

Prof. dr. Yves Desjardins
Laval Université Québec



Updates on health effects of berries: New modes of action linked to the modulation of the gut microbiota

INAF, Université Laval

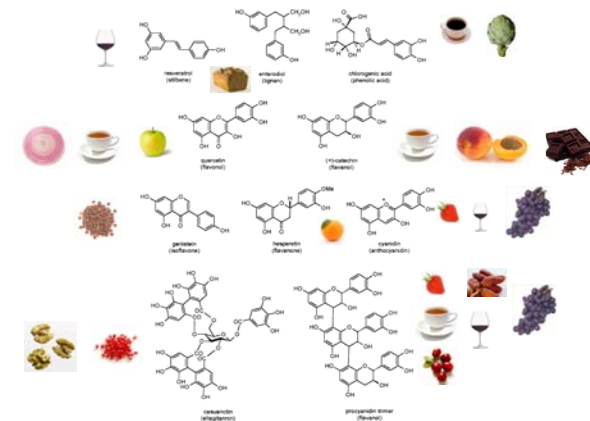
23 January 2019

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Université Laval
Québec, Québec, Canada



Health effects have been attributed to phenolic compounds





British Journal of Nutrition, page 1 of 13
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doi:10.1017/S0007114517000393

Strawberry and cranberry polyphenols improve insulin sensitivity in insulin-resistant, non-diabetic adults: a parallel, double-blind, controlled and randomised clinical trial

Martine Paquette^{1,2}, Ana S. Medina Larqué^{1,2}, S. J. Weisnagel^{2,3}, Yves Desjardins¹, Julie Marois^{1,2}, Geneviève Pilon^{1,4}, Stéphanie Dudonné¹, André Marette^{1,4} and Hélène Jacques^{1,2*}

¹Institute of Nutrition and Functional Foods, Laval University, Quebec, Canada, G1V 0A6

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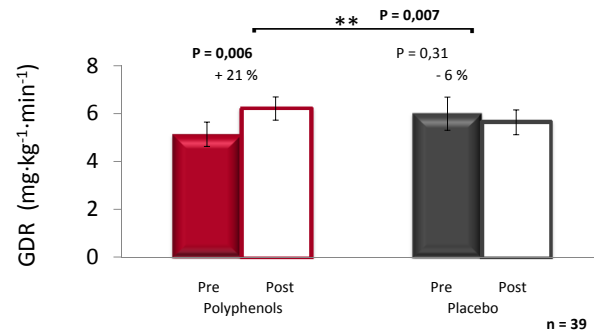
⁴Quebec Heart and Lung Institute, Quebec, Canada, G1V 4G5

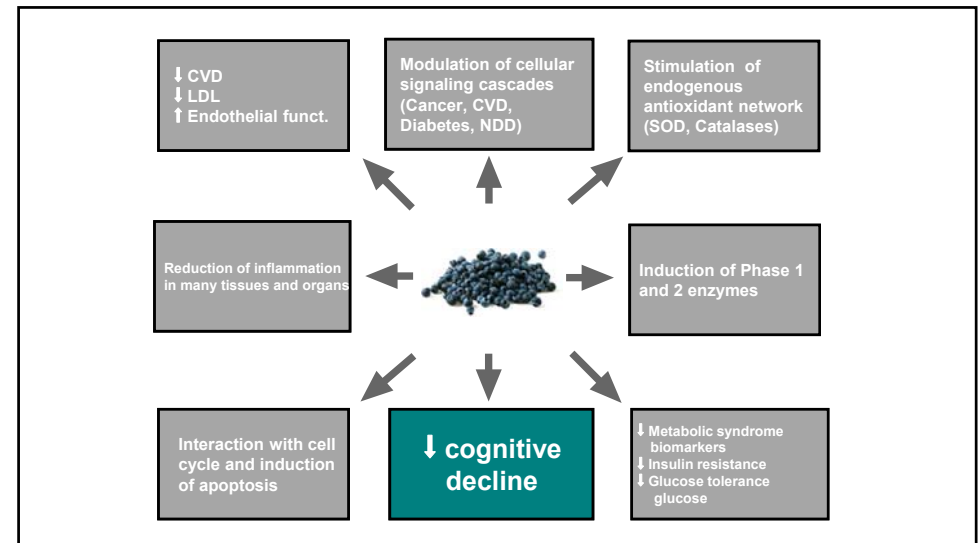
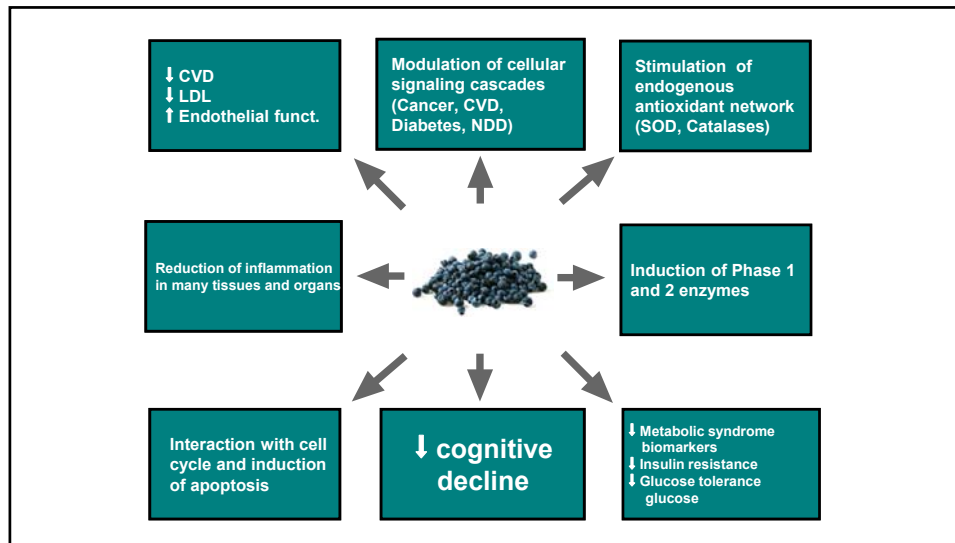
(Submitted 3 June 2016 – Final revision received 13 January 2017 – Accepted 28 January 2017)



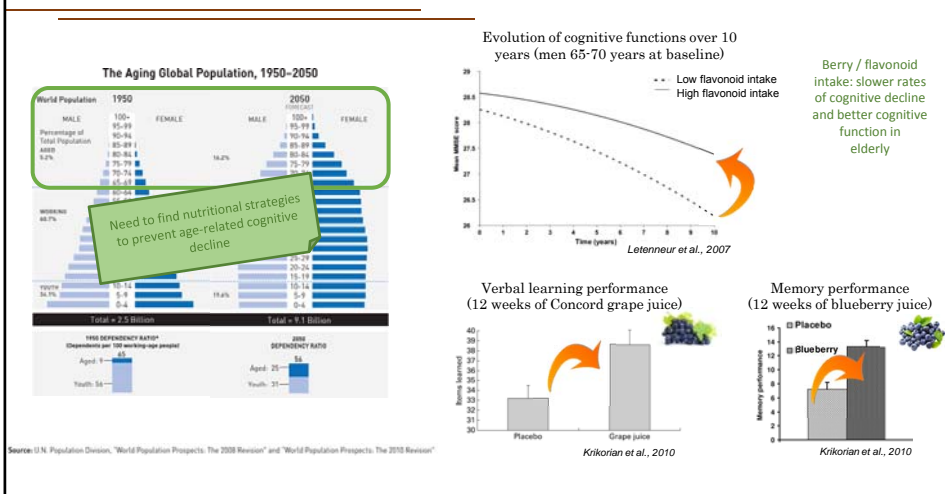
Glucose disposal rate (GDR)

Metformin = 25 % GDR





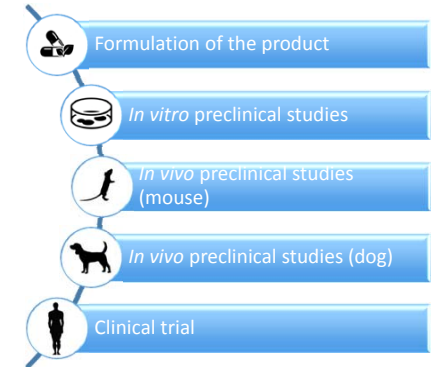
Preventive effect of berry polyphenols on cognitive decline



Neurophenols Research Consortium



- ▶ France-Canada collaborative project (2011-2015)
- ▶ Academic institutions: phytochemistry, neuroscience, psychology and nutrition
- ▶ Companies: active ingredients and food supplements
- ▶ Development of a nutritional formulation of blueberry and grape polyphenols with a beneficial effect on cognitive decline in humans and pets



Neurophenols Research Consortium



Cognitive-Enhancing Effects of a Polyphenols-Rich Extract from Fruits without Changes in Neuropathology in an Animal Model of Alzheimer's Disease

Alexandre Dal-Pan^{a,b,c}, Stéphanie Dudonné^{a,b}, Philippe Bonneau^{a,b,c,d}, Margarete Brandebauer^a, Cynthia Tremblay^a, Yves Desjardins^{a,b} and Frédéric Calvez^{a,b,c,d,e} on behalf of the Neurophenols consortium[†]

Journal of Alzheimer's Disease 55 (2017) 115–135

A mixed grape and blueberry extract is safe for dogs to consume

Anne-Sophie Martineau^a, Véronique Leray^a, Anne Lepoutre^a, Géraldine Blanchard^a, Julien Bensalem^a, David Gaudou^a, Khadija Ouguenam^a, Patrick Nguyen^{a,b} and On behalf of Neurophenols Consortium

BMC Veterinary Research (2016) 12:162



Original Article

Polyphenols From Grape and Blueberry Improve Episodic Memory in Healthy Elderly with Lower Level of Memory Performance: A Bicentric Double-Blind, Randomized, Placebo-Controlled Clinical Study

Julien Bensalem^{a,b}, Stéphanie Dudonné^{a,b}, Elodie Gillard^a, Frédéric Calvez^{a,b,c}, David Gaudou^a, Khadija Ouguenam^a, Patrick Nguyen^{a,b} and On behalf of Neurophenols Consortium

Journal of Alzheimer's Disease 55 (2017) 115–135

Potential of the bioavailability of blueberry phenolic compounds by co-ingested grape phenolic compounds in mice, revealed by targeted metabolomic profiling in plasma and feces†

Stéphanie Dudonné^{a,b}, Alexandre Dal-Pan^{a,b}, Pascal Dubé^a, Thibault V. Varin^a, Frédéric Calvez^{a,b} and Yves Desjardins^a

Food Funct., 2016, 7, 3421



Dietary Polyphenol Supplementation Prevents Alterations of Spatial Navigation in Middle-Aged Mice

Julien Bensalem^{1,2,3}, Laure Servant^{1,2}, Serge Alfaro^{1,2,4}, David Gaudou⁵, Sophie Lape^{1,2}, Pauline Lafenetre^{1,2,4,6} and Véronique Pallat^{1,2,4,6}

Front. Behav. Neurosci. 10:9.

Protective effects of berry polyphenols against age-related cognitive impairment

Julien Bensalem^{a,b}, Alexandre Dal-Pan^{a,b}, Elodie Gillard^a, Frédéric Calvez^{a,b,c} and Véronique Pallat^{a,b,c,d,e}

Nutrition and Aging, 2015

Clinical trial

- Randomized, placebo-controlled, double-blinded study
- Bi-center : France and Quebec (50-50%)
- Inclusion criteria:
 - Age : 60 to 70 years old
 - 20 ≤ BMI ≤ 30
 - 26 < MMSE (Mini Mental State Examination) ≤ 29
 - WMS (Wechsler Memory Scale) < 29 (immediate recall score)
 - WMS < 16 (delayed recall score)
- Exclusion criteria:
 - Consumption of food supplements containing polyphenols or omega-3
 - Depression, schizophrenia, Alzheimer's disease, dementia...
 - Treatment affecting cognitive functions (anti-depressants, neuroleptics...)
 - Unbalanced or restrictive diet
 - Alcohol consumption > 2 glasses /day
 - High level of physical activity (> 5h /week)
- Food restrictions:
 - Polyphenol rich foods: berries ≤ 2 servings per week, tea ≤ 1 cup per day, dark chocolate (≥ 70% cocoa) ≤ 140 g per week
 - Omega-3 rich foods (fish, algae...) : ≤ 3 servings per week

Table 1 | Baseline characteristics (n=190).

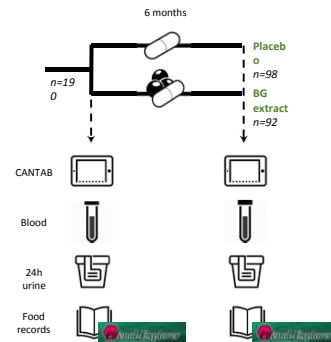
	MV	mean	(SD)	n (%)
Age (years)	0	64.66	(2.91)	
Gender	0			
Men				55 (28.9)
Women				135 (71.1)
Investigation center	0			
France				95 (50.0)
Quebec				95 (50.0)
Education years	0			
< 15 years				114 (60.0)
≥ 15 years				76 (40.0)
PASE	10	141.36	(54.52)	
MMSE	0	28.14	(0.79)	
WMS immediate recall	0	18.65	(4.67)	
WMS delayed recall	0	7.94	(3.12)	
BMI (kg/m ²)	0	24.71	(2.24)	

MV: missing value, n: frequency, SD: standard deviation.

BMI: Body Mass Index, MMSE: Mini-Mental State Examination, PASE: Physical Activity Scale for the Elderly, WMS: Wechsler Memory Scale.

Clinical trial

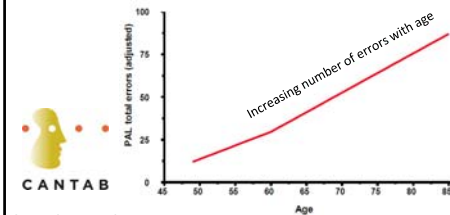
- Supplementation : 300 mg of BG extract twice a day or placebo
- Duration : 6 months (evaluation at baseline and after 6 months)
- Cognitive performances evaluation (CANTAB battery):
 - PAL test (Paired Associates Learning) = **primary outcome**
 - VRM (Verbal recognition memory) immediate and delayed recall, free recall (18 words)
 - SSP (Spatial Span) and Reverse SSP
- Biological measurements: heart rate, blood pressure, hematology (cholesterolemia, triglyceridemia, insulinemia, glycemia...)
- Targeted metabolomics analysis (24h urine, UHPLC-MS/MS)
- Food records (dietary habits, polyphenol consumption)



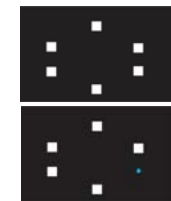
PAL test

Paired Associates Learning test (PAL) assesses **episodic memory** and **learning** = association of an event with place and time

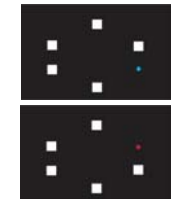
Outcome measures include the errors made by the participant, the number of trials required to locate the pattern(s) correctly, memory scores and stages completed.



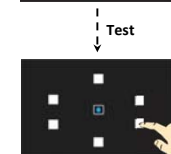
Source: Cambridge Cognition, PAL sensitivity to age



Boxes are displayed on the screen

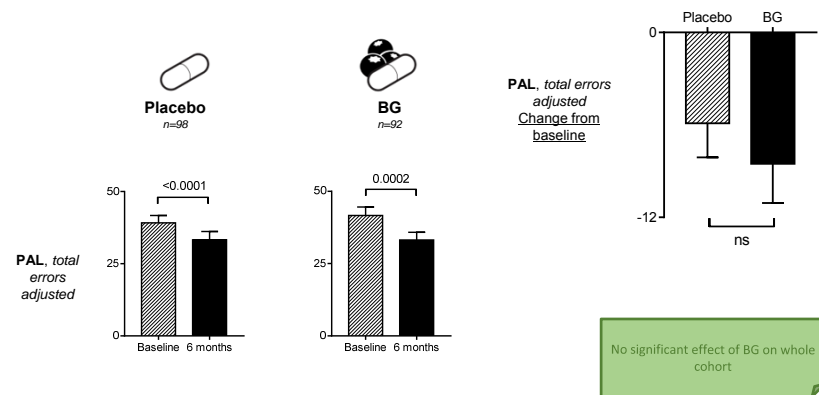


Boxes are automatically opened (randomized order) to show the patterns. The difficulty level increases through the test (patterns increasing from 1 to 8)

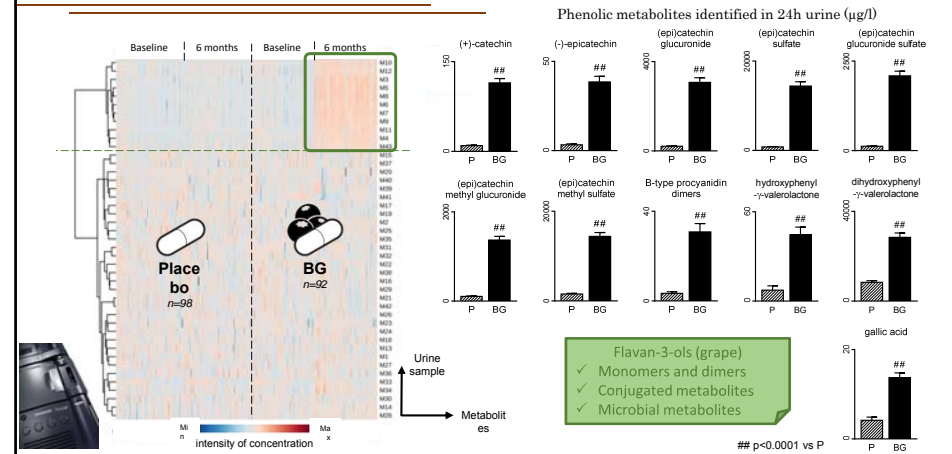


Once all the boxes have been opened, the participants have to associate the patterns with their respective location

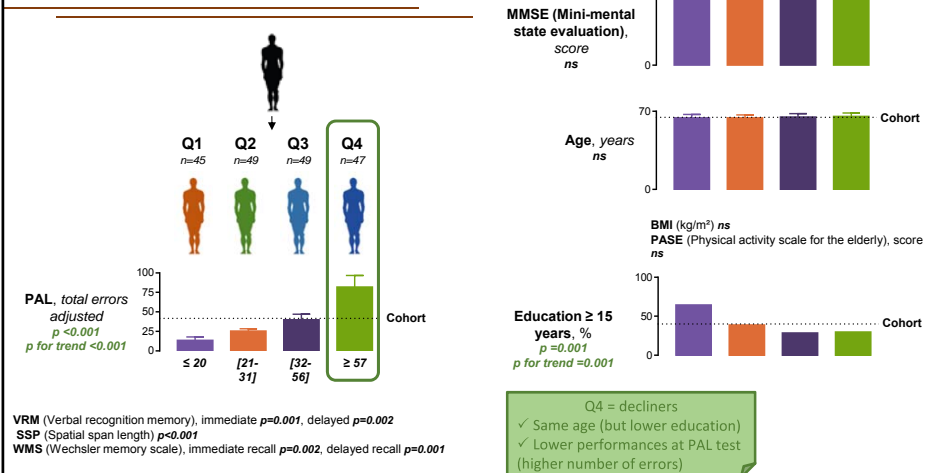
Effect of BG extract on whole cohort



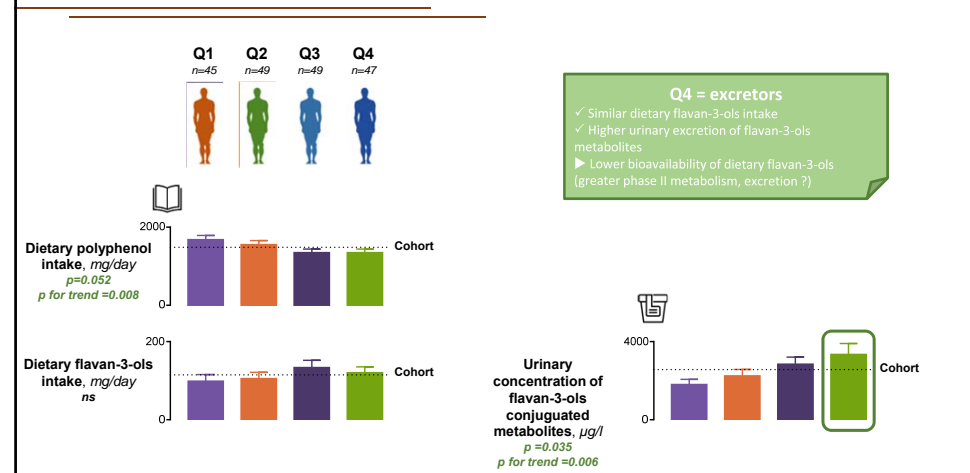
Biomarkers of BG consumption: targeted metabolomic analysis



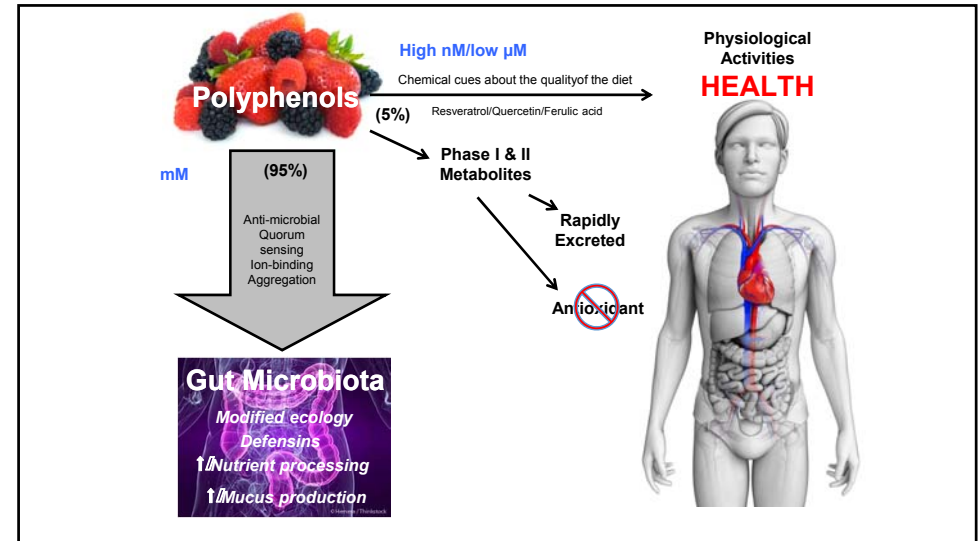
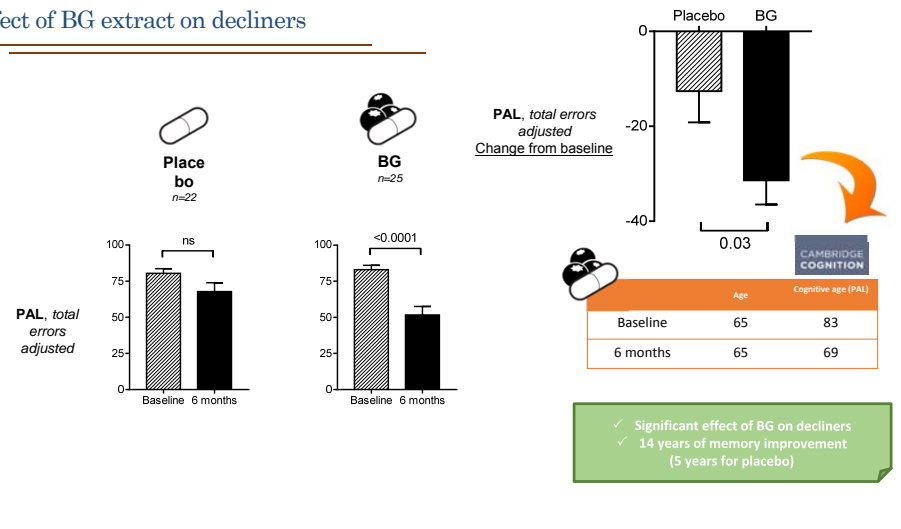
Stratification of the cohort (PAL baseline)



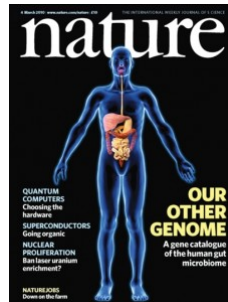
Stratification of the cohort (PAL baseline)



Effect of BG extract on decliners



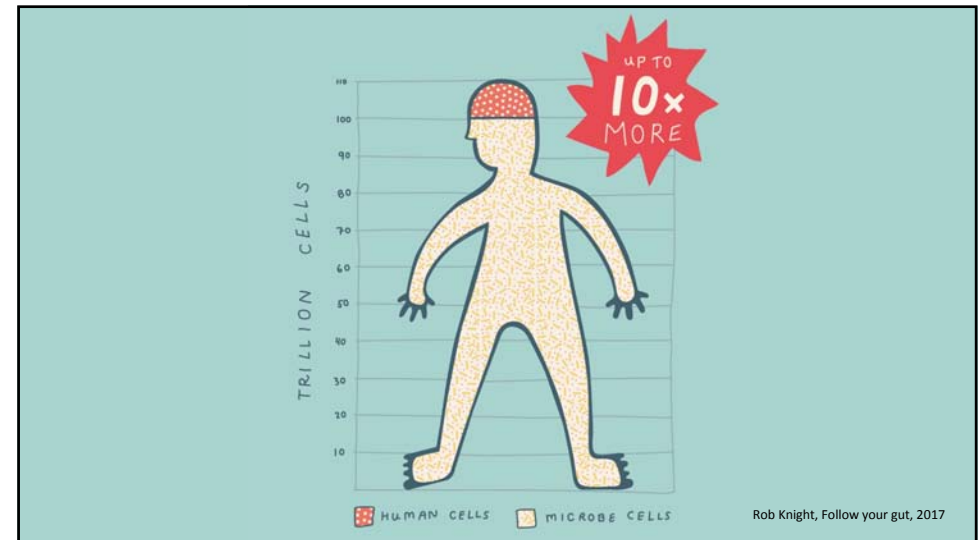
Our genome: the microbiome



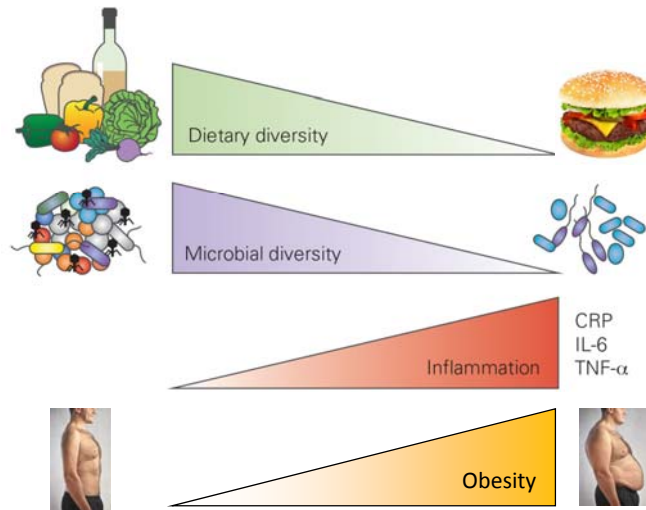
Adapted from Backhed et al. Science 307, 1915-1920.

The hidden organ

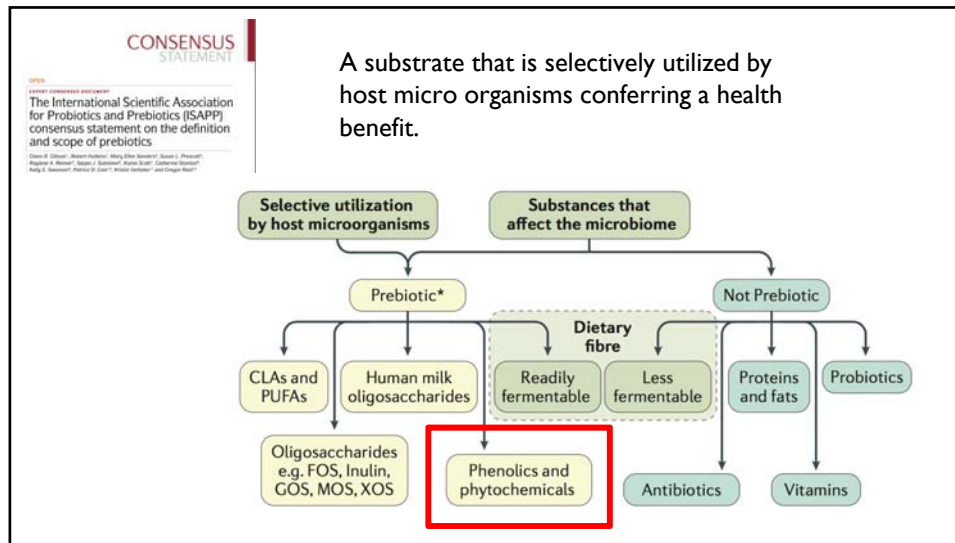
- 1.5-2.0 kg microorganisms
- 100 trillion bacteria in our gut...



99 % +

[illegible]

Zhernakova et al. Science, 2016



Impact
Factor
17.016

Downloaded from gut.bmj.com on August 4, 2014 - Published by group.bmj.com
 Gut Online First, published on July 30, 2014 as 10.1136/gutjnl-2014-307142

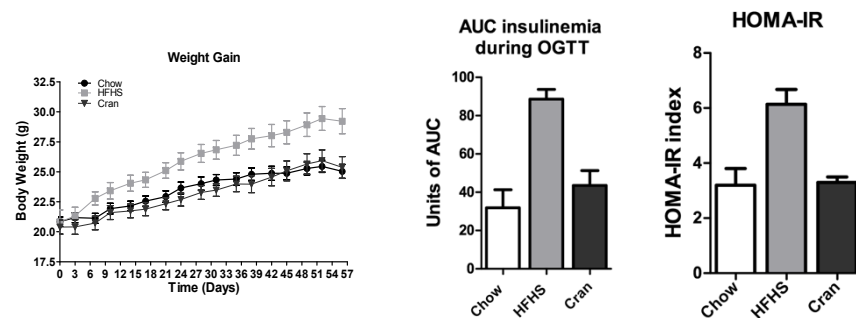
Gut microbiota

ORIGINAL ARTICLE

A polyphenol-rich cranberry extract protects from diet-induced obesity, insulin resistance and intestinal inflammation in association with increased *Akkermansia* spp. population in the gut microbiota of mice

Fernando F Anhe^{1,2}, Denis Roy², Geneviève Pilon^{1,2}, Stéphanie Dudonné², Sébastien Matamoros², Thibault V Varin², Carole Garofalo³, Quentin Moine³, Yves Desjardins², Emile Levy^{3,4}, André Marette^{1,2}

Effect of cranberry extract on Weight Gain and Glycemia



Effect of a cranberry extract on hepatic steatosis

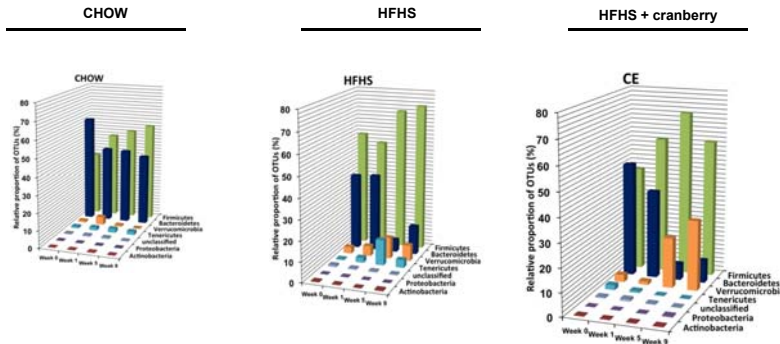
Chow

HFHS
+
Cranberry



HFHS

Evolution of the gut microbiota under a HFHS diet or a diet supplemented with cranberry extract.



Cross-talk between *Akkermansia muciniphila* and intestinal epithelium controls diet-induced obesity

Amandine Everard^a, Clara Belzer^b, Lucie Geurts^a, Janneke P. Ouwerkerk^b, Céline Druart^a, Laure B. Bindels^a, Yves Guiot^c, Muriel Derrien^b, Giulio G. Muccioli^d, Nathalie M. Delzenne^e, Willem M. de Vos^{b,h}, and Patrice D. Cani^{a,h,1}

^aMetabolism and Nutrition Research Group, Walloon Excellence in Life sciences and BioTechnology (WELBIO), Louvain Drug Research Institute, Université catholique de Louvain, B-1200 Brussels, Belgium; ^bLaboratory of Microbiology, Wageningen University, 6703 HB, Wageningen, The Netherlands; ^cDepartment of Pathology, Cliniques Universitaires Saint-Luc, Université catholique de Louvain, B-1200 Brussels, Belgium; ^dBioanalysis and Pharmacology of Bioactive Lipids Research Group, Louvain Drug Research Institute, Université catholique de Louvain, B-1200 Brussels, Belgium; and ^eDepartments of Bacteriology and Immunology and Veterinary Biosciences, University of Helsinki, 00014 Helsinki ylipisto, Helsinki, Finland

Edited* by Todd R. Klaenhammer, North Carolina State University, Raleigh, NC, and approved March 28, 2013 (received for review November 8, 2012)

NATURE | NEWS

Gut microbe may fight obesity and diabetes

Bacterium helps to regulate metabolism in mice.

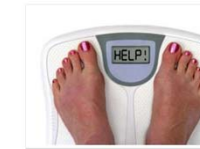
Brian Owens

13 May 2013

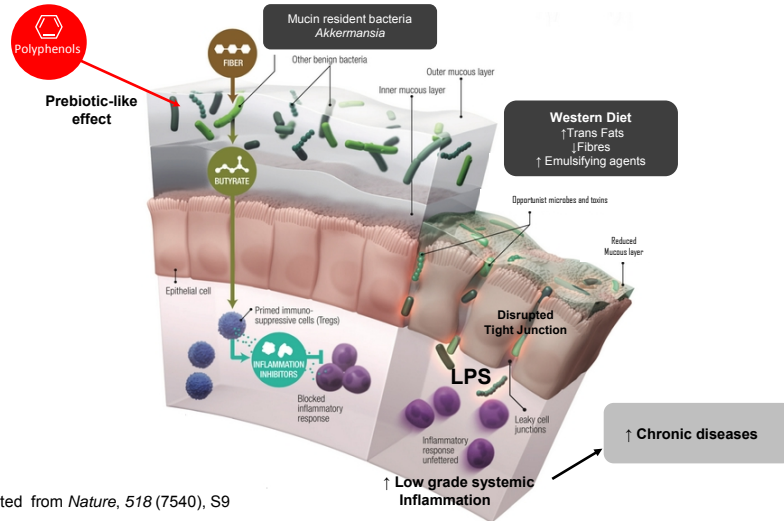
The Buzz About *Akkermansia muciniphila*: It's More Than Just Weight Loss

May 17, 2013 by Terri Sundquist

★★★★☆ 3 Votes



The bacterium *Akkermansia muciniphila* is creating quite a stir in science news, with people calling it the "weight loss bacterium". While it's exciting to think about a bacterium that has the ability to reduce body weight with no change in food intake, there's another reason to get excited: The potential to treat obesity-related metabolic disorders such as type-2



Adapted from Nature, 518 (7540), S9

More and more evidences point to the fact that polyphenols have a prebiotic action and particularly stimulate *Akkermansia muciniphila*

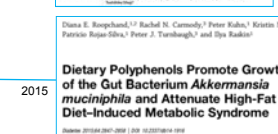
Pomegranate



Apples



Concord Grapes



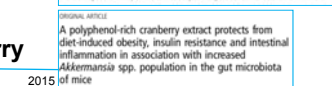
Caffeic acid



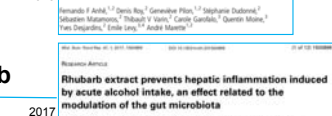
Table Grapes



Cranberry



Rhubarb



Lingonberry



Exploration of Nordic Ressources



Contents lists available at ScienceDirect

2015, 44:214-224.

Journal of Food Composition and Analysis

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

Original Research Article

Comprehensive analysis of phenolic compounds and abscisic acid profiles of twelve native Canadian berries



Stéphanie Dudonné^{a,*}, Pascal Dubé^a, Fernando Forato Anhê^{a,b}, Geneviève Pilon^{a,b},
André Marette^{a,b}, Mélanie Lemire^c, Cory Harris^d, Eric Dewailly^c, Yves Desjardins^a

^a Institute of Nutrition and Functional Foods (INAF), Laval University, 2440 boulevard Hochelaga, Québec (QC) G1V0A6, Canada

^b Department of Medicine, Quebec Heart and Lung Institute (CRIUCPQ), Laval University, 2725 Chemin Ste-Foy, Québec (QC) G1V4G5, Canada

^c Populations Health and Optimal Health Practices Axis, CHU de Québec Research Center, 2875 Boulevard Laurier, Québec (QC) G1V2M2, Canada

^d Department of Biology, University of Ottawa, 30 Marie Curie, Ottawa (ON) K1N6N5, Canada

Arctic fruits



Cloudberry (CLE)



Alpine Bearberry (ABE)



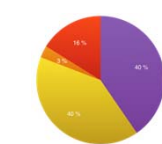
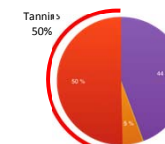
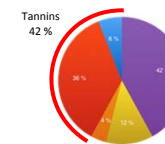
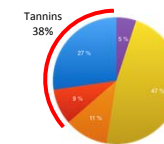
Lingonberry (LGE)



Crowberry (CRB)



Bog blueberry (BBE)



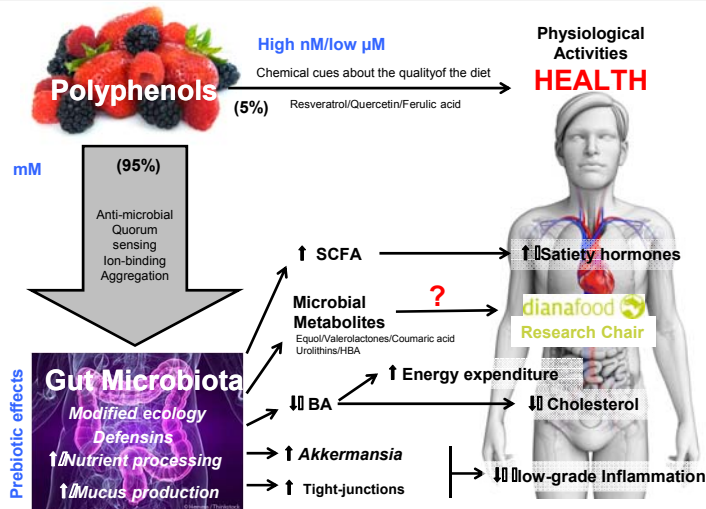
■ Ellagitannins

■ Procyanidins

■ Anthocyanins

■ Phenolic acids

■ Flavonols/Flavanols



Acknowledgements

Y. Desjardins

Stéphanie Dudonné
Pascale Dubé
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Bruno Marcotte

