and Health Care Management, Boone, NC, 28608
[b] Dept. of Health and Exercise Science Appalachian State University, Boone, NC, 28608
[c] Boone Dermatology, Clinic, Boone, NC, 28608

25 men and women 18-50 years of age
High Bush BB powder equivalent to 250 g berries

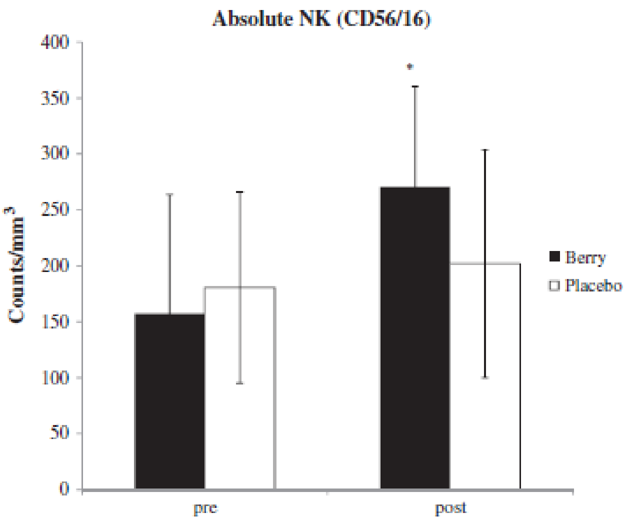
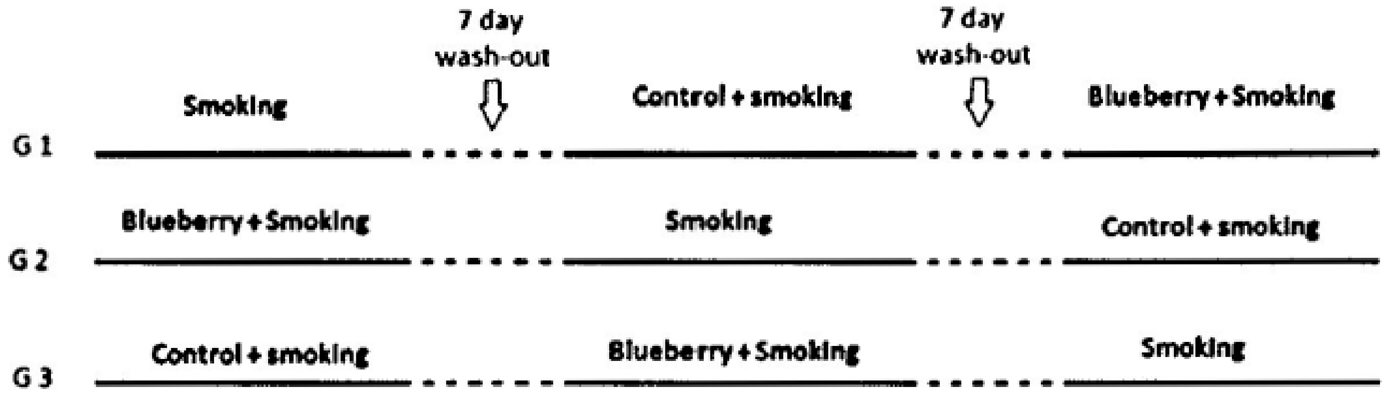


Fig. 3 – Absolute NK cell counts (BB–n, 13) and (PL–n, 12). Values are before and after BB or PL administration. Two-by-two repeated-measures ANOVA main effects were treatment, $P = .494$; time, $P = .001$; and treatment-time interaction, $P = .012$. Because of significant treatment-time interaction, preevaluations to postevaluations were performed. *Indicates significant difference vs pretreatment ($P \leq .001$). Values are means ± SD.

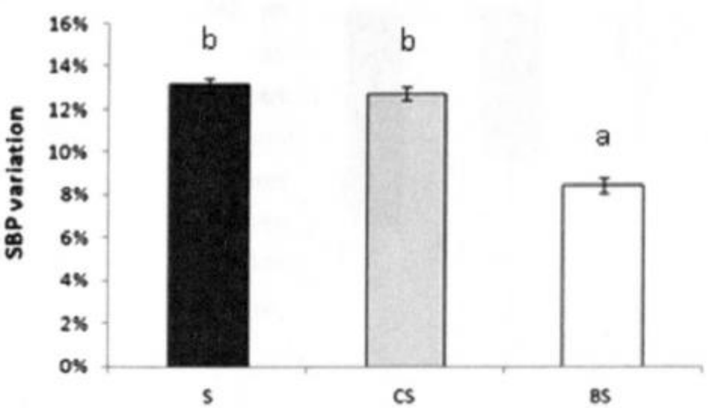
Blueberries Improve Cardiovascular Function

Food & Function

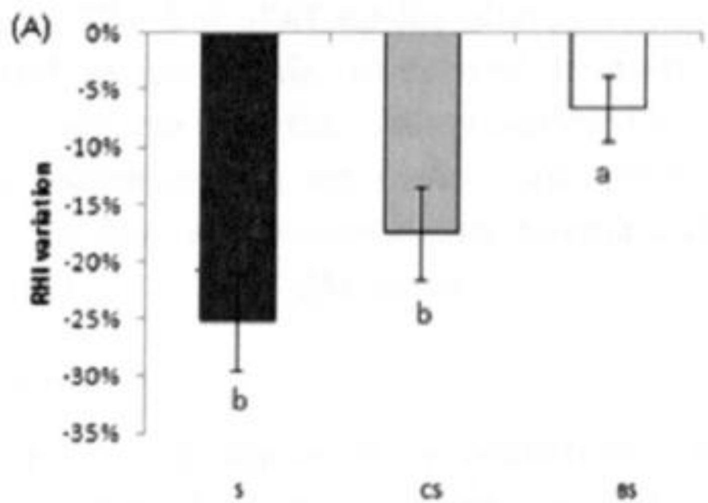
16 healthy young smokers
300 gram of high bush BB

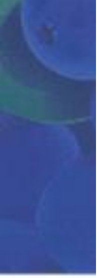


Variation in Systolic BP



Reactive Hyperemia Index





Clinical Nutrition xxx (2014) 1–8

Contents lists available at ScienceDirect

Clinical Nutrition

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Original article

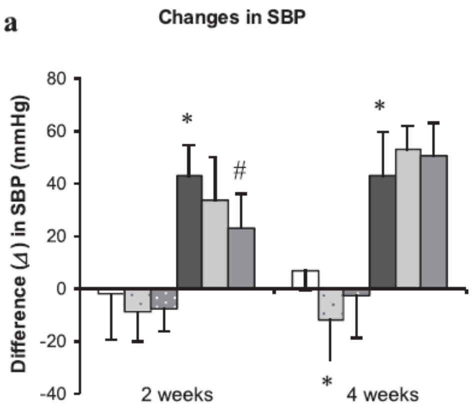
Antihypertensive activity of blueberries fermented by *Lactobacillus plantarum* DSM 15313 and effects on the gut microbiota in healthy rats

Irini Lazou Ahrén [a], Jie Xu [b,*], Gunilla Önning [a], Crister Olsson [c], Siv Ahrné [b], Göran Molin [b]

[a] Probi AB, Lund, Sweden
[b] Laboratory of Food Hygiene, Department of Food Technology, Engineering and Nutrition, Lund University, Box 124, SE-221 00 Lund, Sweden
[c] Department of Biosystem and Technology, Swedish University of Agricultural Science, P.O. Box 103, 23053 Alnarp, Sweden

Rats were fed standard chow (R36; Lantmännen, Sweden) with or without added freeze-dried fermented blueberry powder at 2 g/rat/day. The blueberries had been fermented over night after incubation with *L. plantarum* DSM 15313 (=HEAL19). Two different fermented blueberry powders were tested and were described as product A and product B.

a



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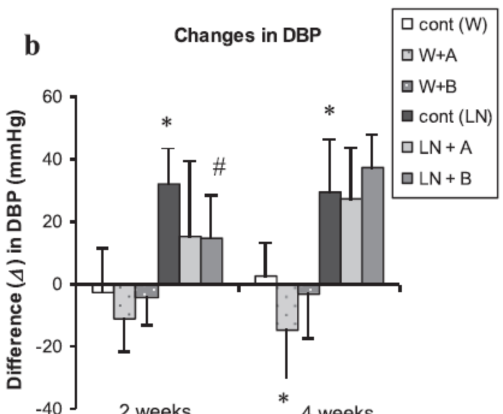


Table 3
Quantification of caecal bacteria by SYBR green qPCR.

	Cont W		W + A		W + B	
	Median	25–75%	Median	25–75%	Median	25–75%
Lactobacillus (log copy/g)	8.12	7.98–8.69	8.14	7.63–8.32	8.32	8.23–8.46
Enterobacteriaceae (log copy/g)	9.97	9.32–10.33	9.16	8.34–9.78	9.23	8.91–9.32
Bacteroides fragilis group (log copy/g)	9.68	9.44–9.88	9.92	9.74–10.24	9.80	9.55–10.10
Clostridium leptum group (log copy/g)	9.14	8.78–9.24	8.51	7.47–9.05	8.61[a]	7.0–8.64
Desulfovibrio (log copy/g)	7.06	6.98–7.15	6.99	6.70–7.26	6.73[a]	6.43–6.97

[a] denotes $p < 0.05$ compared to cont W.

Table – Anthropometric and vascular measures

	BB Pre	BB Post	PL Pre	PL Post	P
Height (m)	1.71 + 0.11		1.72 + 0.05		.679
Age (y)	46.15 + 11.92		39.92 + 13.38		.166
Weight (kg)	81.34 + 18.16	80.62 + 17.44	72.01 + 10.54	72.36 + 10.83	.127
% Body fat	31.8 + 11.32	32.51 + 10.71	23.7 + 10.78	23 + 11.27	.054
Body Mass Index (kg/m^2)	27.8 + 5.46	27.54 + 5.17	24.23 + 3.44	24.36 + 3.59	.113
Systolic BP (mm Hg)	117.23 + 7.85	114.15 + 11.47[a]	113.53 + 10.39	112.92 + 8.42	.515
Diastolic BP (mm Hg)	74.61 + 11.46	73.07 + 5.8	70.15 + 12.39	74.15 + 9.77	.646
AIx (m/s^2)	18.91 + 11	14.66 + 13.8[b]	23.2 + 7.79	24.58 + 10.15	.024
ASP (mm Hg)	112.4 + 10.2	101.5 + 7.1[c]	110.06 + 6.5	109.88 + 8.3	.046
cPWV (m·s^2)	8.4 + 1.1	7.9 + 1.3	8.8 + 1.9	8.9+ 0.9	.279

Abbreviation: BP, blood pressure.
Values are means ± SD for pre- (Pre) and post- (Post) tests. BB–n, 13 and PL–n, 12. Differences in height, age, weight, and %body fat were tested using t tests. Systolic BP, AIx, ASP, and cPWV were tested using 2 × 2 repeated-measures ANOVA. P values represent the collapsed means for each group in comparison with each other for main effects of treatment only. To address variation in initial measures, a δ value (pre – post) was obtained for all variables in BB and PL, respectively, and this absolute difference in the magnitude of the change compared between the 2.
No variables were statistically significant with the exception of
[a] Systolic BP, P = .047.
[b] AIx, P = .011.
[c] ASP, P ≤ .001.

25 men and women 18-50 years of age
High Bush BB powder equivalent to 250 g berries

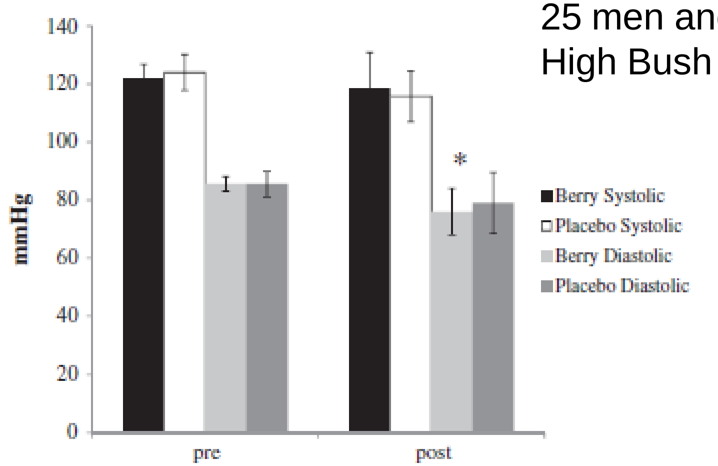


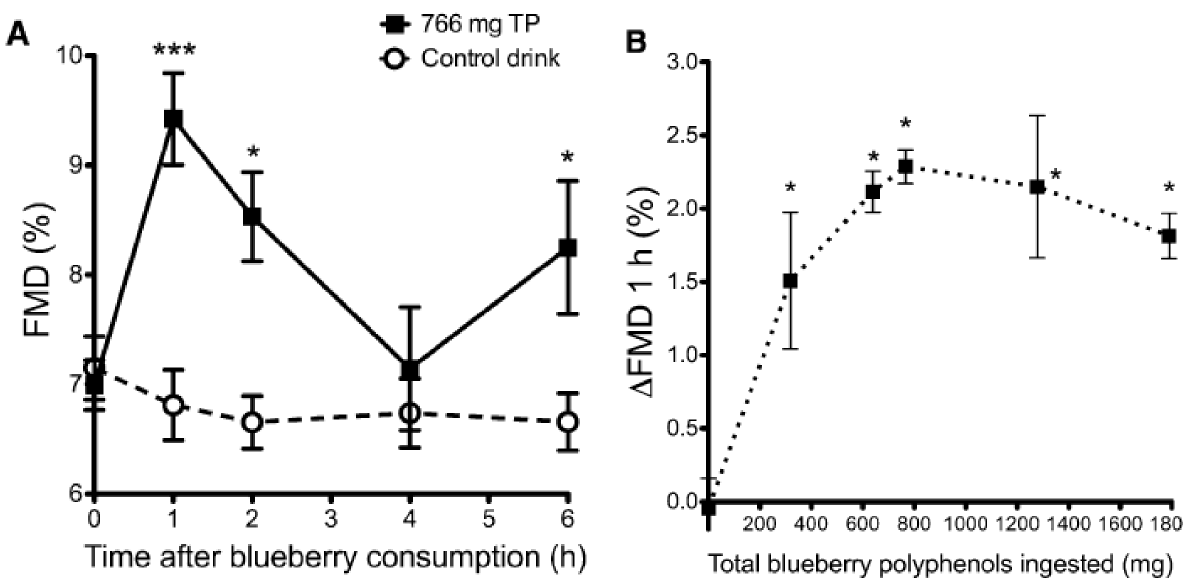
Fig. 1 – Blood pressure changes in participants with prehypertensive systolic and diastolic pressures in response to BB (n, 5) and PL (n, 4) supplementation. Significantly different from presupplementation (*P = .038). Values are means ± SD.

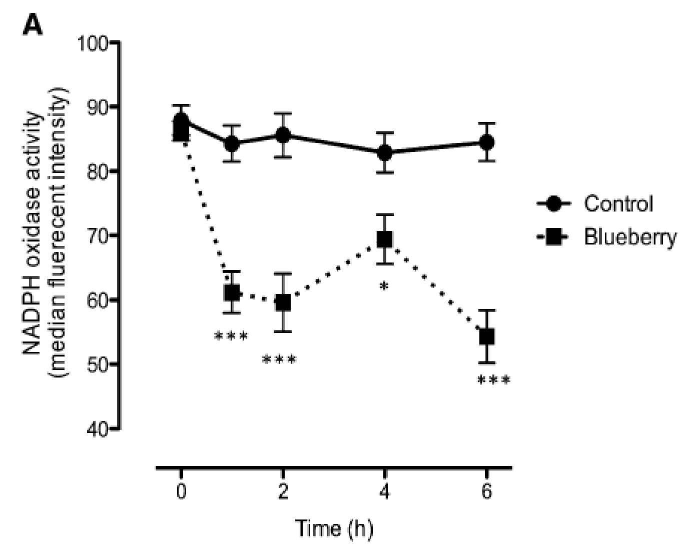
Intake and time dependence of blueberry flavonoid–induced improvements in vascular function: a randomized, controlled, double-blind, crossover intervention study with mechanistic insights into biological activity[1–3]

Ana Rodriguez-Mateos, Catarina Rendeiro, Triana Bergillos-Meca, Setareh Tabatabaee, Trevor W George, Christian Heiss, and Jeremy PE Spencer

Am J Clin Nutr doi: 10.3945/ajcn.113.066639. Printed in USA.

21 young healthy men; wild BB powder drink





RESEARCH ARTICLE

10 young males; wild BB powder

Impact of processing on the bioavailability and vascular effects of blueberry (poly)phenols

Ana Rodriguez-Mateos[1,2], Raquel Del Pino-García[1,3], Trevor W. George[4], Alberto Vidal-Diez[5], Christian Heiss[2] and Jeremy P. E. Spencer[1]

Table 1. Phytochemical content of the test products

	Blueberry drink	Blueberry bun (×3)
Freeze-dried blueberry (g)	34	34
Total polyphenols (mg)	692 ± 13	637 ± 28
Total anthocyanins (mg)	339 ± 6.1	196 ± 7.7*
Total procyanidins (mg)	111 ± 4.1	140 ± 7.4
Monomers (mg)	22 ± 1.1	29 ± 0.8
Dimers (mg)	26 ± 1.1	42 ± 1.4*
Trimers (mg)	15 ± 0.6	23 ± 1.6*
Tetramers (mg)	14 ± 0.6	17 ± 1.5
Pentamers (mg)	9 ± 0.5	11 ± 1.5
Hexamers (mg)	8 ± 0.4	8 ± 0.8
Heptamers (mg)	6.5 ± 0.4	5 ± 0.5
Octamers (mg)	5 ± 0.8	4 ± 0.5
Nonamers (mg)	4 ± 0.8	0*
Decamers (mg)	2 ± 0.6	0*
Total oligomers (mg)	89 ± 2.9	111 ± 6.6
Quercetin (mg)	24 ± 0.2	25 ± 0.9
Chlorogenic acid (mg)	179 ± 1	221 ± 10*
Caffeic acid (mg)	16 ± 0.3	17 ± 0.9
Ferulic acid (mg)	22 ± 1.0	38 ± 1.3

Results are expressed as mean ± SEM ($n = 3$).
*Significantly different from the blueberry drink, $p < 0.05$.

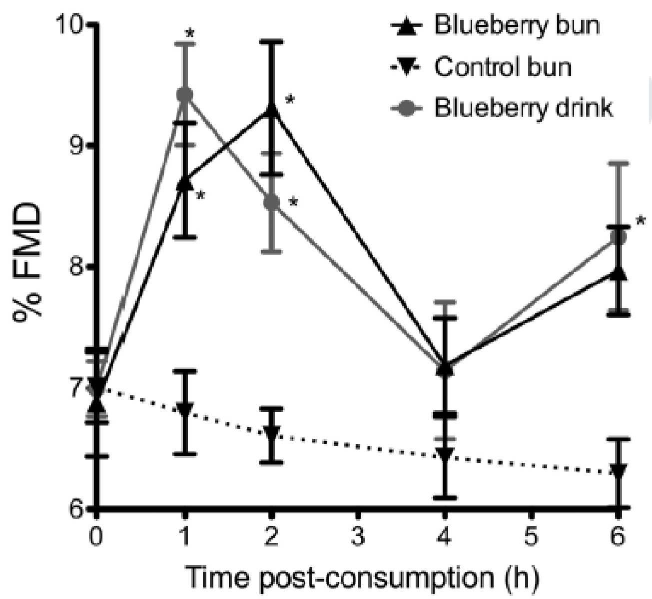


Figure 1. Time-course of FMD after consumption of three blueberry baked products (blueberry bun) containing 637 mg of total (poly)phenols, three baked control products (control bun), or a blueberry drink containing 692 mg of total (poly)phenols in healthy men ($n = 10$). Data are mean values ± SEM. *$p < 0.05$ significantly different with respect to processed control at the specified time point.

Blueberries Attenuate Bone Loss

Wild BBs Increase Bone Mineral Content and Density

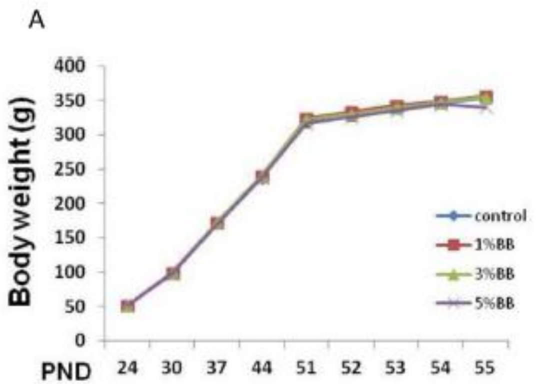
OPEN ACCESS Freely available online PLOS | ONE

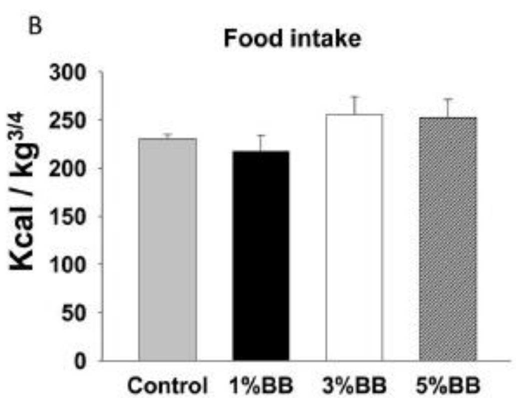
Feeding Blueberry Diets to Young Rats Dose-Dependently Inhibits Bone Resorption through Suppression of RANKL in Stromal Cells

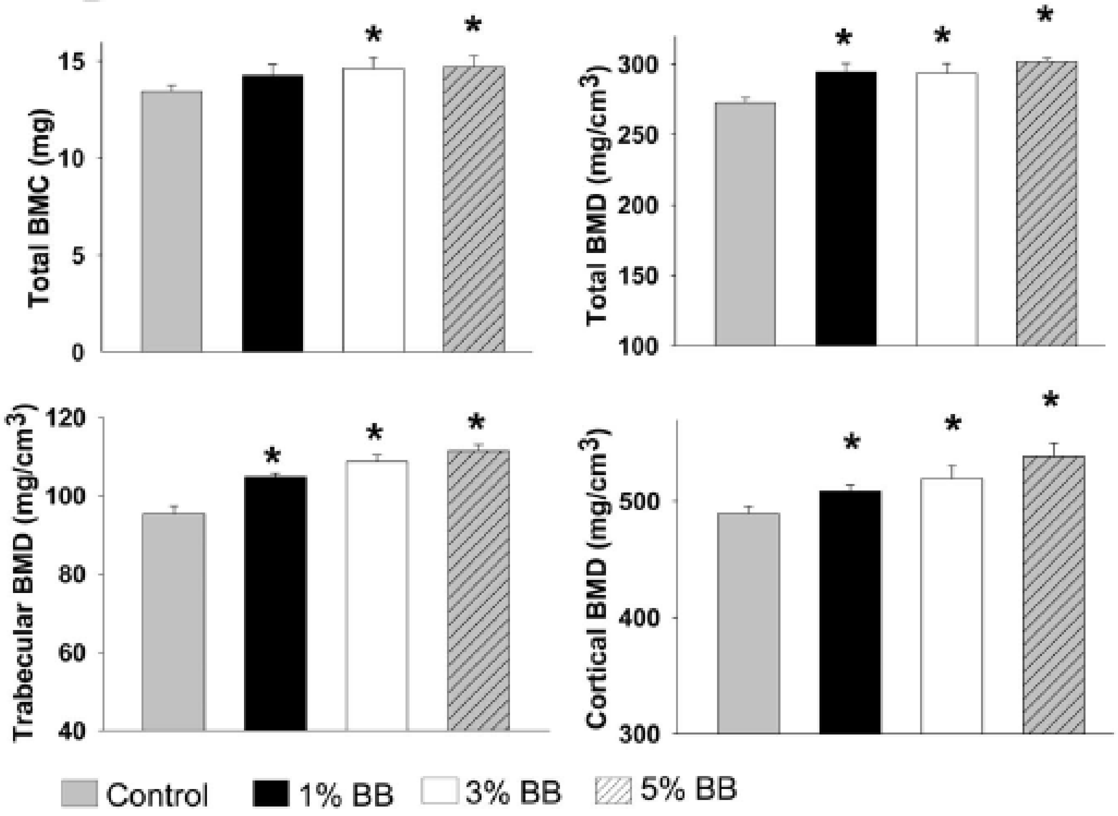
Jian Zhang[1,2], Oxana P. Lazarenko[1,2], Jie Kang[1,2], Michael L. Blackburn[1,2], Martin J. J. Ronis[1,2,3], Thomas M. Badger[1,2], Jin-Ran Chen[1,2]*

1 Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, Arkansas, United States of America, 2 Arkansas Children's Nutrition Center, Little Rock, Arkansas, United States of America, 3 Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences, Little Rock, Arkansas, United States of America

Female Sprague-Dawley rats fed BB diets from 3-8 weeks of age







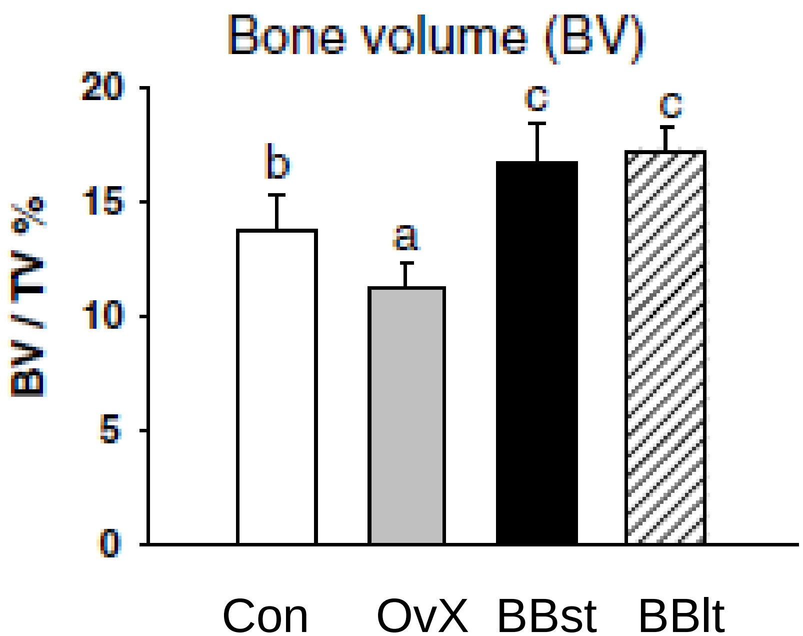
Wild BBs Maintain Bone Mineral Content and Density after OvX

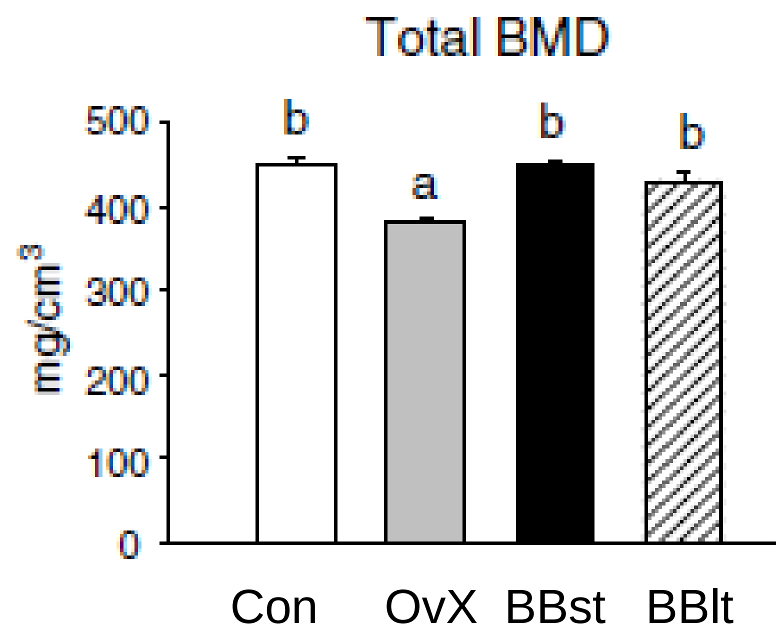
AGE (2013) 35:807–820
DOI 10.1007/s11357-012-9412-z

Blueberry consumption prevents loss of collagen in bone matrix and inhibits senescence pathways in osteoblastic cells

Jian Zhang · Oxana P. Lazarenko ·
Michael L. Blackburn · Thomas M. Badger ·
Martin J. J. Ronis · Jin-Ran Chen

Female Sprague-Dawley rats fed BB diets from 21-34 days of age followed by ovariectomy (OvX) at 60 days and followed for 3 more weeks.





Li *et al. Journal of Orthopaedic Surgery and Research* 2014, **9**:56
http://www.josr-online.com/content/9/1/56

JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH

RESEARCH ARTICLE Open Access

Rabbiteye blueberry prevents osteoporosis in ovariectomized rats

Tao Li[1†], Shou-Mian Wu[2†], Zhi-Yuan Xu[2*] and Sheng Ou-Yang[2*]

Help against bone loss? Blueberries ripe for study

Shari Rudavsky, The Indianapolis Star *8:27 p.m. EDT September 30, 2014*

(Photo: Kelly Wilkinson, The Indianapolis Star)

INDIANAPOLIS — Nearly $4 million can buy a lot of blueberries. Purdue University researchers are hoping it also will help find a way to reduce bone loss (http://www.indystar.com/story/life/diet-fitness/2014/09/30/purdue-gets-million-study-blueberries/16491327/)in older women.

The National Institutes of Health recently awarded $3.7 million over five years to a team from Purdue and the Indiana University School of Medicine to study whether berries contain compounds that could help fight the loss of bone that typically happens to post-menopausal women.

Animal studies suggest that blueberries may contain substances known as polyphenols and flavonoids that help the body's immune system combat the bone loss that can lead to osteoporosis.

"We're going to see if some natural product can help prevent that without drugs; that would be the idea," said Connie Weaver, distinguished professor and head of nutrition science at Purdue and the principal investigator on the project, which was funded by the National Center for Complementary and Alternative Medicine.

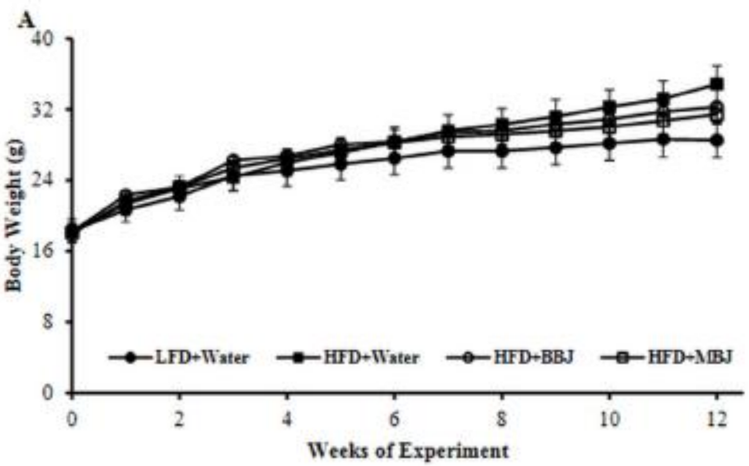
Blueberries Attenuate Pathology of Obesity

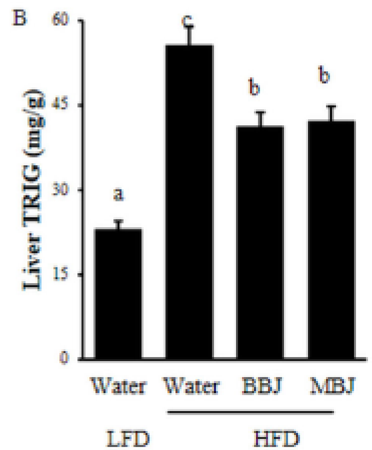
OPEN ACCESS Freely available online
October 2013 | Volume 8 | Issue 10 | e77585
PLOS ONE

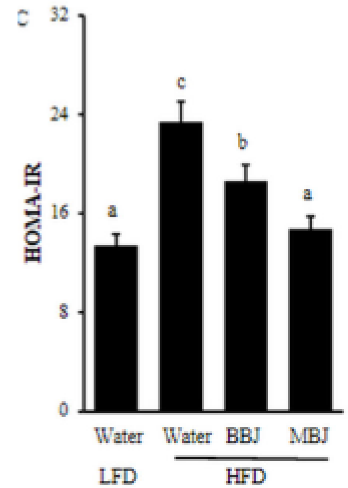
Blueberry and Mulberry Juice Prevent Obesity Development in C57BL/6 Mice

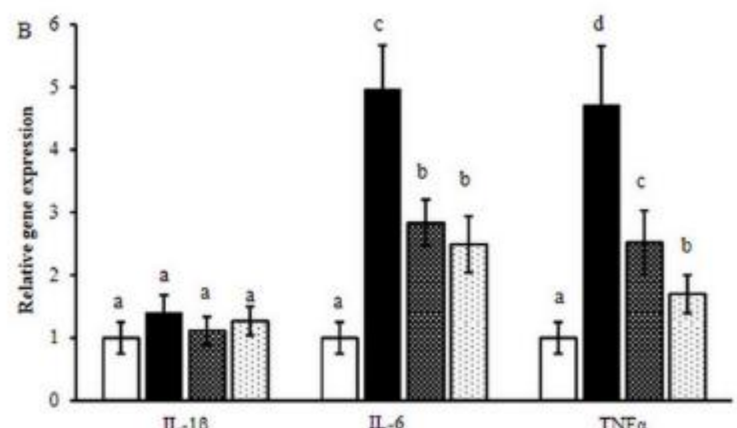
Tao Wu[1,2], Qiong Tang[1], Zichun Gao[1], Zhuoping Yu[1], Haizhao Song[1], Xiaodong Zheng[1,2*], Wei Chen[1,2*]

1 College of Biosystems Engineering and Food Science, Zhejiang University, Hangzhou, Zhejiang, China, **2** Fuli Institute of Food Science, Zhejiang University, Hangzhou, Zhejiang, China









High Bush BB juice

NRC Research Press

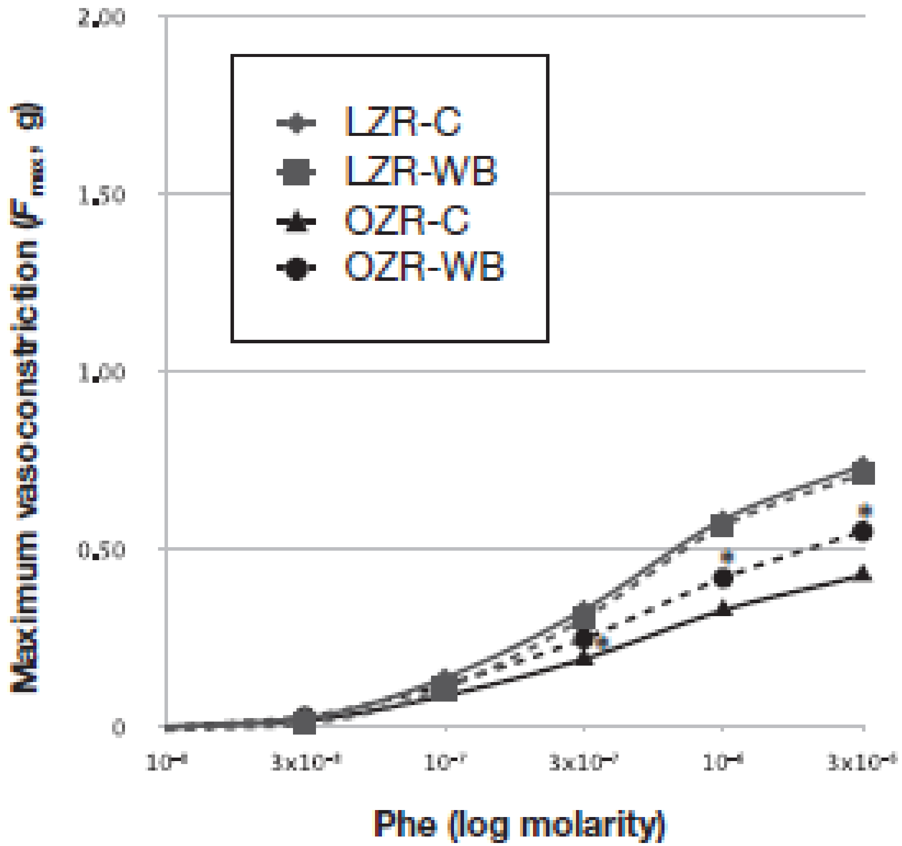
ARTICLE

Wild blueberry consumption affects aortic vascular function in the obese Zucker rat

Stefano Vendrame, Aleksandra S. Kristo, Dale A. Schuschke, and Dorothy Klimis-Zacas

8 weeks; 8% Wild BB diet

Phenylephrine Stimulation



Blueberries Improve Cognition

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Article

pubs.acs.org/JAFC

dx.doi.org/10.1021/jf404565s | *J. Agric. Food Chem.* 2014, 62, 3972−3978

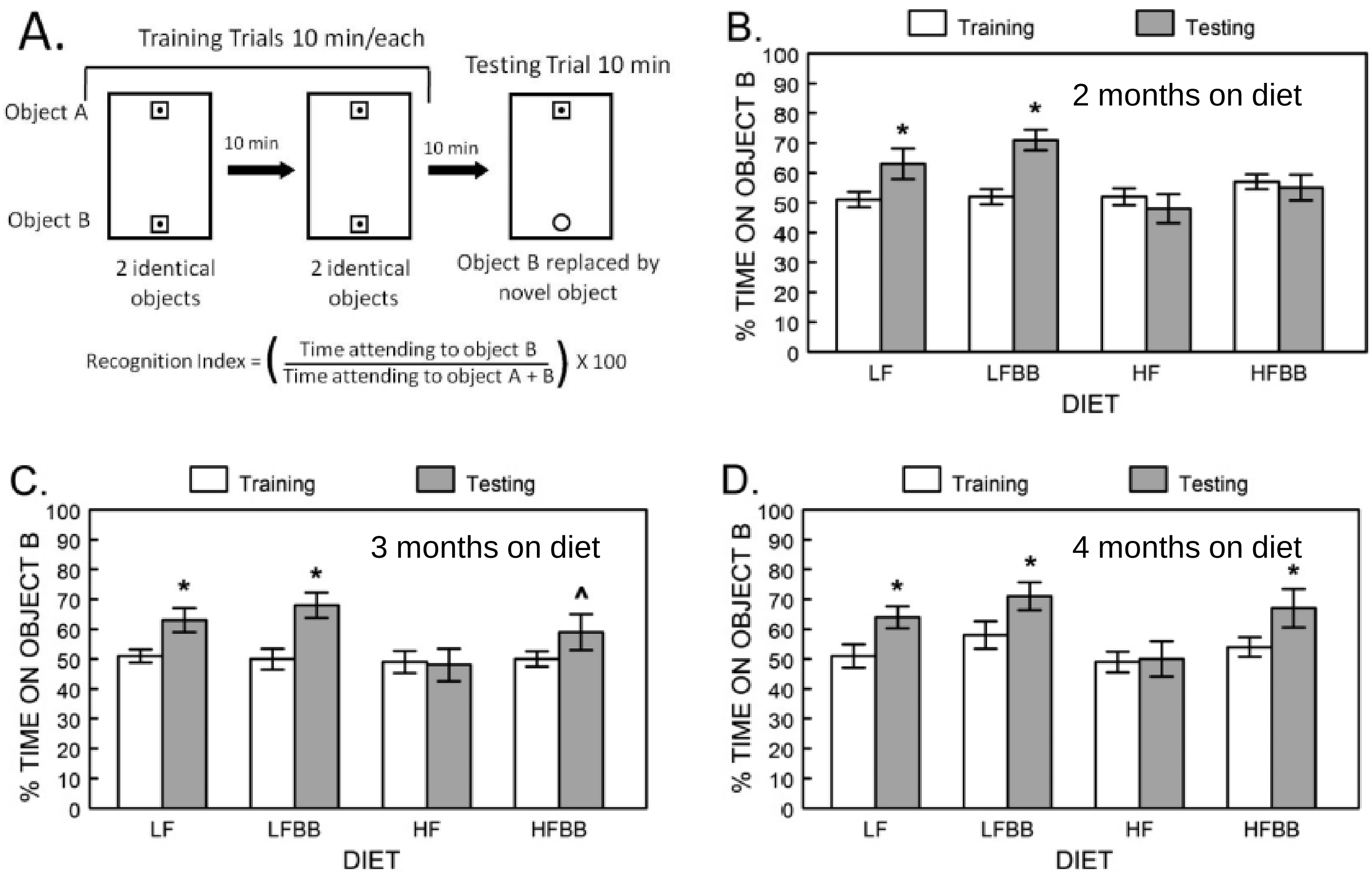
Blueberry Supplementation Improves Memory in Middle-Aged Mice Fed a High-Fat Diet

Amanda N. Carey,[*,†,§] Stacey M. Gomes,[†] and Barbara Shukitt-Hale[†]

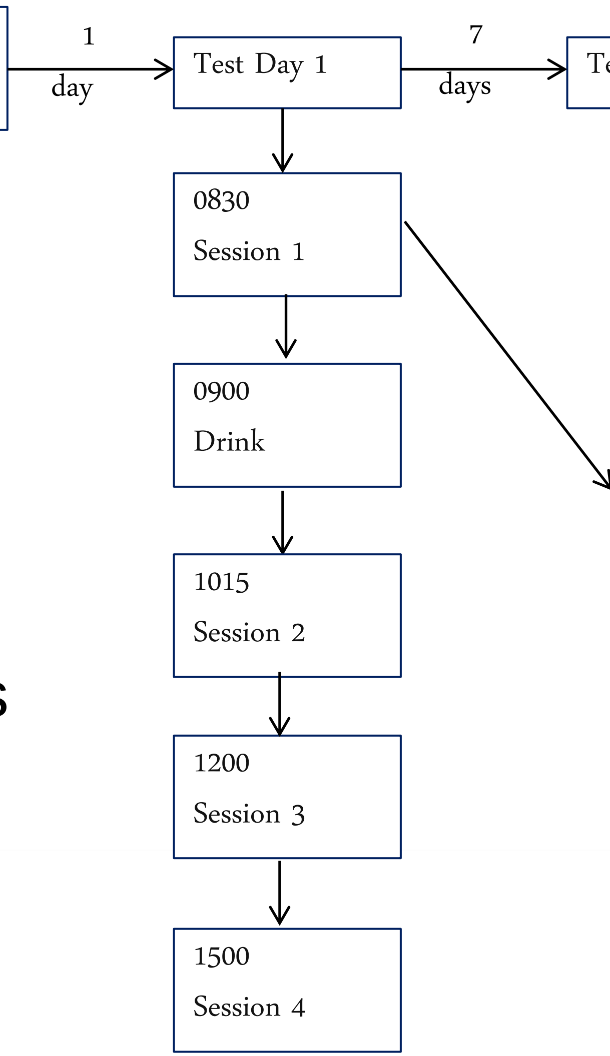
[†]Human Nutrition Research Center on Aging at Tufts University, Agricultural Research Service, U.S. Department of Agriculture, Boston, Massachusetts 02111, United States

[§]Department of Psychology, Simmons College, Boston, Massachusetts 02115, United States

9-mo old mice; high bush BB prep 4%



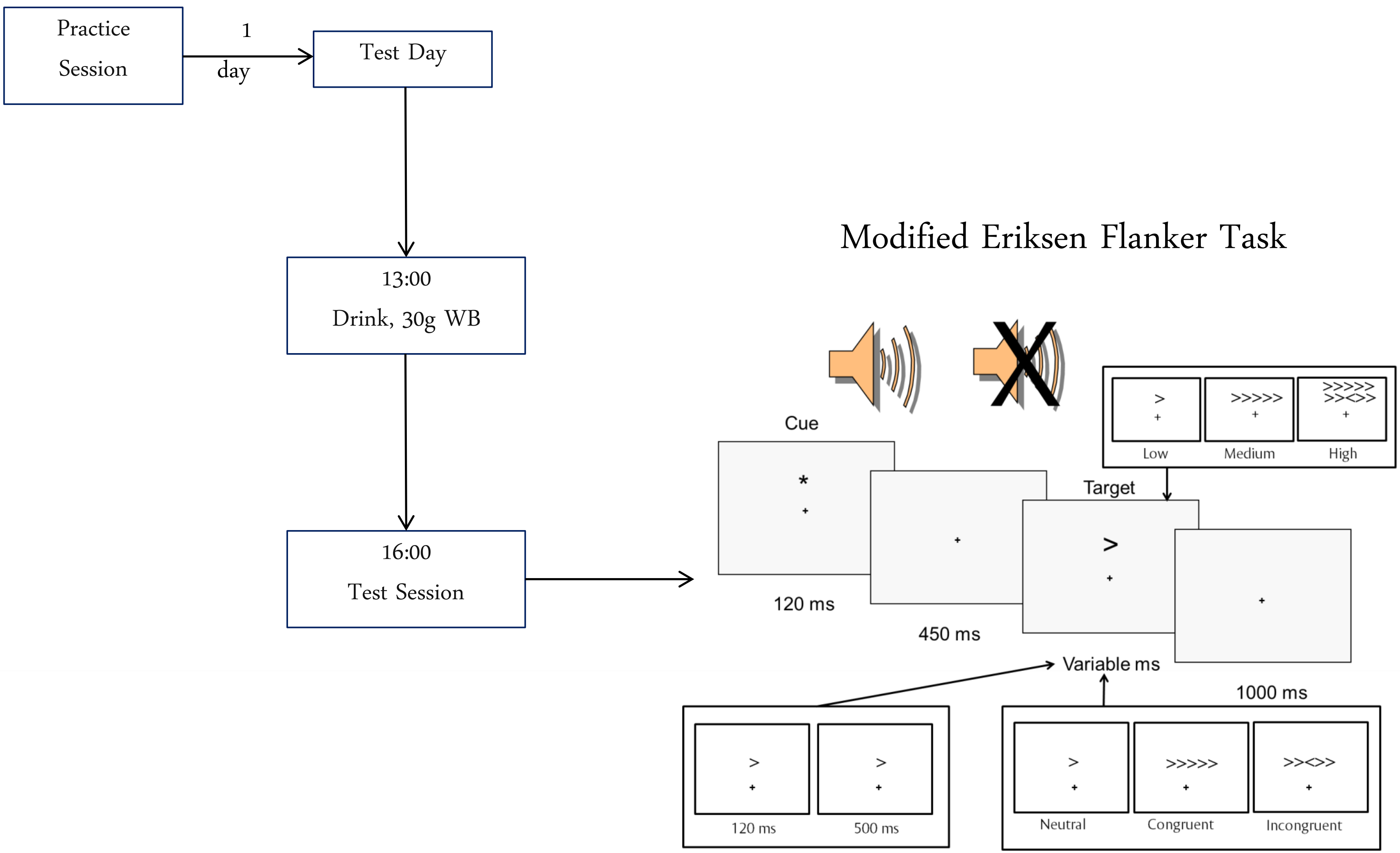
Experiment 1: Time-course & dose response study in healthy 7-10 year olds



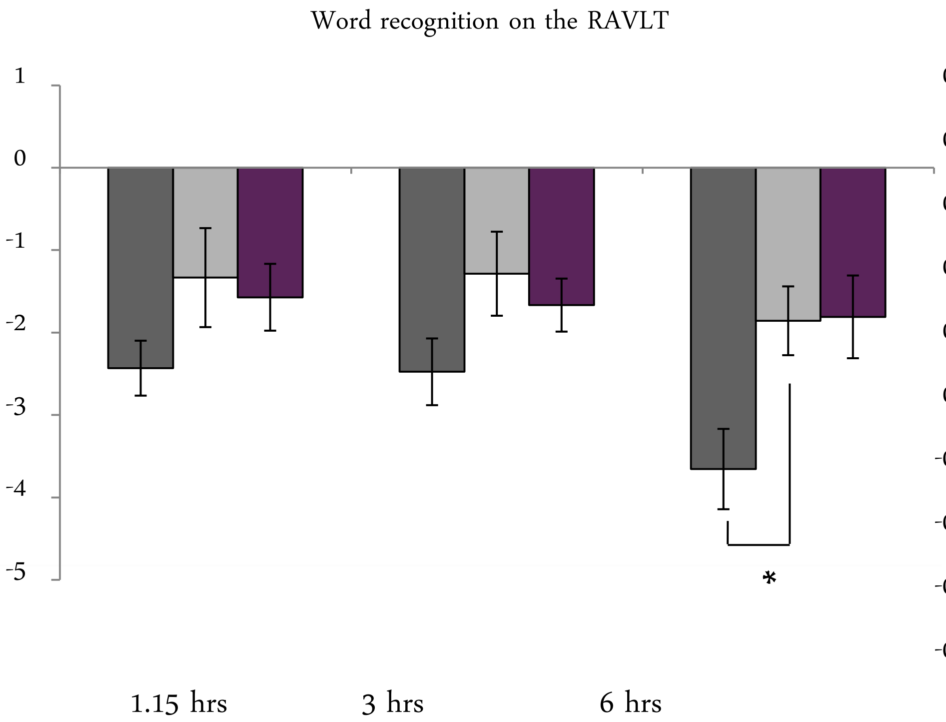
Claire Williams
U. of Reading

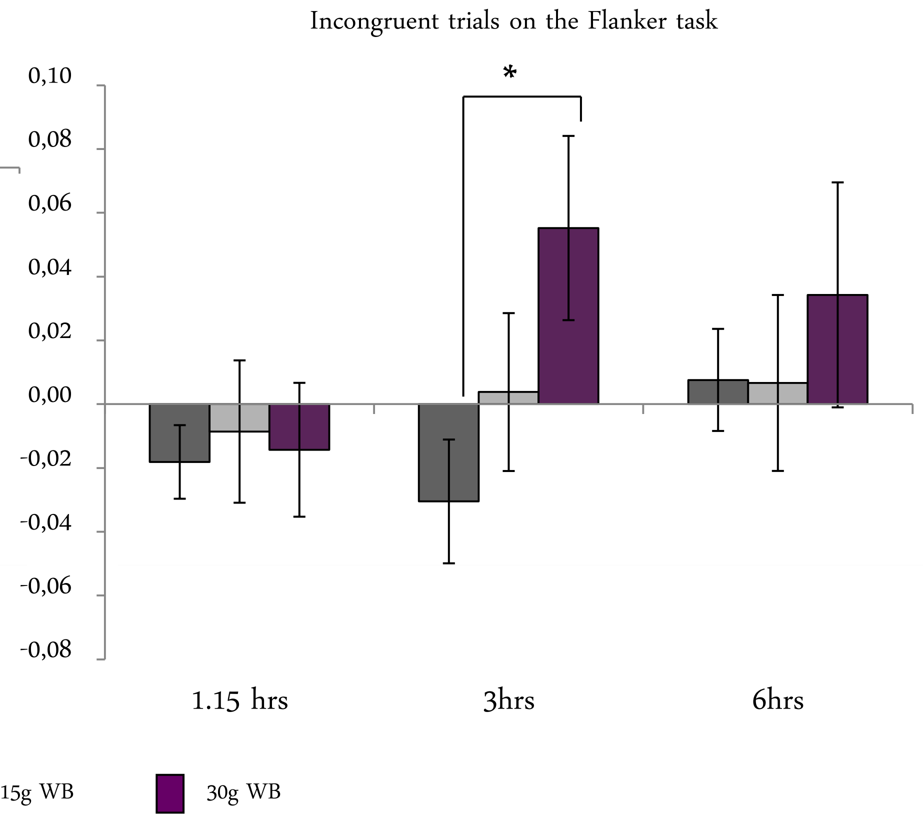
Test	Function
Go-NoGo	Executive Function – Response inhibition
Flanker	Executive Function – Interference effects
AVLT	STM / LTM / Word Recognition
Picture-matching	Levels of processing & response interference

Experiment 2: Investigation of WB effects on executive function in ADHD and non-ADHD children

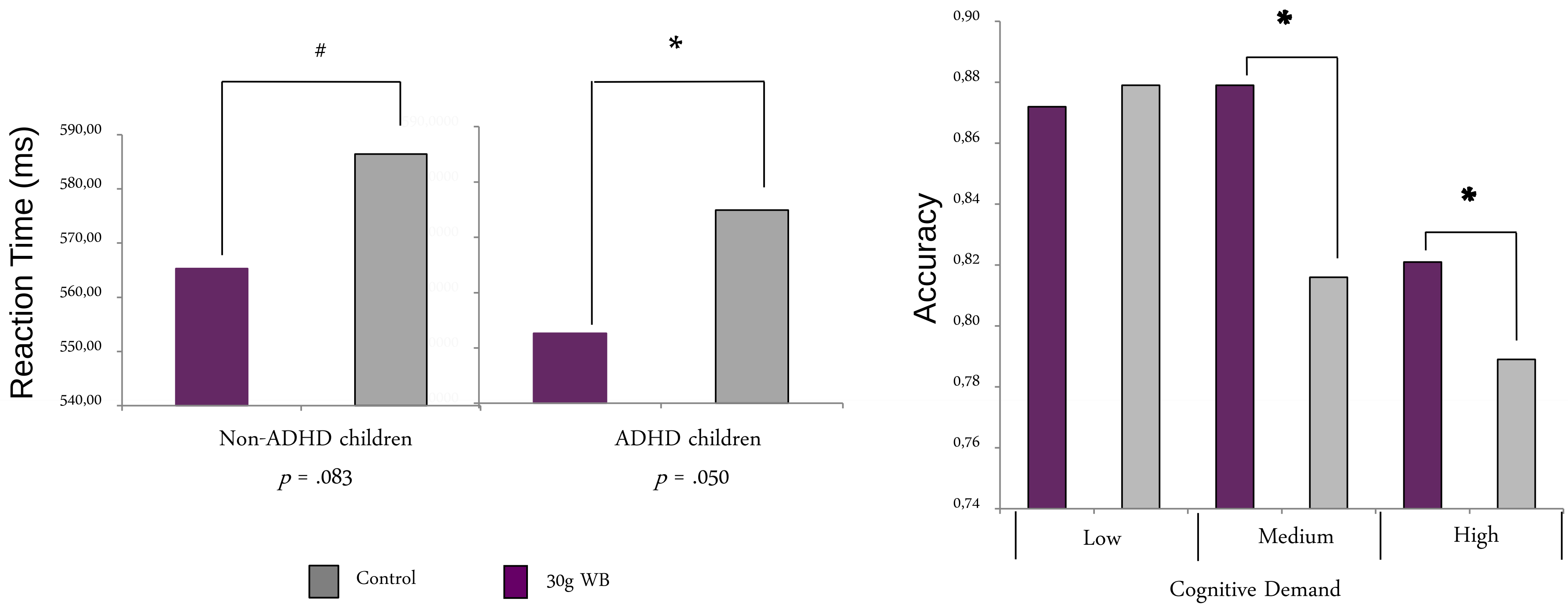


- This is the first time-course study investigating effects of WB on cognition in children (aged 7-10 years old). Children were tested at baseline and then 1.15, 3 and 6 hours after receiving a WB drink or matched control drink.
- At each timepoint children performed a battery of cognitive tasks targeting attention (flanker task & Go-NoGo task) or memory (Reyes auditory verbal learning task [RAVLT] & picture-matching task)
- Significant benefits of WB treatment were seen including better 'delayed' memory and better word recognition on the RAVLT 6 hours post-treatment, and better accuracy on incongruent trials of a flanker task 3 hours post-treatment.
- Importantly, regardless of cognitive task, WB treatment led to an overall improvement in cognition, with the best performance associated with 30g WB, and worst performance with the control drink.





- In further experiments we have specifically investigated attention-related benefits of WB treatment. Here, we examined the effects of WB treatment on both non-ADHD and ADHD children.
- Children were treated with 30g WB or matched control drink and tested on a Modified Eriksen Flanker Task 3 hours after receiving their treatment- derived from our earlier studies showing that we see benefits on executive function at this dose and at 3 hours.
- In line with our previous findings, children show increased attention following WB treatment. Importantly benefits were seen for both non-ADHD and ADHD populations.
- Intriguingly, these benefits to attention-related processing were exaggerated as the cognitive demands of the task increased i.e when the task was easy then treatment with WB had little effect, but as task difficulty increased then WB-treated children outperformed children treated with control.



16,010 participants, aged 70 years; assessments conducted twice at 2-yr intervals over 4 yrs

ANN NEUROL 2012;00:000–000

Dietary Intakes of Berries and Flavonoids in Relation to Cognitive Decline

Elizabeth E. Devore, ScD,[1] Jae Hee Kang, ScD,[1] Monique M. B. Breteler, MD, PhD,[2] and Francine Grodstein, ScD[1]

From the [1]Channing Laboratory, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA; and [2]German Center for Neurodegenerative Diseases, Bonn, Germany.

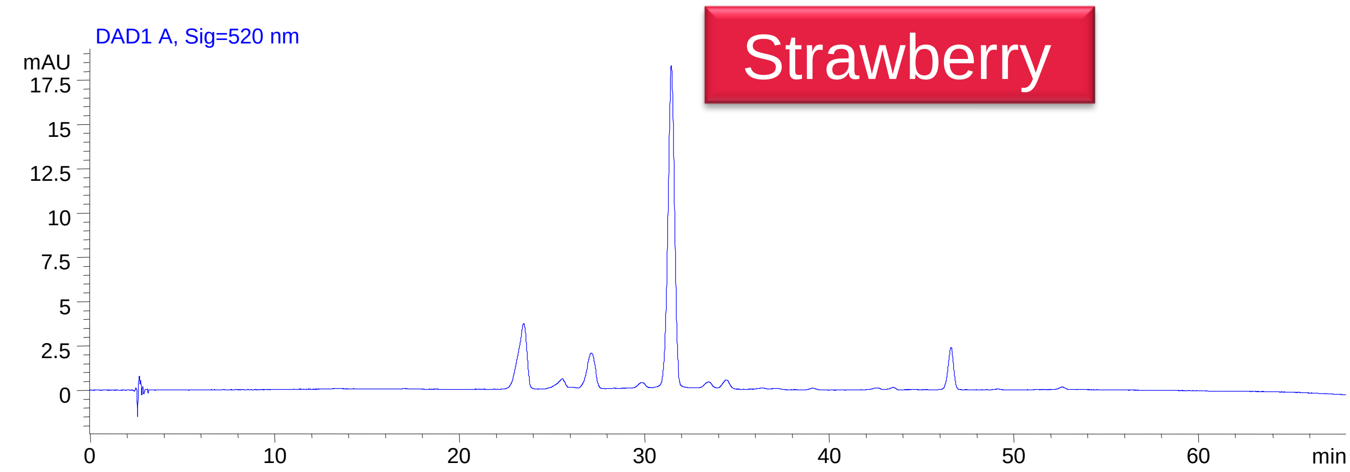
TABLE 2: Mean Differences (95% CI) in Rates of Cognitive Decline over 4 Years of Follow-up, across Categories of Berry Intake[a,b]

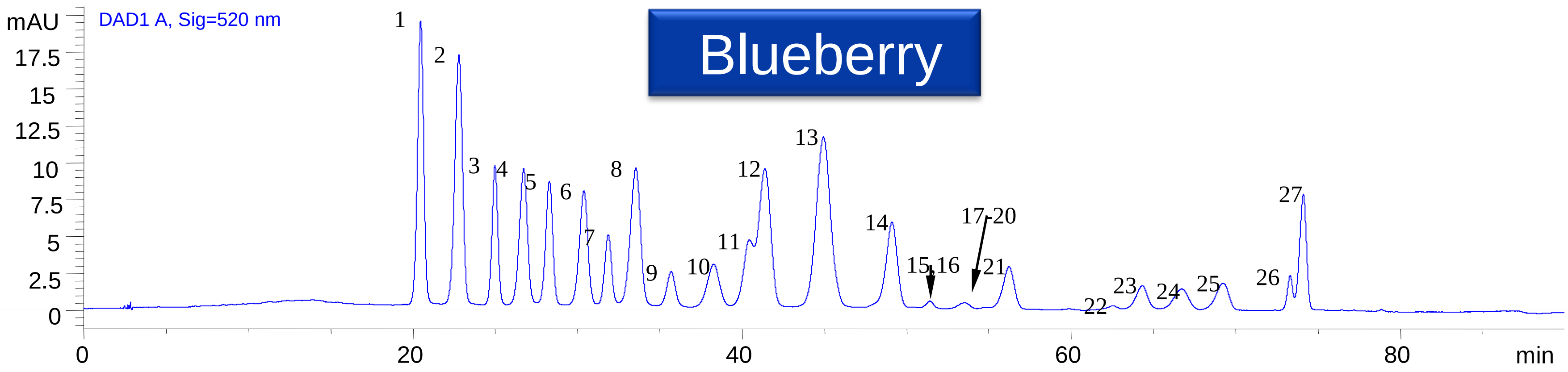
Score	Blueberries			*p*-trend
	<1 Serving/mo, 35.2%	1–3 Servings/mo, 44.8%	≥1 Serving/wk, 20.0%	
Global score				
Model 1[c]	0.00	0.02 (−0.01 to 0.04)	0.04 (0.01 to 0.07)	0.010
Model 2[d]	0.00	0.02 (−0.01 to 0.04)	0.04 (0.01 to 0.07)	0.014
Verbal memory score				
Model 1[c]	0.00	0.02 (−0.01 to 0.05)	0.05 (0.01 to 0.09)	0.016
Model 2[d]	0.00	0.02 (−0.01 to 0.06)	0.05 (0.01 to 0.09)	0.022
Telephone Interview of Cognitive Status				
Model 1[c]	0.00	0.11 (−0.01 to 0.22)	0.16 (0.02 to 0.31)	0.027
Model 2[d]	0.00	0.11 (−0.01 to 0.23)	0.17 (0.03 to 0.32)	0.022

What About Blueberry Metabolism?

Anthocyanin Profile of Strawberry and Blueberry

Mass spec analysis



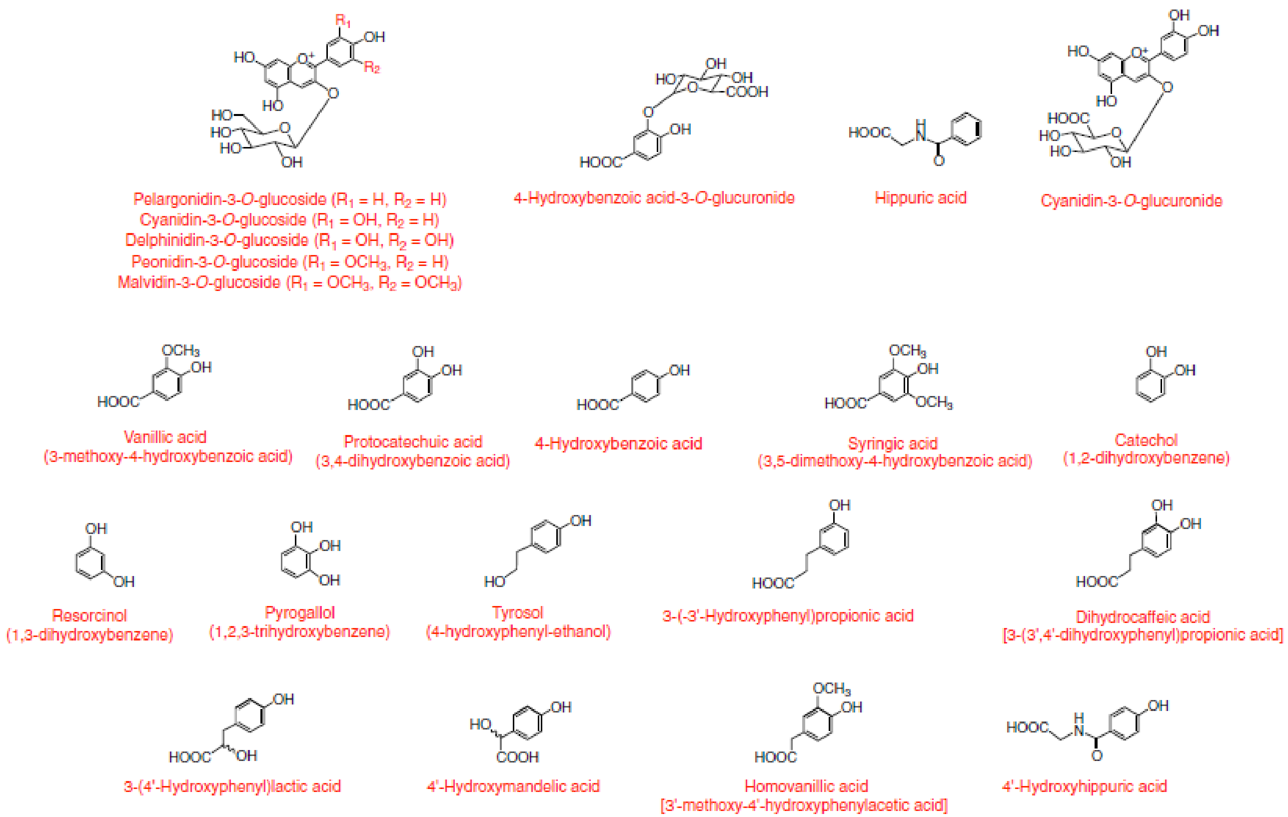


Arch Toxicol (2014) 88:1803–1853
DOI 10.1007/s00204-014-1330-7

REVIEW ARTICLE

Bioavailability, bioactivity and impact on health of dietary flavonoids and related compounds: an update

Ana Rodriguez-Mateos · David Vauzour · Christian G. Krueger · Dhanansayan Shanmuganayagam · Jess Reed · Luca Calani · Pedro Mena · Daniele Del Rio · Alan Crozier



JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Article

ubs.acs.org/JAFC

(Table 1). The next day, volunteers consumed 250 mL of single-strength BJ containing 216 mg of C3g equivalents. The nonacylated

Anthocyanin Metabolites Are Abundant and Persistent in Human Urine

Wilhelmina Kalt,*[†] Yan Liu,[§] Jane E. McDonald,[†] Melinda R. Vinqvist-Tymchuk,[†] and Sherry A. E. Fillmore[†]

[†]Atlantic Food and Horticulture Research Centre, Agriculture and Agri-Food Canada, 32 Main Street, Kentville, NS B4N 1J5, Canada

[§]Institute of Special Economic Animal and Plant Sciences, CAAS, 4899 Juye Street, Changchun 130112, China

ABSTRACT: LC-MS/MS revealed that metabolites of anthocyanins (Acn) were abundant in human urine ($n = 17$) even after 5 days with no dietary Acn. After intake of 250 mL of blueberry juice, parent Acn were 4% and Acn metabolites were 96% of the total urinary Acn for the following 24 h. Multiple reaction monitoring revealed 226 combinations of mass transition × retention times for known Acn and predicted Acn metabolites. These were dominated by aglycones, especially aglycone glucuronides. The diversity of Acn metabolites could include positional isomers of Acn conjugates and chalcones. The persistence of Acn metabolites suggested enterohepatic recycling leading to prolonged residence time. The prevalence of Acn metabolites based on pelargonidin, which is not present in blueberry juice, may reflect ongoing dehydroxylation and demethylation of other Acn via xenobiotic and colonic bacterial action. The results suggest that exposure to Acn-based flavonoid moieties is substantially greater than suggested by earlier research.

INTERNATIONAL JOURNAL OF FOOD SCIENCES and NUTRITION

http://informahealthcare.com/ijf
ISSN: 0963-7486 (print), 1465-3478 (electronic)

Int J Food Sci Nutr, 2014; 65(4): 440–448

DOI: 10.3109/09637486.2013.869798

informa healthcare

FOOD COMPOSITION AND ANALYSIS

Stability and absorption of anthocyanins from blueberries subjected to a simulated digestion process

Yixiang Liu[1], Di Zhang[2], Yongpei Wu[1], Dan Wang[2], Ying Wei[3], Jiulin Wu[4], and Baoping Ji[2]

[1]*College of Biological Engineering, Jimei University, Xiamen, Fujian, P.R. China,* [2]*College of Food Science & Nutritional Engineering, China Agricultural University, Beijing, P.R. China,* [3]*Chinese National Research Institute of Food & Fermentation Industries, Beijing, P.R. China, and* [4]*Institute of Biomedical and Pharmaceutical Technology, Fuzhou University, Fuzhou, Fujian, P.R. China*

Abstract

Numerous studies have shown that anthocyanins usually have better *in vitro* bioactivity than *in vivo* bioactivity. This may be due to physiochemical degradation during gastrointestinal digestion and their poor bioavailability in *in vivo* studies. Therefore, this study aims to investigate the effects of anthocyanin structure on their stability under simulated gastrointestinal digestion and to assess their absorption in the intestines using Caco-2 human intestinal cell monolayers. The results show that gastric digestion does not significant affect blueberry anthocyanins in terms of composition and antioxidative activity. However, approximately 42% of the total anthocyanin and 29% of the antioxidative activity were lost during intestinal digestion. Structural analysis indicated that fewer free hydroxyl groups and more methoxy groups in the B-ring improve anthocyanin stability. The absorption trials demonstrated that more hydrophobic anthocyanins have better absorption efficiency than more hydrophilic anthocyanins. Furthermore, the glycoside structure also determines the absorption efficiency of anthocyanins.

Contents lists available at ScienceDirect

Food Chemistry

journal homepage: www.elsevier.com/locate/foodchem

Analytical Methods

Stability and biological activity of wild blueberry (*Vaccinium angustifolium*) polyphenols during simulated *in vitro* gastrointestinal digestion

J. Correa-Betanzo [a], E. Allen-Vercoe [b], J. McDonald [b], K. Schroeter [b], M. Corredig [a], G. Paliyath [c,*]

[a] *Department of Food Science, University of Guelph, Ontario N1G2W1, Canada*
[b] *Department of Molecular and Cellular Biology, University of Guelph, Ontario N1G2W1, Canada*
[c] *Department of Plant Agriculture, University of Guelph, Ontario N1G2W1, Canada*

Frozen wild blueberries (low-bush)

A B S T R A C T

Wild blueberries are rich in polyphenols and have several potential health benefits. Understanding the factors that affect the bioaccessibility and bioavailability of polyphenols is important for evaluating their biological significance and efficacy as functional food ingredients. Since the bioavailability of polyphenols such as anthocyanins is generally low, it has been proposed that metabolites resulting during colonic fermentation may be the components that exert health benefits. In this study, an *in vitro* gastrointestinal model comprising sequential chemostat fermentation steps that simulate digestive conditions in the stomach, small intestine and colon was used to investigate the breakdown of blueberry polyphenols. The catabolic products were isolated and biological effects tested using a normal human colonic epithelial cell line (CRL 1790) and a human colorectal cancer cell line (HT 29). The results showed a high stability of total polyphenols and anthocyanins during simulated gastric digestion step with approximately 93% and 99% of recovery, respectively. Intestinal digestion decreased polyphenol- and anthocyanin- contents by 49% and 15%, respectively, by comparison to the non-digested samples. During chemostat fermentation that simulates colonic digestion, the complex polyphenol mixture was degraded to a limited number of phenolic compounds such as syringic, cinnamic, caffeic, and protocatechuic acids. Only acetylated anthocyanins were detected in low amounts after chemostat fermentation. The catabolites showed lowered antioxidant activity and cell growth inhibition potential. Results suggest that colonic fermentation may alter the biological activity of blueberry polyphenols.

"You can't be serious!!!!"

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

41 studies found for: blueberry

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Rank	Status	Study
2	Completed	**Impact of Blueberries on Uric Acid and Quality of Life** **Condition:** Hyperuricemia **Interventions:** Dietary Supplement: Blueberry Powder; Other: Placebo Powder **Study Start:** January 2012
3	Active, not recruiting	**The Health Effects of a Blueberry Enriched Diet on Obese Children** **Condition:** Obesity **Interventions:** Other: Blueberry Smoothie; Other: Sham Smoothie **Study Start:** March 2013
4	Active, not recruiting	**Effects of Blueberry on Cognition and Mobility in Older Adults** **Conditions:** Aging; Age-Related Memory Disorders **Interventions:** Dietary Supplement: Freeze-dried Blueberry; Dietary Supplement: Blueberry Placebo **Study Start:** January 2013
5	Completed	**Dose-dependent Effects of Blueberry Polyphenols on Endothelial Function in Healthy Individuals** **Condition:** Endothelial Function **Interventions:** Dietary Supplement: Freeze-dried blueberry powder dissolved in water; Dietary Supplement: Control **Study Start:** May 2012
6	Completed	**Effect of Blueberries on Vascular Function in Healthy Men** **Condition:** Healthy **Intervention:** Dietary Supplement: Blueberries **Study Start:** October 2010


OPEN
PUSH DOWN & TURN
CLOSE

Dr. Blueberry

Pennington Biomedical Research Center
Louisiana State University System
Baton Rouge, Louisiana USA

But what about Aging and Longevity?

Aging Cell (2006) 5, pp59–68

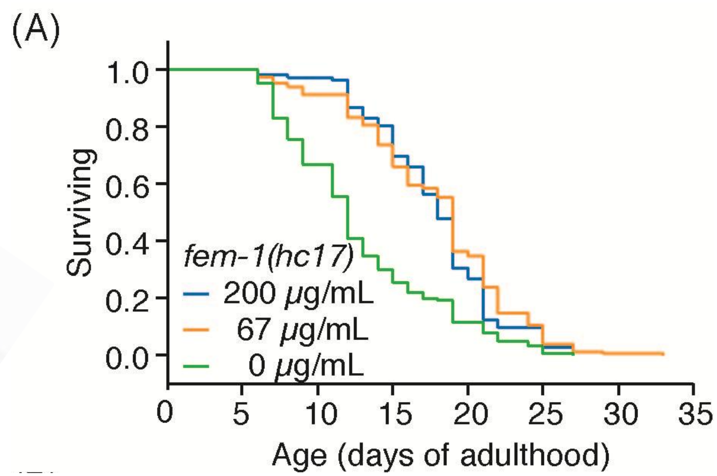
Doi: 10.1111/j.1474-9726.2006.00192.x

Blueberry polyphenols increase lifespan and thermotolerance in *Caenorhabditis elegans*

OnlineOpen: This article is available free online at www.blackwell-synergy.com

Mark A. Wilson,[1] Barbara Shukitt-Hale,[2] Wilhelmina Kalt,[3] Donald K. Ingram,[4] James A. Joseph[2] and Catherine A. Wolkow[1]

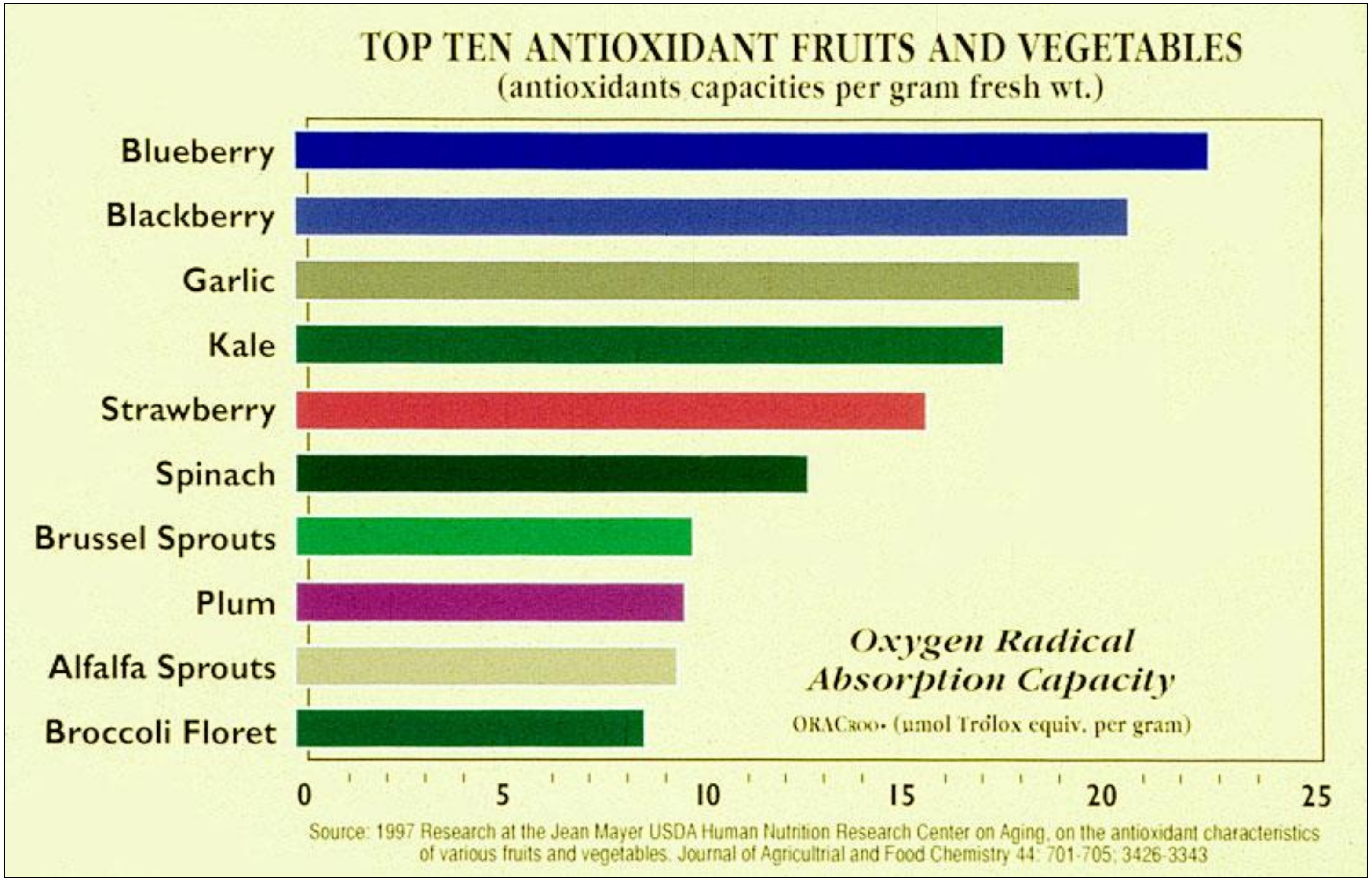
[1]Laboratory of Neurosciences, National Institute on Aging, Intramural Research Program, Baltimore, MD 21224, USA [2]United States Department of Agriculture, Human Nutrition Research Center on Aging, Tufts University, Boston, MA 02111, USA [3]Agriculture and Agri-Food Canada, 32 Main Street, Kentville, Nova Scotia, Canada [4]Laboratory of Experimental Gerontology, National Institute on Aging, Intramural Research Program, Baltimore, MD 21224, USA



USDA/ORAC - The Antioxidant Assay

Oxygen Radical Absorbance Capacity

Ron Prior



Wang H, Cao, G, Prior, RL. (1996) J. Agric. Food Chem. 44:701-705.


O
S

June, 2012

USDA removes ORAC reference values from their website:

There is no evidence that the beneficial effects of polyphenol-rich foods can be attributed to the antioxidant properties of these foods. The data for antioxidant capacity of foods generated by in vitro (test-tube) methods cannot be extrapolated to in vivo (human) effects and the clinical trials to test benefits of dietary antioxidants have produced mixed results. We know now that antioxidant molecules in food have a wide range of functions, many of which are unrelated to the ability to absorb free radicals

OPEN ACCESS Freely available online PLoS one

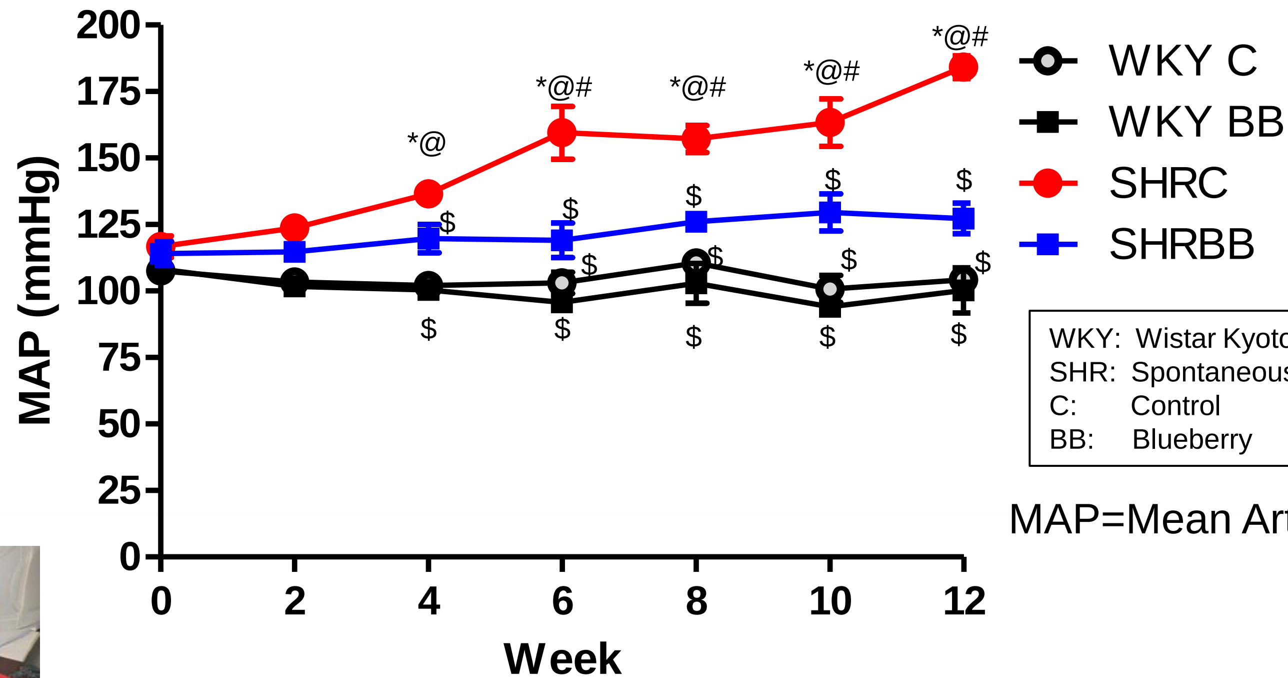
A Blueberry-Enriched Diet Attenuates Nephropathy in a Rat Model of Hypertension via Reduction in Oxidative Stress

September 2011 | Volume 6 | Issue 9 | e24028

Carrie M. Elks[1,4], Scott D. Reed[2], Nithya Mariappan[1], Barbara Shukitt-Hale[3], James A. Joseph[3], Donald K. Ingram[4]*, Joseph Francis[1]*

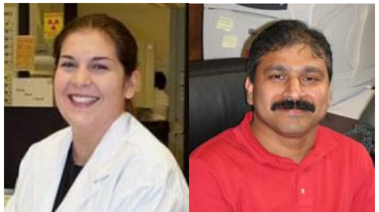
1 Comparative Biomedical Sciences, Louisiana State University School of Veterinary Medicine, Baton Rouge, Louisiana, United States of America, 2 Neurosignaling Laboratory, Pennington Biomedical Research Center, Louisiana State University System, Baton Rouge, Louisiana, United States of America, 3 United States Department of Agriculture-Agriculture Research Services, Human Nutrition Research Center on Aging, Tufts University, Boston, Massachusetts, United States of America, 4 Nutritional Neuroscience and Aging Laboratory, Pennington Biomedical Research Center, Louisiana State University System, Baton Rouge, Louisiana, United States of America

BB freeze dried powder—2% NIH-31 diet

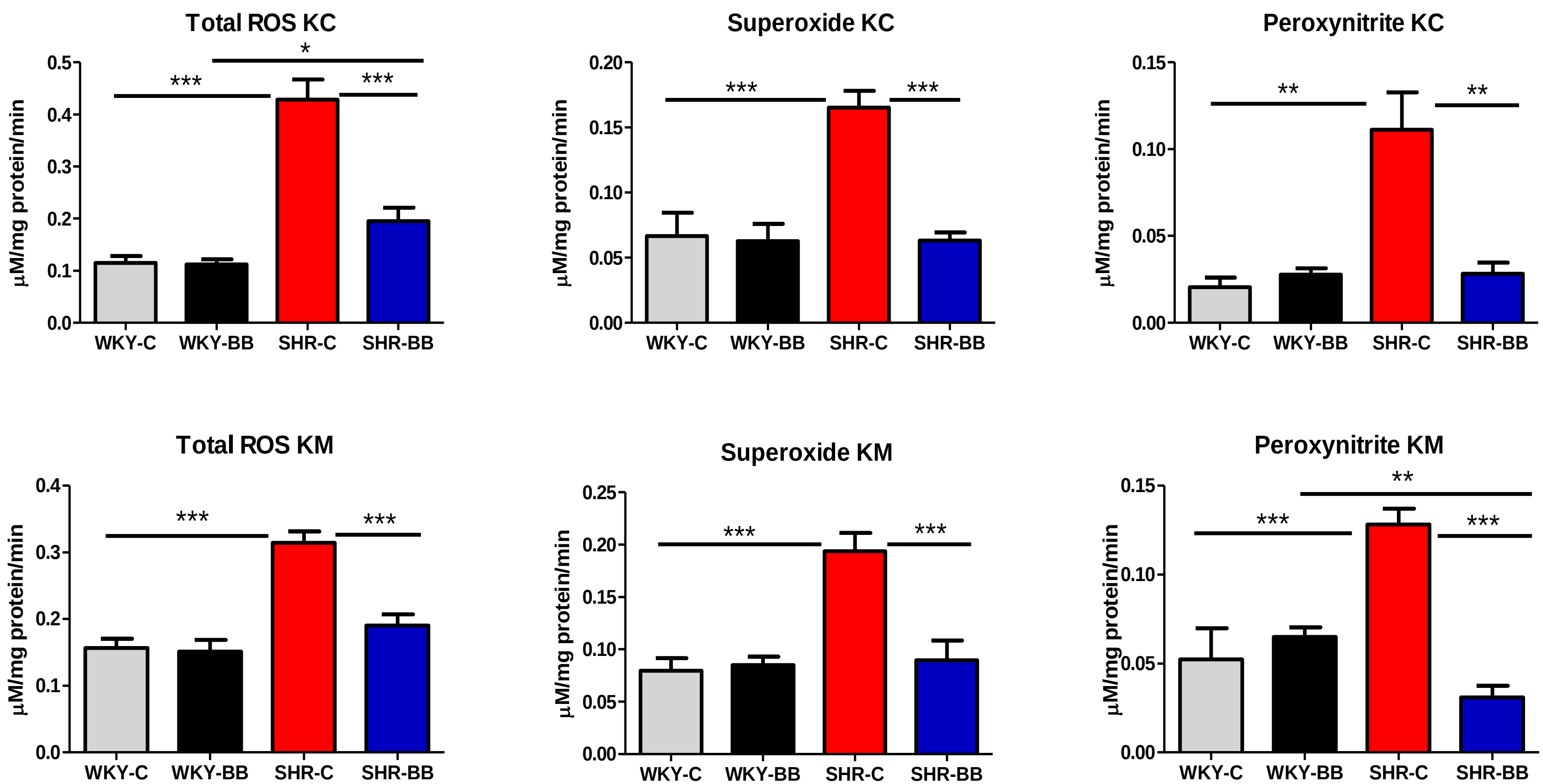


WKY: Wistar Kyoto Rat Control
SHR: Spontaneously Hypertensive Rat
C: Control
BB: Blueberry

MAP=Mean Arterial Pressure

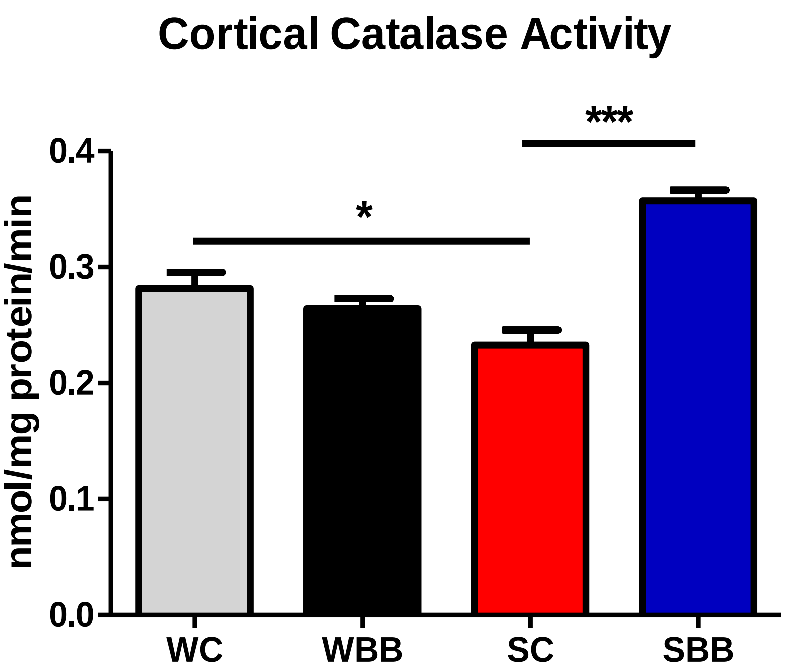


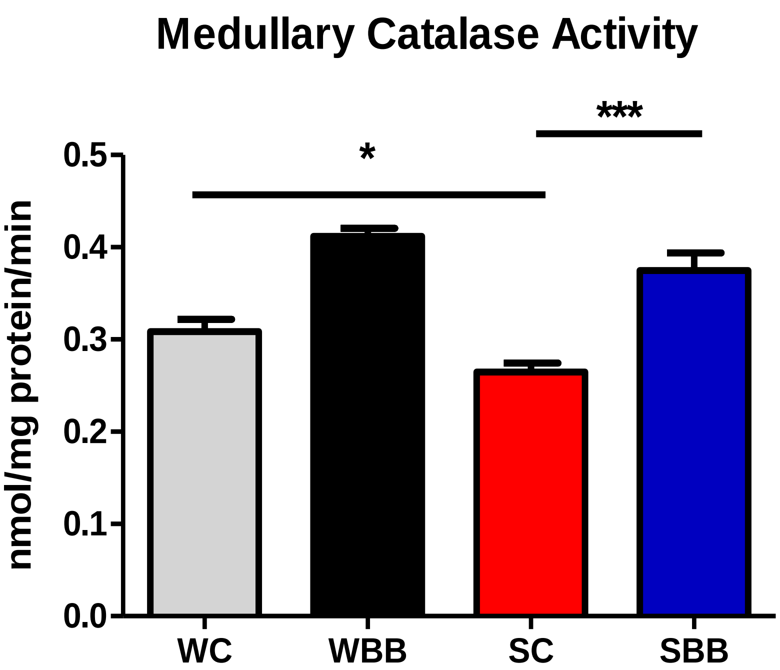
Rats fed BB-enriched diets for 12 weeks exhibited decreased renal free radical production.



* p<0.05; ** p<0.01; ***p<0.001

Rats fed BB-enriched diets for 12 weeks exhibited increased renal catalase activity.





* p<0.05; ***p<0.001

Cell
PRESS

Cell Metabolism
Minireview

Stress-Response Hormesis and Aging: "That which Does Not Kill Us Makes Us Stronger"

David Gems[1] and Linda Partridge[1,*]
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Hormesis refers to the beneficial effects of a treatment that at a higher intensity is harmful. In one form of hormesis, sublethal exposure to stressors induces a response that results in stress resistance. The principle of stress-response hormesis is increasingly finding application in studies of aging, where hormetic increases in life span have been seen in several animal models.

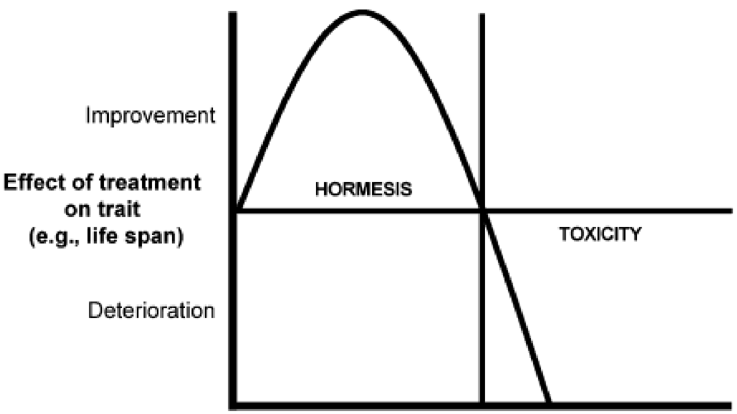

Figure 1. Dose-Response Curve of a Treatment with a Hormetic Effect
Low doses result in enhanced function, whereas higher doses result in dys-function.

Cell Metabolism
Minireview

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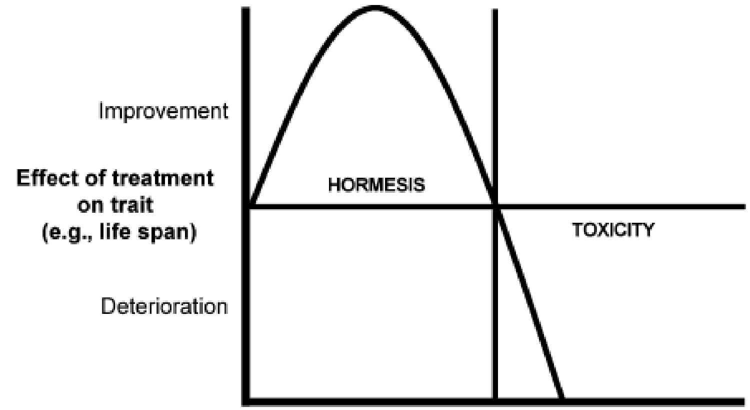

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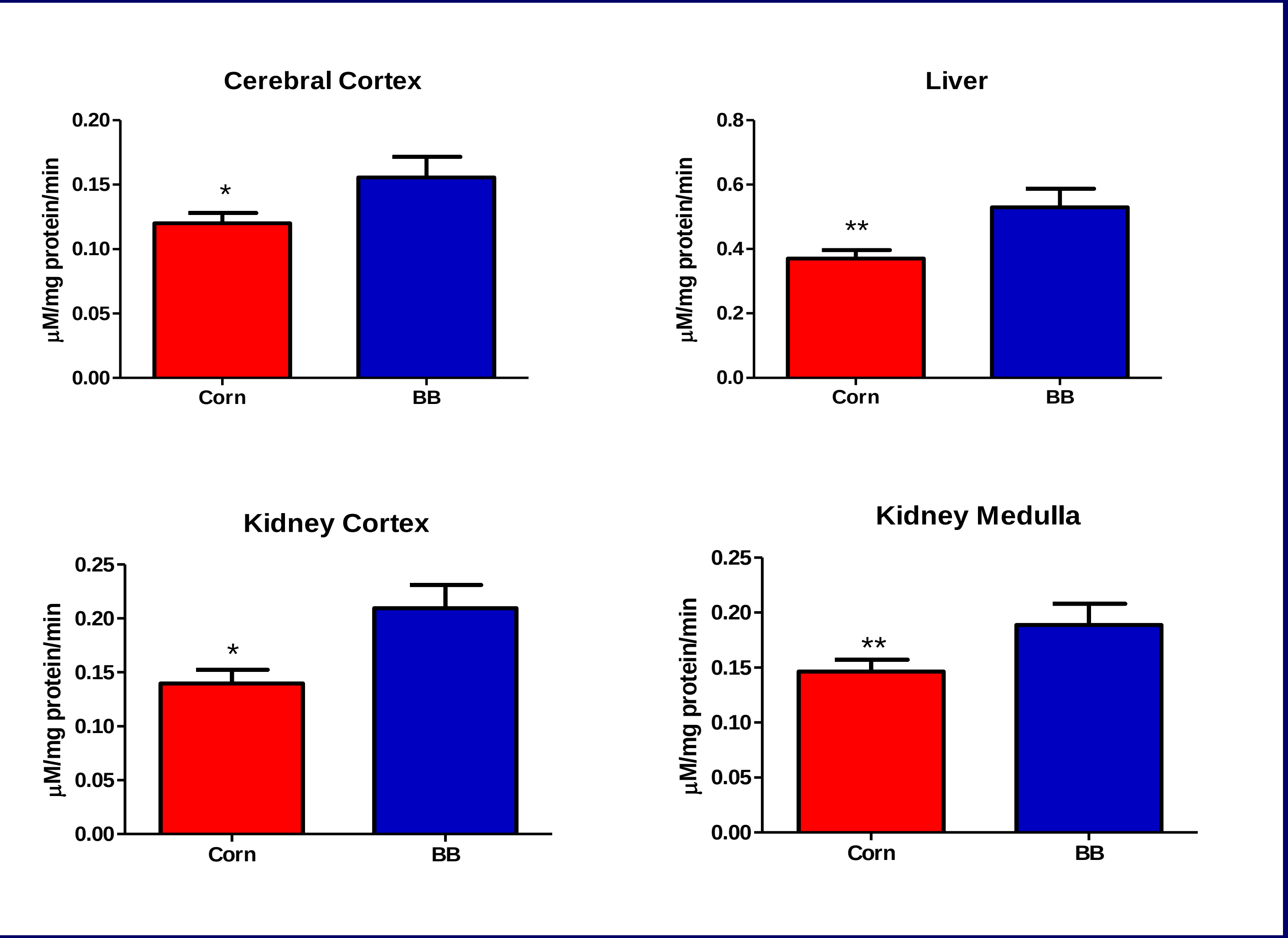
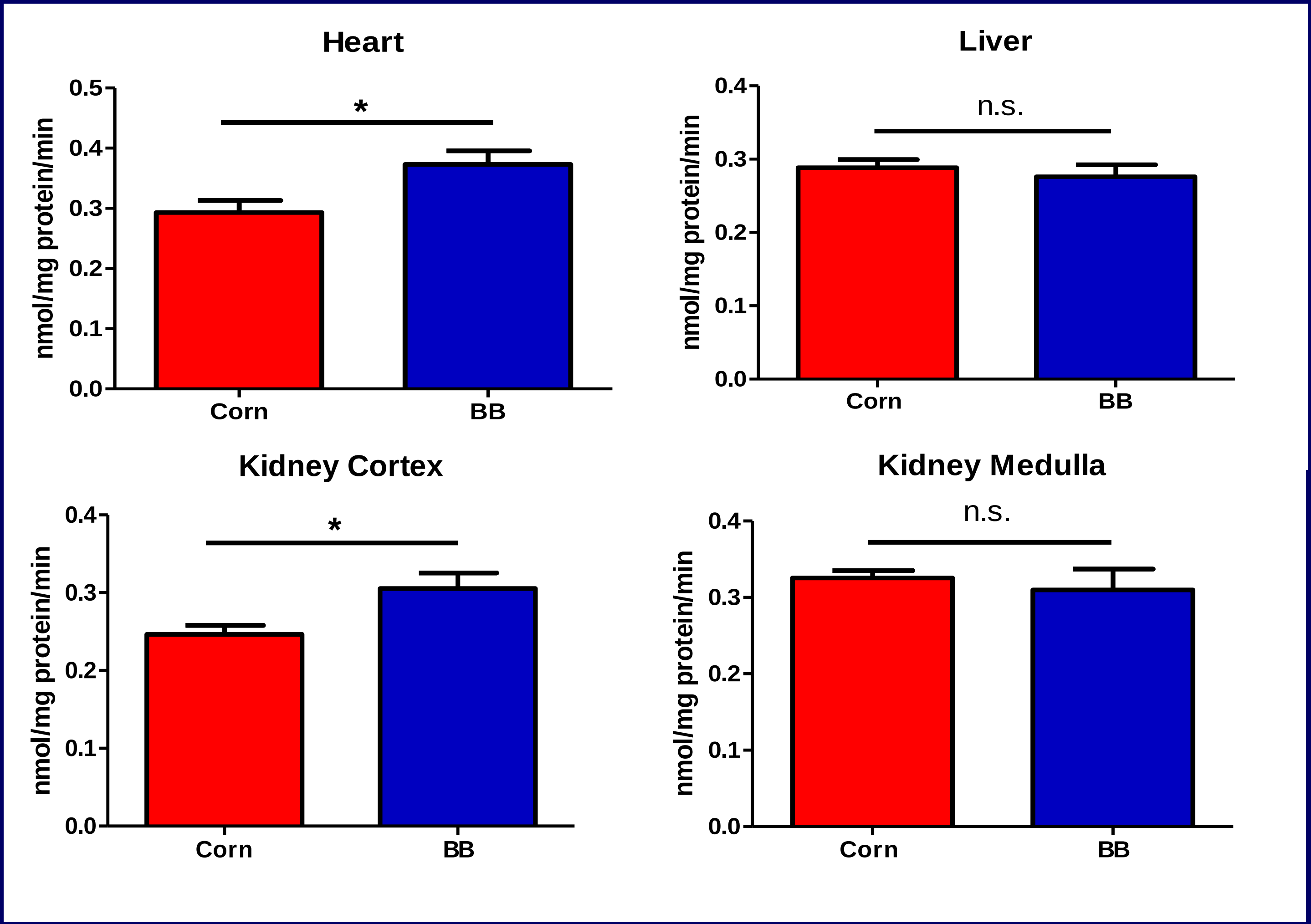
Low doses result in enhanced function, whereas higher doses result in dysfunction.

Rats fed BB-enriched diets for 2 days exhibited increased total ROS production.



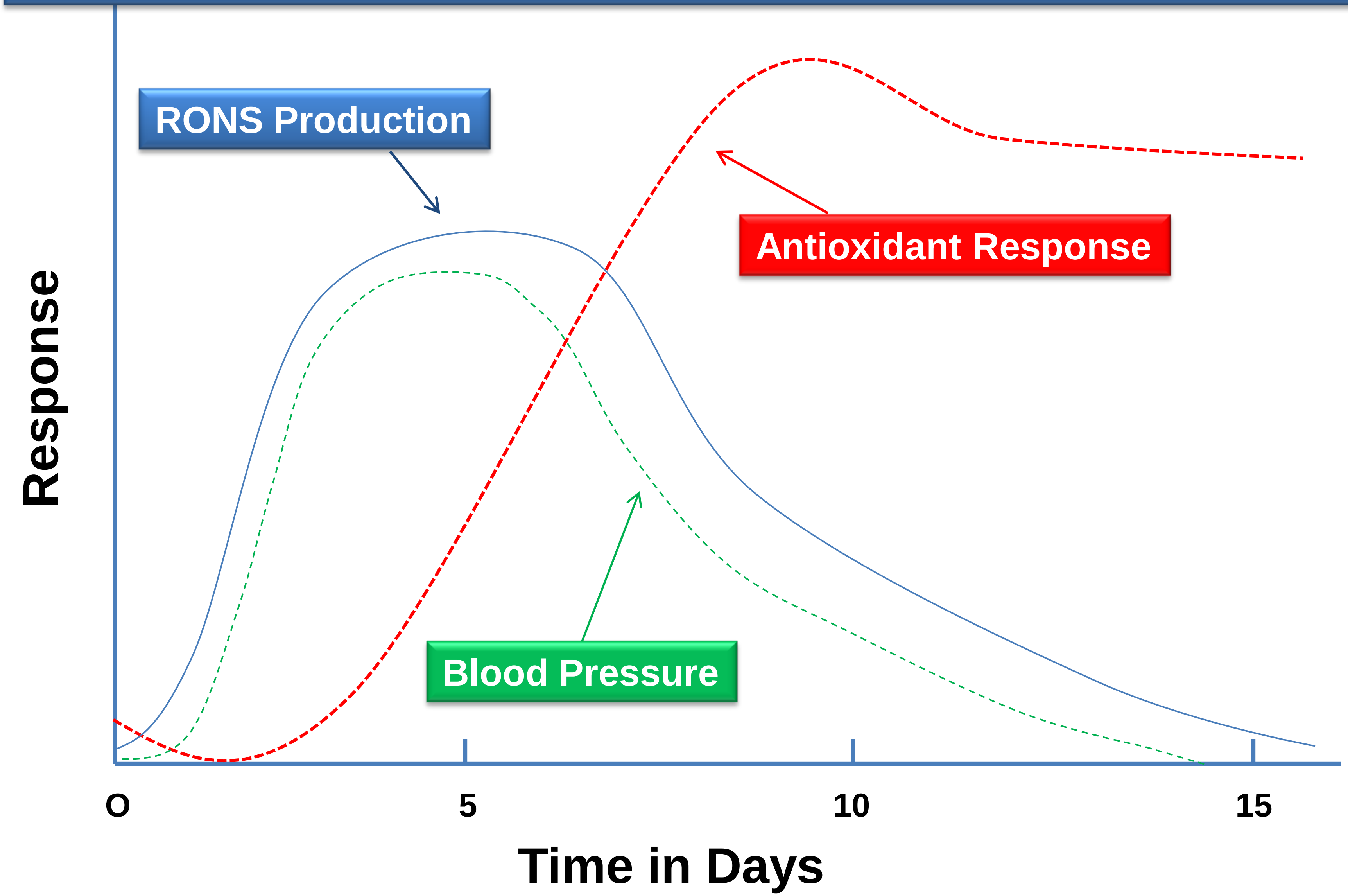
* $p<0.05$; ** $p<0.01$

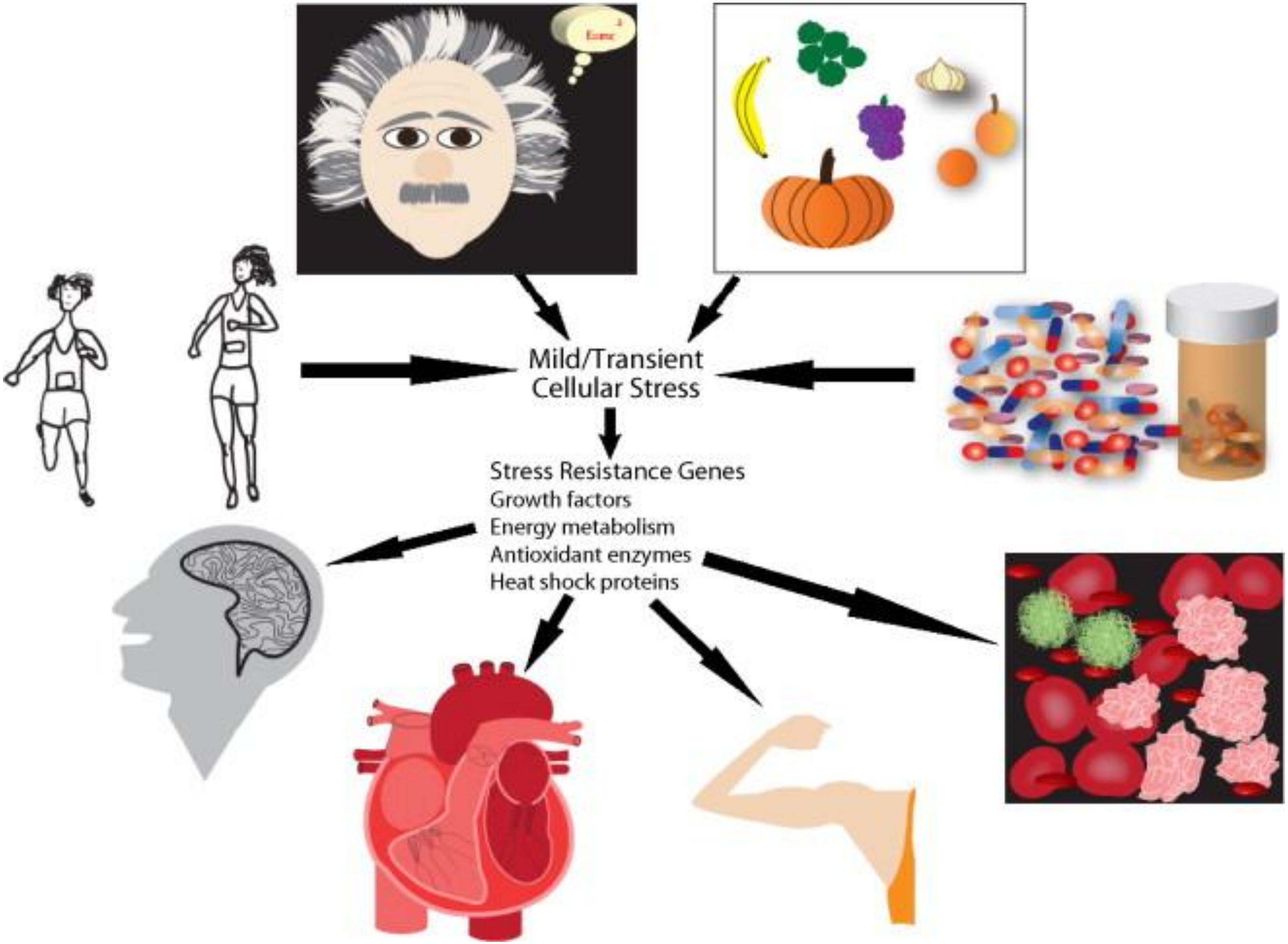
Rats fed BB-enriched diets for 2 days had varied alterations in tissue catalase activities.



* $p<0.05$

Kinetics of Hypothetical Hormetic Response to BBs:
Production of Reactive Oxygen and Nitrogen Species (RONS) Stimulates Increased Blood Pressure and Antioxidant Defensive Response




Mild/Transient
Cellular Stress
Stress Resistance Genes
Growth factors
Energy metabolism
Antioxidant enzymes
Heat shock proteins