

# Cocoa, Chocolate and Health



*Debra Miller, PhD  
Director of Nutrition, Health & Regulatory  
The Hershey Company*



# Outline

- Nature to Nutrition: Where does cocoa come from?
- How cocoa & chocolate are made
- Bioactive ingredients
- Review of the literature
- Emerging areas with benefit
- Alkalization
- % Cacao
- From the science bench to clinical practice



Where does natural cocoa  
& chocolate come from?



# Why would chocolate have healthy components?

- In English, Cocoa is both the plant and the powder
- Cacao is commonly used term from the romance languages
- “% Cacao” is the proportion of the product made from the cocoa bean
- *Theobroma cacao* is the scientific name
- “Food of the gods”

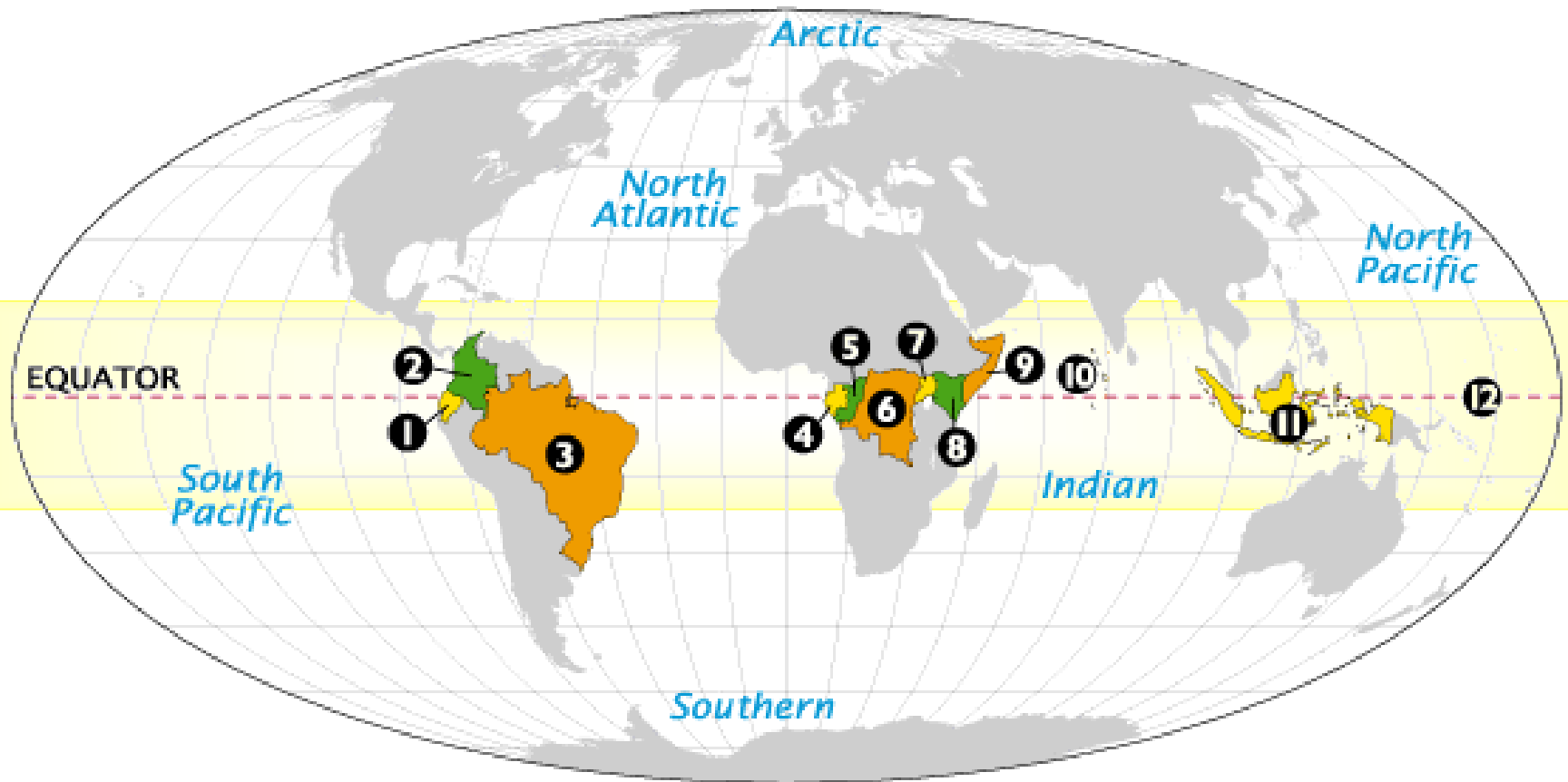




# The Cocoa Pod (It's a plant!)



# Geographical Origins of Cocoa



Cocoa trees grow only in tropical regions  $\pm 20^\circ$  latitude from the Equator in tropical rain forests. Major regions are Central & South America, Central Africa and Indonesia.



How do you get from a cocoa  
bean to a chocolate bar?





# Cocoa's Natural Origins

***Cocoa comes from the Theobroma cacao tree***



- ***The tree grows in the tropical rainforest between 20° N & S of the equator***
- ***The tree grows to 40-50 ft***
- ***Their life expectancy is +100 years***

***Cacao flowers produce the cocoa pods***



- ***Hundreds of flowers appear, but only 1-2% ripen to become mature cocoa pods***
- ***The pollinated flower takes 180 days to mature into a cocoa pod***

***Cocoa pods are the fruit, cocoa beans are the seeds***



- ***The pods range between 4-16 inches in length***
- ***The cocoa pod has a hard, thick outer rind like acorn squash***



# Natural Cocoa Harvesting is a Hand Craft

*The cocoa bean is removed from the pod*



- *Cocoa pods are broken open by a machete or by striking them*
- *About 30-50 cocoa beans are developed in each pod*

*Cocoa 'beans' are fermented between banana leaves*



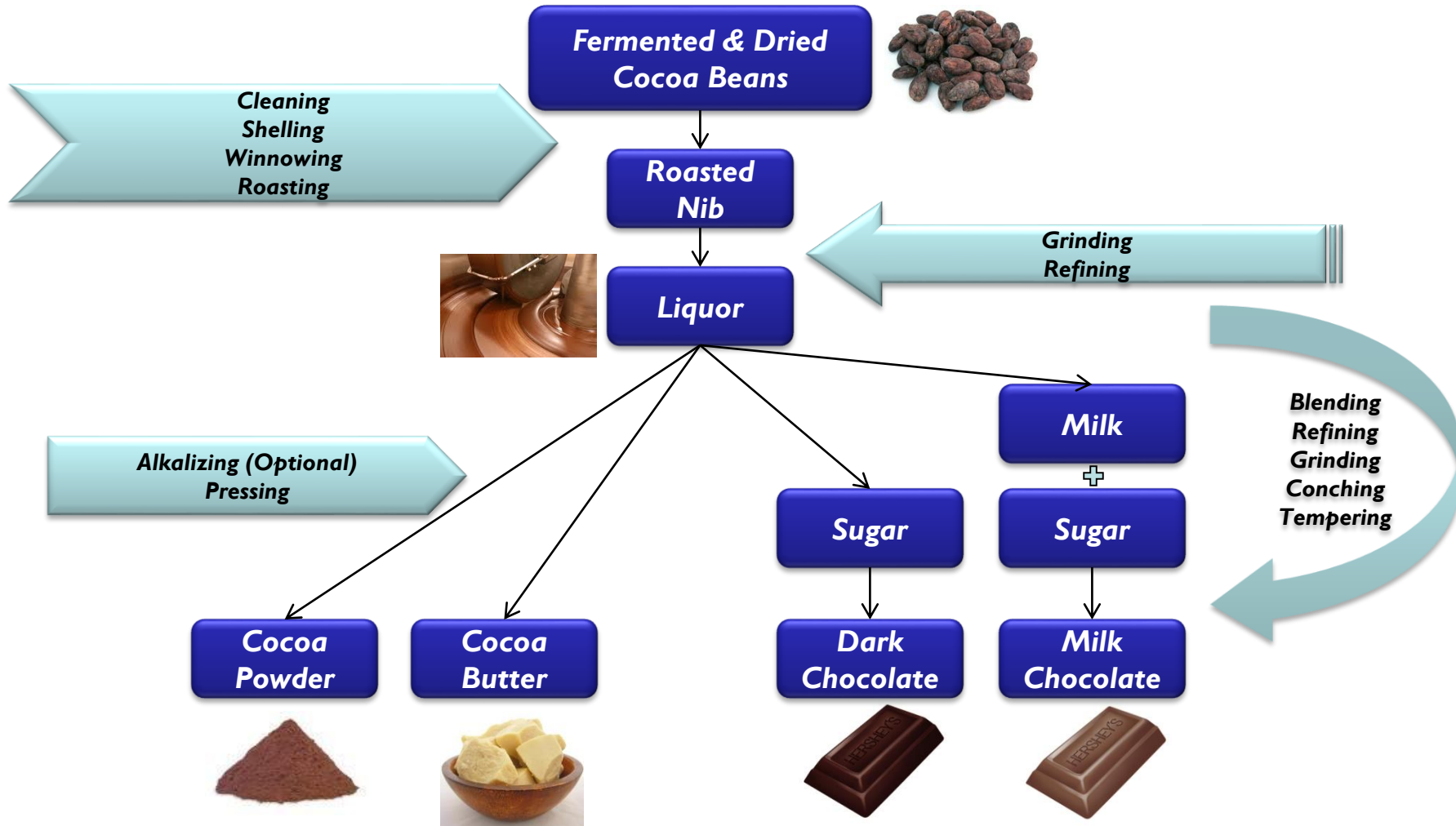
- *Duration depends on the tradition of the growing region*
- *Fermentation begins the development of 'chocolate' flavor*

*Cocoa beans are then dried in the sun*



- *Some cultures dry over fires*
- *Freshly fermented beans contain 40% moisture and are dried to 8%*

# From Cocoa Beans to Chocolate



# Ancient Medicinal Uses of Cocoa

Dillinger et al. J Nutr 2000.

- >150 medicinal uses of cacao
- Cardiovascular Disease (CVD) Related uses:
  - “faint of heart”
  - Angina (reduces)
  - Blood (generates/produces)
  - Heart palpitations (relieves)
  - Heart (strengthens/vivifies)
  - Longevity (prolongs)



# What nutritional compounds are in the cocoa bean?

by weight...

52% Cocoa Butter

34% Oleic Acid  
33% Stearic Acid  
27% Palmitic Acid  
6% Other

21% Carbohydrates

~1% Sugar, 20% Fiber

17% Protein

Arginine, Glutamine, Leucine

10% Polyphenols

2% Proanthocyanins

Minerals

Fe, Mg, P, K, Cu





# Partial List of Compounds in Cacao

711 identified

- Acetic-acid, aesculetin, alanine, alkaloids, alpha-sitosterol, alpha-theosterol, amyl-acetate, amyl-alcohol, amyl-butyrate, amylase, apigenin-7-o-glucoside, arabinose, arachidic-acid, arginine, ascorbic-acid, ascorbic-acid-oxidase, aspariginase, beta-carotene, beta-sitosterol, beta-theosterol, biotin, caffeic-acid, caffeine, calcium, campesterol, catalase, catechins, catechol, cellulase, cellulose, chlorogenic-acid, chrysoeriol-7-o-glucoside, citric-acid, coumarin, cyanidin, cyanidin-3-beta-l-arabinoside, cyanidin-3-galactoside, cyanidin-glycoside, cycloartanol, d-galactose, decarboxylase, dextrinase, diacetyl, dopamine, epigallocatechin, ergosterol, ferulic-acid, formic-acid, fructose, furfural, galacturonic-acid, galocatechin, gentisic-acid, glucose, glutamic-acid, glycerin, glycerophosphatase, glycine, glycolic-acid, glycosidase, haematin, histidine, i-butyric-acid, idaein, invertase,

## Resveratrol Found in Chocolate

09/09/08-

The ingredient that is thought to provide many of the health benefits of red wine and red grapes has now been identified in chocolate and chocolate products as well. Recent reports have noted small amount of reveratrol in peanuts and peanut skins, however chocolate products are seemingly more concentrated than not, but do not contain as

acetate, isovitexin, kaempferol, l-epicatechin, ic-acid, lipase, luteolin, luteolin-7-o-glucoside, lysine, mannan, manninotriose, mannose, melibiose, ylacetate, n-nonacosane, niacin, nicotinamide, l, o-hydroxyphenylacetic-acid, octoic-acid, oleic-rin, oxalic-acid, p-anisic-acid, p-coumaric-acid, p-c-acid, p-hydroxyphenylacetic-acid, palmitic-acid, n, pentose, peroxidase, phenylacetic-acid, tidyl-choline, phosphatidyl- ethanolamine, phosphorus, phytase, planteose, polygalacturonate, ine, propionic-acid, propyl-acetate, protocatechuic-

acid, punine, p, quercetin, quercetin-3-o-galactoside, quercetin-3-o-glucoside, quercitrin, raffinase, raffinose, reductase, rhamnose, riboflavin, rutin, rutoside, saccharose, salsolinol, serine, sinapic-acid, stachyose, stearic-acid, stearodiolin, stigmasterol, sucrose, syringic-acid, tannins, tartaric-acid, theobromine, theophylline, thiamin, threonine, trigonelline, tyramine, tyrosine, valerianic-acid, valine, vanillic-acid, verbascose, verbascotetrose, vitexin



# Active compounds occur within natural foods

## Fish Oil Model

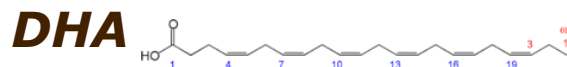
**Salmon**



**Crude Fish Oils**



**Distilled Fish Oils**



## Cocoa Model



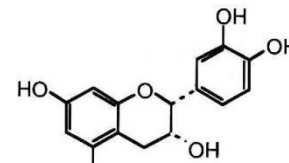
**Chocolate**



**Cocoa Powder**



**Cocoa Extracts**



**Flavanols**



# Antioxidant or Flavanol?



# Polyphenols

## Flavonoids

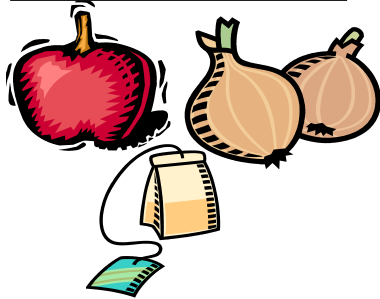
### Anthocyanin



### Flavanone



### Flavonol



### Flavanol



### Isoflavone



### Flavone



## Antioxidants





Why would natural cocoa  
have benefits to health?



# Ancient Uses of Cocoa: A Modern Example

Hollenberg et al. J Food Comp Anal, 2001.

## ■ KUNA Amerinds:

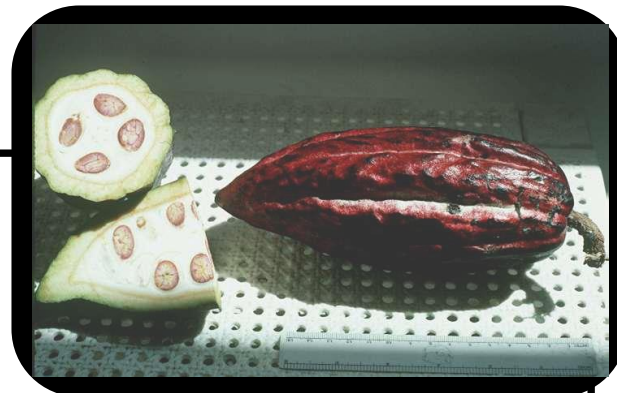
- Indigenous population off the coast of Panama
- Traditional high salt diet
- Showed no rise in blood pressure with age
- Immigrants did develop hypertension

**Island dwelling Kuna's consume an average of 5 cups of cocoa per day**



# Cocoa Seeds are a “Super Fruit”

Crozier, SJ., et. al., *Chemistry Central Journal*, 2011.



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Research article

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Abstract

## Cacao seeds are a "Super Fruit": A comparative analysis of various fruit powders and products

Background

Results and Discussion

**Stephen J Crozier** ✉, **Amy G Preston** ✉, **Jeffrey W Hurst** ✉, **Mark J Payne** ✉, **Julie Mann** ✉, **Larry Hainly** ✉ and **Debra L Miller** ✉

The Hershey Center for Health & Nutrition, 1025 Reese Avenue, Hershey, PA, 17033, USA

Conclusions

✉ author email   ✉ corresponding author email

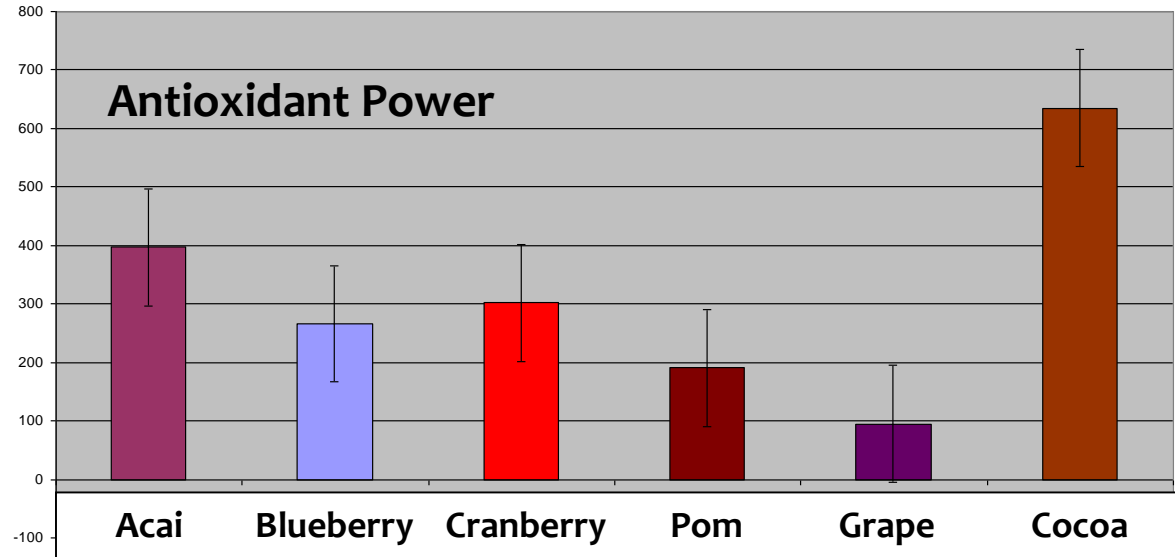
Methods

*Chemistry Central Journal* 2011, **5**:5   doi:10.1186/1752-153X-5-5

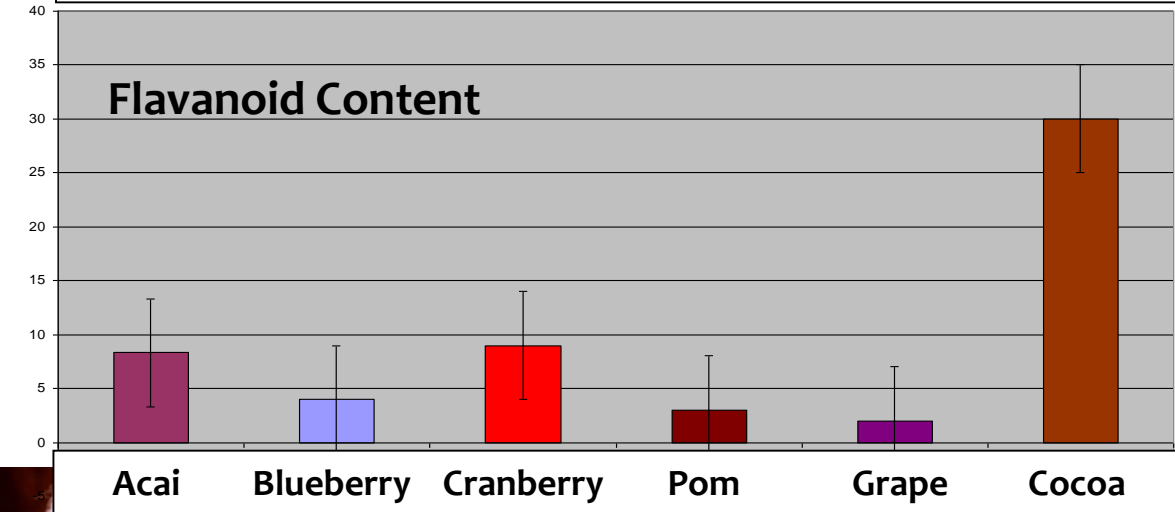


# Cocoa Compared to “Super Fruit” Powders

ORAC $\mu$ MTE/g

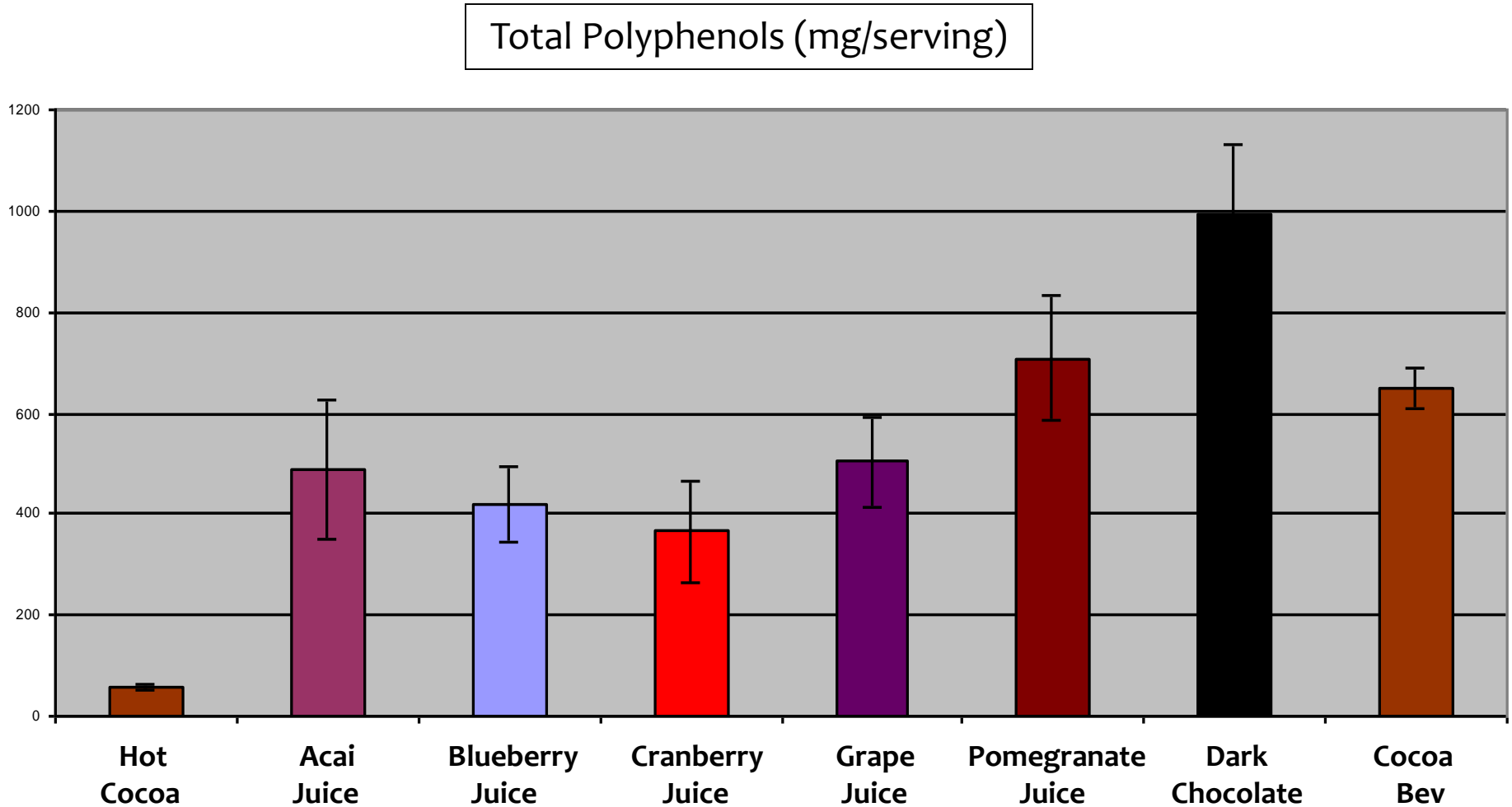


Flavanoids mg/g



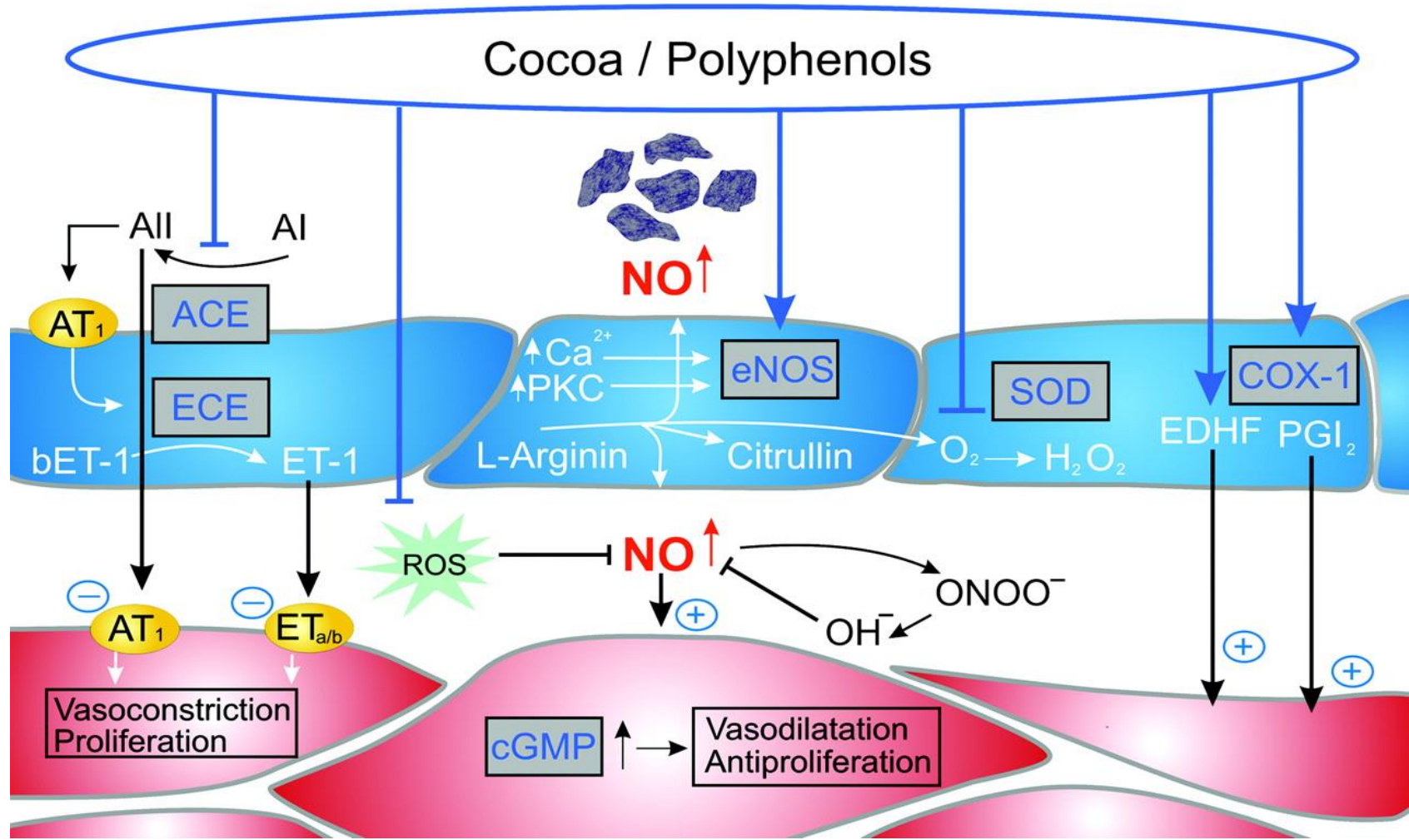


# What about foods that people buy?

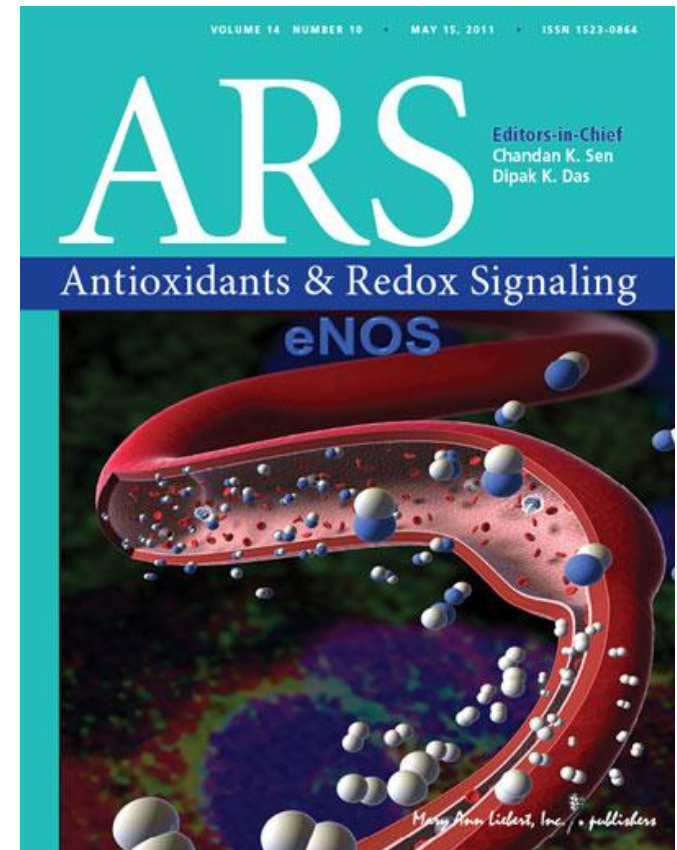
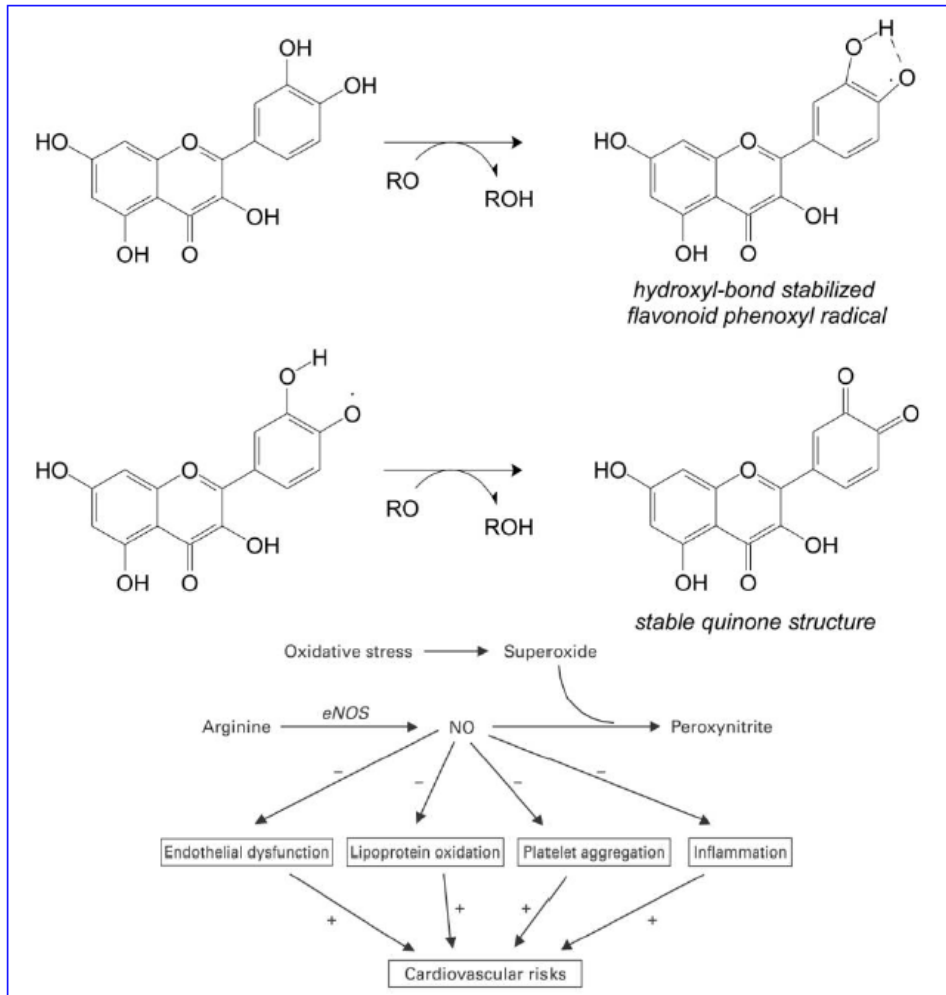


# Mechanisms of Action

Corti R et al. Circulation 2009;119:1433-1441



# 2011 Yale University Review



A scientific consensus  
is building

Has it arrived?





# Cocoa & Chocolate Cardiovascular SCIENCE is MOUNTING

## Low vs. Higher-Dose Dark Chocolate and Blood Pressure in Cardiovascular High-Risk Patients

Steffen Desch<sup>1</sup>, Daniela Kobler<sup>1</sup>, Johanna Schmidt<sup>1</sup>, Melanie Sonnabend<sup>1</sup>, Volker Adams<sup>1</sup>, Mahdi Sareban<sup>1</sup>, Ingo Eitel<sup>1</sup>, Matthias Blüher<sup>2</sup>, Gerhard Schuler<sup>1</sup> and Holger Thiele<sup>1</sup>

### BACKGROUND

Dark chocolate may have blood pressure-lowering properties. We conducted a prospective randomized open-label blinded end-point design trial to study a potential dose dependency of the presumed antihypertensive effect of dark chocolate by directly comparing low vs. higher doses of dark chocolate over the course of 3 months.

(6 g/day –2.3 mm Hg, 95% confidence interval –4.1 to –0.4, 25 g/day –1.9 mm Hg, 95% confidence interval –3.6 to –0.2). There were no significant differences in blood pressure changes between groups. In the higher-dose group, a slight increase in body weight (0.8 kg, 95% confidence interval 0.3 to 1.3 kg) was observed.

### METHODS

We enrolled a total of 102 patients with prehypertension/stage 1 hypertension and established cardiovascular end-organ damage or diabetes mellitus. Patients were randomly assigned to receive either 6 or 25 g/day of flavanol-rich dark chocolate for 3 months. The difference in 4-h mean blood pressure between groups was defined as the primary outcome measure.

### CONCLUSIONS

The findings are consistent with the hypothesis that the beneficial effects of dark chocolate are due to the lack of a dose effect. The results should be interpreted with caution. Keywords: blood pressure, hypertension

Am J Hypertens 2010;23:1029-1034

## Hypertension

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association  
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### Agings, Acculturation, Salt Intake, and Hypertension in the K...

Gregorio Martinez, Mary M. Coogan, Frank Preston, Alicia Rivera, David Taplin and Alicia Clement  
Hypertension 1997;29:171-176  
© 1997 American Heart Association, 7272 Greenville Avenue, Dallas, TX 75223  
DOI: 10.1161/01.HYP.0000011711.17117.17  
All rights reserved. Print ISSN: 0893-9700. Online ISSN: 1531-0199

This article, along with updated information located on the World Wide Web at <http://ahajournals.org/cgi/content/full/29/1/17>

## JAMA

Online article and related content current as of April 6, 2009.

### Chocolate and Blood Pressure in Elderly Individuals With Isolated Systolic Hypertension

Dirk Taubert, Reinhard Berkeles, Renate Roessen, et al.  
JAMA. 2003;290(8):1029-1030 (doi:10.1001/jama.290.8.1029)  
<http://jama.ama-assn.org/cgi/content/full/290/8/1029>

If this article is corrected,

has been cited 65 times,

when this article is cited.

Articles, Nutritional and Metabolic Disorders, Nutrition/ Malnutrition: Open new articles are published in these topic areas.

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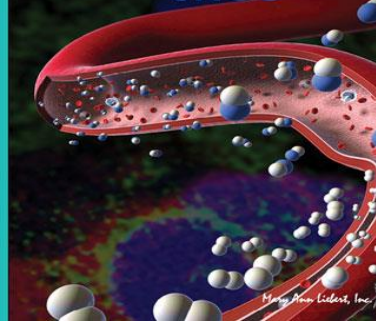
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10.1161

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Antioxidants & Redox Signal  
eNOS



Editors-in-Chief  
Chandan K. Sen  
Dipak K. Das

## BMJ

BMJ 2011;342:e9448. doi:10.1136/bmj.e9448

Page 1 of 8

### RESEARCH

## Chocolate consumption and cardiometabolic disorders: systematic review and meta-analysis

OPEN ACCESS

Adriana Butrago-Lopez visiting research assistant<sup>1,2,3,4</sup>, Jean Sanderson research associate<sup>1,2,3,4</sup>, Laura Johnson research associate<sup>1,2,3,4</sup>, Samantha Wamukula PhD student<sup>1,2,3,4</sup>, Angela Wood university lecturer in biostatistics<sup>1,2,3,4</sup>, Emanuele Di Angelantonio university lecturer in medical screening<sup>1,2,3,4</sup>, Oscar H Franco clinical lecturer in public health<sup>1,2,3,4</sup>

<sup>1</sup>Department of Public Health and Primary Care, <sup>2</sup>Cardiovascular Epidemiology Unit, University of Cambridge, <sup>3</sup>Strangeways Research Laboratory, Cambridge CB2 1RN, UK, <sup>4</sup>Univision Universidad de Cundinamarca de Salud, Hospital de San Jose, Bogota, Colombia, <sup>5</sup>Thorax Unit, Liverpool, UK, Colombia

### Abstract

**Objective:** To evaluate the association of chocolate consumption with the risk of developing cardiometabolic disorders.

**Design:** Systematic review and meta-analysis of randomised controlled trials and observational studies.

**Data sources:** Medline, Embase, Cochrane Library, Pubmed, Citeline, CINA, Web of Science, Scopus, Proquest, reference lists of relevant studies in October 2010, and email contact with authors.

**Study selection:** Randomised trials and cohort, case-control, and cross-sectional studies carried out in human adults, in which the association between chocolate consumption and the risk of outcomes related to cardiometabolic disorders were reported.

**Data extraction:** Data were extracted by two independent investigators, and a consensus was reached with the involvement of a third. The primary outcome was cardiometabolic disorders, including cardiovascular disease (coronary heart disease and stroke), diabetes, and metabolic syndrome. A meta-analysis assessed the role of flavonoid consumption in cardiometabolic disorders by comparing the highest and lowest level of chocolate consumption.

**Results:** From 4076 reference screen studies that the inclusion criteria (including 114 000 participants), none of the studies was a randomised trial, six were cohort studies, and one a cross-sectional study. Large reduction was observed between flavonoid studies for measurement of chocolate consumption, methods, and outcomes measured. Five of the seven studies reported a beneficial association between higher levels of chocolate consumption and risk of cardiometabolic disorders. The higher levels of chocolate consumption were associated with a 37% reduction in cardiovascular disease relative risk (95% confidence interval 0.64 to 0.63) and a 20% reduction in stroke compared with the lowest levels.

Correspondence to: O H Franco [ohf23@medsch.cam.ac.uk](mailto:ohf23@medsch.cam.ac.uk)  
Extra material supplied by the author: Full text and for publication files (see <http://www.bmj.com/content/342/e9448/DC1>)  
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## Chocolate consumption in relation to blood pressure and risk of cardiovascular disease in German adults

Brian Buijsse<sup>1</sup>, Cornelia Weikert<sup>1</sup>, Dagmar Drogan<sup>1</sup>, Manuela Bergmann<sup>1</sup>, and Heiner Boeing<sup>1</sup>

<sup>1</sup>Department of Epidemiology, German Institute of Human Nutrition (DIFE), Potsdam-Nuthetal, Arthur-Scheunert-Allee 114/116, 14558 Nuthetal, Germany

Received 20 September 2008; revised 10 January 2009; accepted 3 October 2009

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## Circulation

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**Cocoa and Cardiovascular Health**  
Roberto Corti, Andreas J. Flammer, Norman K. Hollenberg and Thomas F. Lüscher  
Circulation 2009;119:1433-1441  
DOI: 10.1161/CIRCULATIONAHA.108.827022  
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75223  
Copyright © 2009 American Heart Association. All rights reserved. Print ISSN: 0009-7332. Online ISSN: 1524-4539

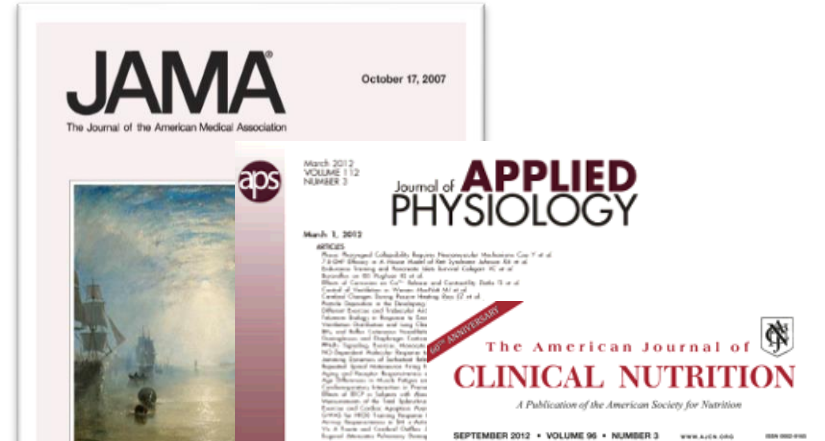
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# Cocoa Flavanols are Associated with Cardiovascular Protection

- Results of a research study published in the *Journal of American Medicine* in 2007 showed that eating a small piece of dark chocolate every day significantly reduced blood pressure after 12 and 18 weeks.
- Enjoying **one to two tablespoons of natural cocoa** a day as an ingredient in beverages, meals or snacks or **20 grams of dark chocolate** may support cardiovascular health (2, 3)



**More than 250 studies have investigated the cardiovascular benefits of natural cocoa and dark chocolate, including beneficial effects for those at risk for cardiovascular disease, high blood pressure, high cholesterol and coronary heart disease.**



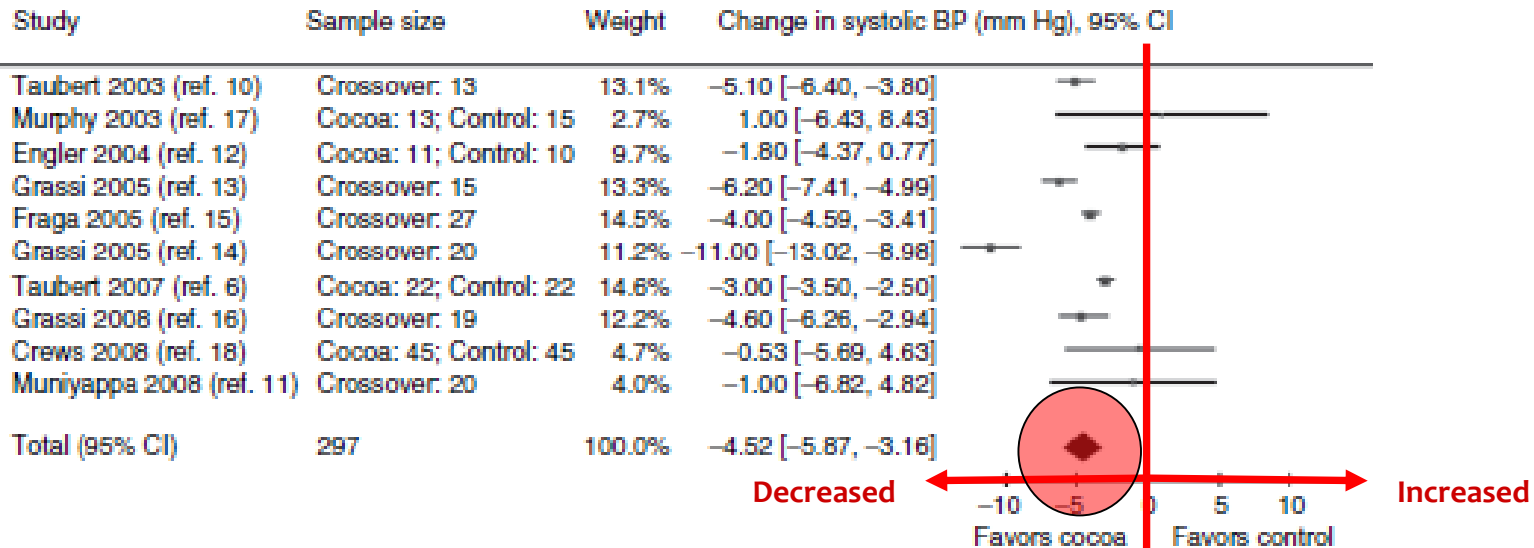
- (1) Taubert, et al. JAMA 2007
- (2) Monahan, et al. J Appl Physiol 2011
- (3) Desch S, et al. Am J Hypertens 2010



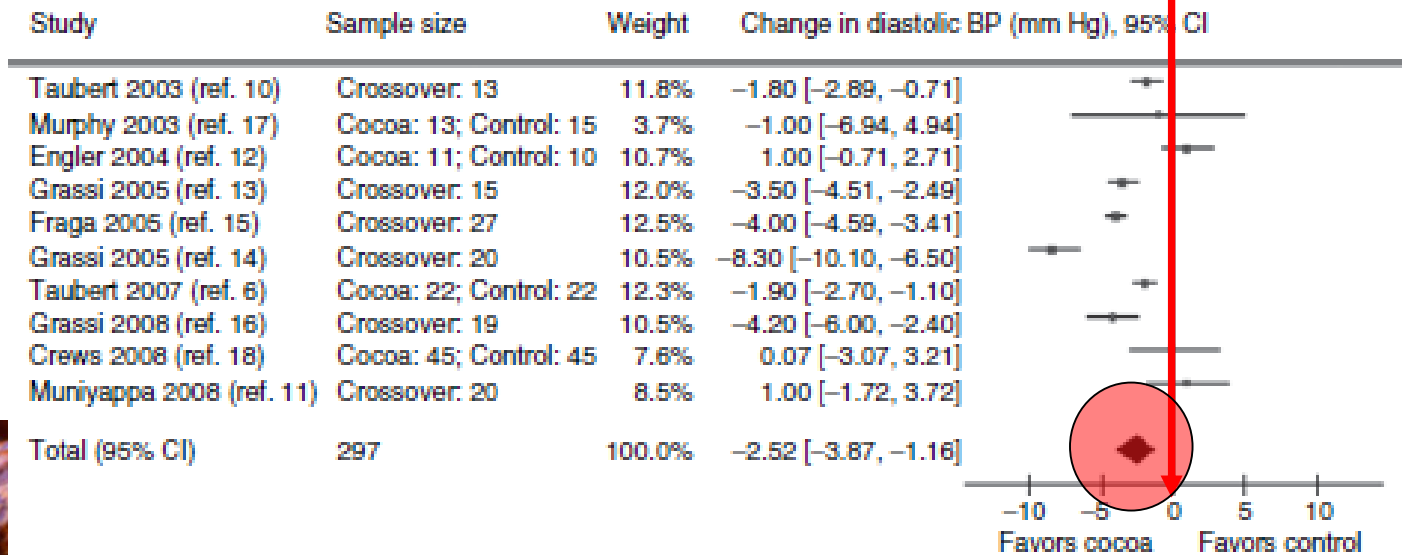
# Meta-Analysis Indicates Cocoa & Dark Chocolate Reduce Blood Pressure

Desch et al. Am J Hypertens 2010

Systolic  
Blood  
Pressure

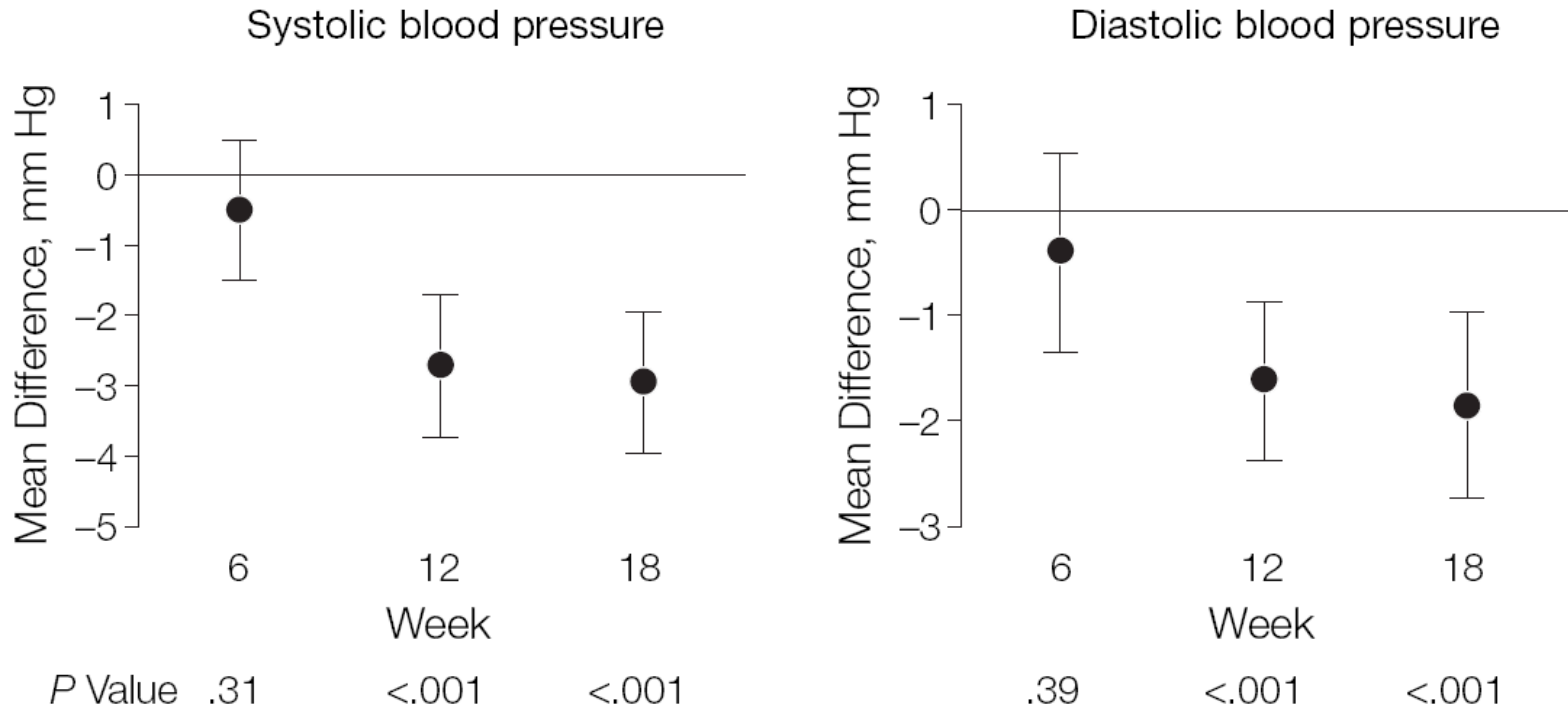


Diastolic  
Blood  
Pressure



# Consuming just 6.3 grams of dark chocolate a day significantly reduced blood pressure after 12 and 18 weeks, compared to white chocolate

*Taubert D et al. JAMA. 2007 Jul 4;298(1):49-60.*



**6.3 g dark chocolate per day = 30 calories**





# Meta-Analysis Indicates Cocoa & Dark Chocolate Reduce Blood Cholesterol

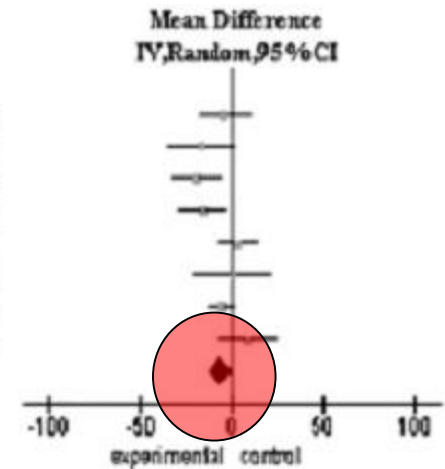
Jia et al. Am J Clin Nutr 2010

Total Cholesterol



Study	Year	N	Experimental Changes in TC		N	Control Changes in TC	
			Mean(mg/dL)	SD		Mean(mg/dL)	SD
Beba(12)	2007	13	-7.33	13.92	12	-3.86	20.06
Balzer(19)	2008	21	-6.30	27.83	20	9.80	31.67
Fraga(17)	2005	27	-18.00	33.13	27	1.00	12.88
Grassi(11)	2005	20	-15.44	21.57	20	0.00	19.65
Grassi(18)	2005	15	3.86	17.81	15	0.00	13.10
Muniyappa(20)	2008	20	-12.00	34.15	20	-13.00	34.15
Taubert(15)	2007	22	-2.70	10.79	22	2.60	14.07
Wan(14)	2001	23	5.79	28.45	23	-3.47	28.45
<b>Total (95% CI)</b>		<b>161</b>			<b>159</b>		

Heterogeneity: Tau<sup>2</sup> = 41.55; Chi<sup>2</sup> = 13.74, df = 7 (P = 0.06); I<sup>2</sup> = 49%  
 Test for overall effect: Z = 1.73 (P = 0.08)

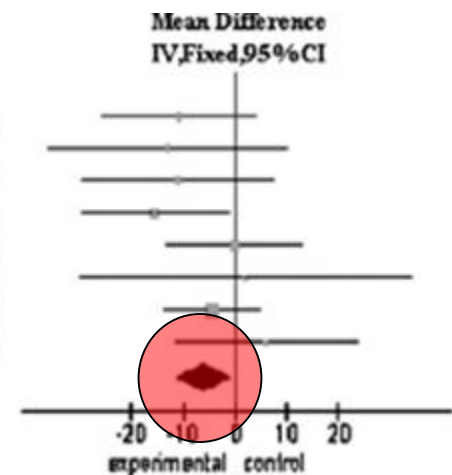


LDL Cholesterol



Study	Year	N	Experimental Changes in LDL		N	Control Changes in LDL	
			Mean(mg/dL)	SD		Mean(mg/dL)	SD
Beba(12)	2007	13	-16.98	19.48	12	-6.18	18.72
Balzer(19)	2008	21	-8.50	33.44	20	4.40	41.01
Fraga(17)	2005	27	-16.00	33.54	27	-5.00	35.43
Grassi(11)	2005	20	-15.44	24.04	20	0.00	21.66
Grassi(18)	2005	15	0.00	19.76	15	0.00	17.33
Muniyappa(20)	2008	20	-9.00	52.84	20	-11.00	50.74
Taubert(15)	2007	22	-2.30	9.38	22	2.00	19.70
Wan(14)	2001	23	8.49	35.92	23	2.32	24.33
<b>Total (95% CI)</b>		<b>161</b>			<b>159</b>		

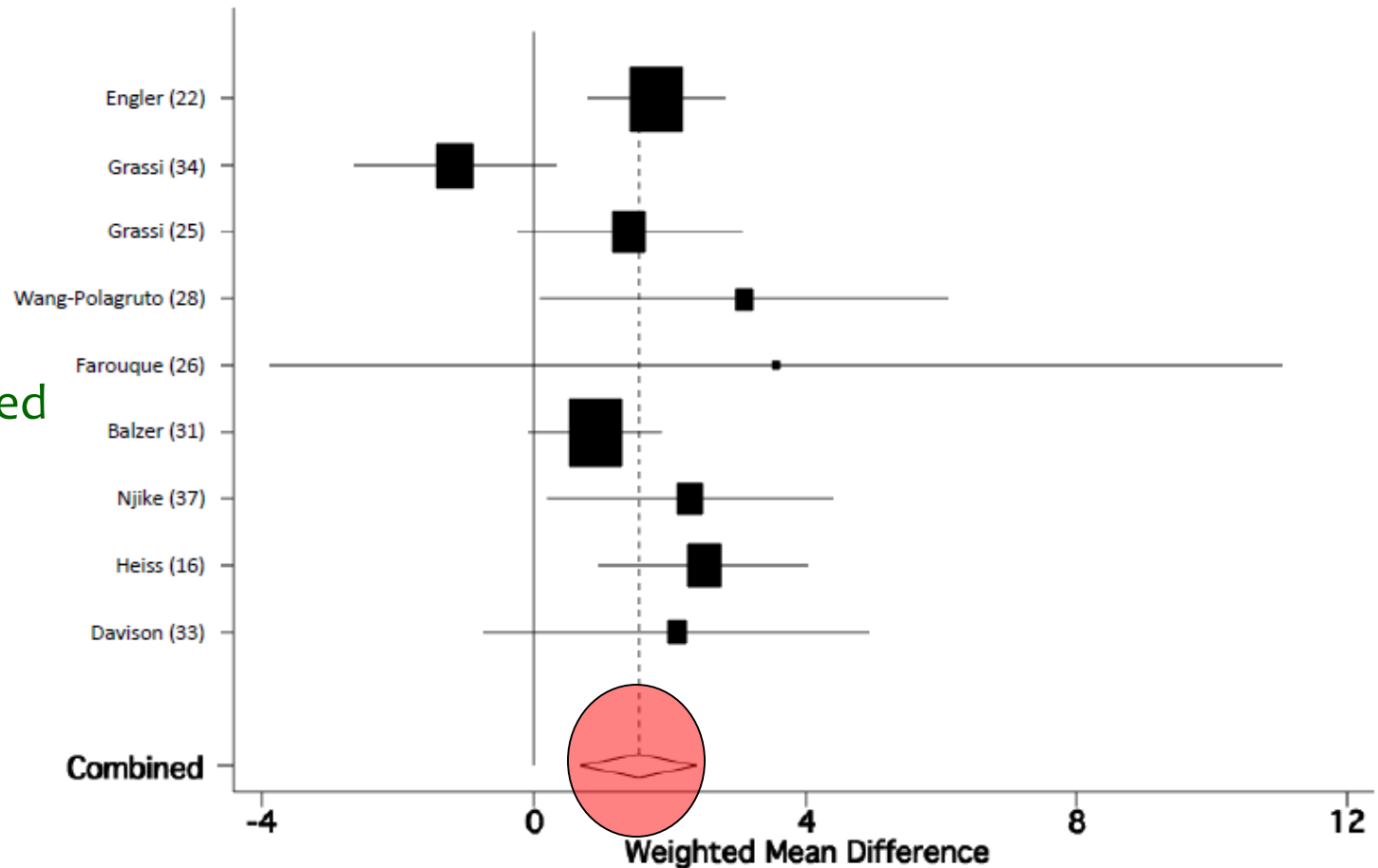
Heterogeneity: Chi<sup>2</sup> = 5.69, df = 7 (P = 0.58); I<sup>2</sup> = 0%  
 Test for overall effect: Z = 2.19 (P = 0.03)



# Meta-Analysis Indicates Cocoa & Dark Chocolate Improve Endothelial Function

Shrime. *J Nutr* 2012

Flow Mediated  
Dilation



Supplemental Figure 12: Forest plot for the effect of consumption of FRC on flow-mediated vascular dilation. Weighted mean differences are reported. The weight of each study is represented by the size of the box; variance is represented by the length of the horizontal line.



# Inflammatory Markers

Effect of cocoa powder on the modulation of inflammatory biomarkers in patients at high risk of cardiovascular disease<sup>1-4</sup>

*Maria Monagas, Nasiruddin Khan, Cristina Andres-Lacueva, Rosa Casas, Mireia Urpi-Sardà, Rafael Llorach, Rosa Maria Lamuela-Raventós, and Ramón Estruch*

AJCN. First published ahead of print September 23, 2009

**Objective:** To evaluate the effects of chronic cocoa consumption on cellular and serum biomarkers related to atherosclerosis in high-risk patients.

## Results:


- No significant changes in expression of adhesion molecules on T lymphocyte surfaces
- Monocytes: VLA-4, CD40 and CD36 were lowered with cocoa treatment ( $p < 0.005$ )
- P-selectin and intercellular adhesion molecule-1 were lowered with cocoa treatment ( $p < 0.007$ )

**Conclusions:** These results suggest that the intake of cocoa polyphenols may modulate inflammatory mediators in patients at high risk of cardiovascular disease. These antiinflammatory effects may contribute to the overall benefits of cocoa consumption against atherosclerosis.



# 2011 Harvard University Review & Cambridge Meta-Analysis

“From an evidence-based review, there is **strong evidence** that high cocoa intake lowers blood pressure, improves vascular endothelial function (circulation/ blood flow), and potentially increases insulin sensitivity.”

**Nutrition & Metabolism**  **Open Access**

Review  
**Chocolate and Prevention of Cardiovascular Diseases: A Systematic Review**  
Eric L. Ding<sup>1,2</sup>, Susan M. Hutflless<sup>1</sup>, Xin Ding<sup>1</sup> and Saket Girotra<sup>3</sup>

Address: <sup>1</sup>Department of Epidemiology, Harvard University, School of Public Health, Boston, MA; <sup>2</sup>Center for Global Health and Development, Harvard University, School of Public Health, Boston, MA; <sup>3</sup>Department of Nutrition, Harvard University, School of Public Health, Boston, MA

Published: 03 January 2011  
Nutrition & Metabolism 2011, 8:10  
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© 2011 Ding et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Abstract**  
**Background:** Consuming cocoa flavanols, flavonoids, and polyphenols may reduce the risk of cardiovascular diseases. However, the effects of chocolate on cardiovascular disease are unclear.  
**Methods:** We reviewed the literature for observational, cohort, case-control, and randomized controlled trials that examined the effect of cocoa consumption on cardiovascular disease risk factors. The search was performed using Medline, Embase, and Cochrane databases. The search criteria for final analysis, in response to PICO, were: P, cocoa consumption; I, cardiovascular disease risk factors; C, control; O, observational study. The search was performed using Medline, Embase, and Cochrane databases. The search criteria for final analysis, in response to PICO, were: P, cocoa consumption; I, cardiovascular disease risk factors; C, control; O, observational study. The search was performed using Medline, Embase, and Cochrane databases. The search criteria for final analysis, in response to PICO, were: P, cocoa consumption; I, cardiovascular disease risk factors; C, control; O, observational study.

**Introduction**  
Cardiovascular disease (CVD), as a cause of the death in the United States

**Journal of Nutrition**. First published ahead of print September 28, 2011 as doi: 10.3945/jn.111.145482.

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**Flavonoid-Rich Cocoa Consumption Affects Multiple Cardiovascular Risk Factors in a Meta-Analysis of Short-Term Studies<sup>1</sup>**

Mark G. Sirtori,<sup>1,2,3\*</sup> Scott B. Reave,<sup>2,3,4</sup> Anna C. McDonald,<sup>2,4</sup> Nabaha H. Chowdhury,<sup>2,4</sup> Carolina E. M. Coker,<sup>2,4</sup> and Eric L. Ding<sup>1,2,4</sup>

<sup>1</sup>Harvard School of Public Health, Boston, MA; <sup>2</sup>Harvard Medical School, Boston, MA; <sup>3</sup>Harvard University, Boston, MA; <sup>4</sup>Harvard University, Boston, MA

**Abstract**  
Aggregating body of evidence suggests that the consumption of foods rich in flavonoids may reduce the risk of cardiovascular disease. However, the effects of cocoa consumption on cardiovascular disease risk factors are unclear. We performed a meta-analysis of randomized, controlled trials to evaluate the effect of cocoa consumption on cardiovascular disease risk factors. The search was performed using Medline, Embase, and Cochrane databases. The search criteria for final analysis, in response to PICO, were: P, cocoa consumption; I, cardiovascular disease risk factors; C, control; O, observational study. The search was performed using Medline, Embase, and Cochrane databases. The search criteria for final analysis, in response to PICO, were: P, cocoa consumption; I, cardiovascular disease risk factors; C, control; O, observational study.

**Introduction**  
The Kuna, an indigenous group of approximately 30,000 people who live permanently on small islands off the coast of Panama, are free of hypertension and cardiovascular disease. Kuna who migrate to nearby Panama City, however, lose this advantage, a loss that cannot be attributed to changes in salt intake (1) or stress (2). The Kuna who live on the Caribbean archipelago, however, consume a striking amount of natural cocoa drinks, whereas those who migrate to the mainland do not (3). The case of the Kuna is but one piece in a growing body of evidence that foods rich in plant-derived polyphenolic compounds may have cardioprotective effects. Three recent meta-analyses have examined these hypotheses. Tschape et al. (4) examined blood pressure in response to cocoa and tea consumption.

**Footnote:** \* Author disclosures of potential conflicts of interest and author contributions are found at the end of this article.  
Address correspondence to: Eric L. Ding, eric.ding@hsph.harvard.edu.  
© 2011 American Society for Nutrition. Manuscript received June 2, 2011; final revision accepted July 5, 2011. Review date: 10/28/11; 11/14/2011.

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**BMJ**  **RESEARCH**

0959-6910/11/343(4):486-494. doi:10.1136/bmj.2011.248486

**Chocolate consumption and cardiometabolic disorders: systematic review and meta-analysis**

**OPEN ACCESS**

Adriana Butrago-Lopez visiting research assistant<sup>1,2</sup>, Jian Sanderson research associate<sup>1</sup>, Laura Johnson research associate<sup>1</sup>, Samantha Wamukulu PhD student<sup>1</sup>, Angela Wood university lecturer in biostatistics<sup>1</sup>, Emanuele Di Angelantonio university lecturer in medical screening<sup>1</sup>, Oscar H Franco clinical lecturer in public health<sup>1</sup>

<sup>1</sup>Department of Public Health and Primary Care, Cardiovascular Epidemiology Unit, University of Cambridge, Strangeways Research Laboratory, Cambridge CB2 1RL, UK; <sup>2</sup>Universidad Veracruzana de Ciencias de la Salud, Hospital de San José, Soquim, Veracruz, Veracruz, Universidad Veracruzana, Jaramena, Soquim, Veracruz

**Abstract**  
**Objective:** To evaluate the association of chocolate consumption with the risk of developing cardiometabolic disorders.  
**Design:** Systematic review and meta-analysis of randomised controlled trials and observational studies.  
**Data sources:** Medline, Embase, Cochrane Library, PubMed, CINAHL, APA, Web of Science, Scopus, Proquest, reference lists of relevant studies (to October 2010), and email contact with authors.  
**Study selection:** Randomised trials and cohort, case-control, and cross-sectional studies carried out in human adults, in which the association between chocolate consumption and the risk of developing cardiometabolic disorders had been reported.  
**Data extraction:** Data were extracted by two independent investigators, and a consensus was reached with the resolution of a third. The primary outcome was cardiometabolic disorders, including cardiovascular disease, coronary heart disease and stroke, diabetes, and metabolic syndrome. A meta-analysis assessed the risk of developing cardiometabolic disorders by comparing the highest and lowest level of chocolate consumption.  
**Results:** From 4278 abstracts seven studies met the inclusion criteria (including 114 088 participants). None of the studies was a randomised trial, six were cohort studies, and one a cross-sectional study. Large majority were observational. These seven studies had measurement of chocolate consumption, methods, and outcomes evaluated. Five of the seven studies reported a beneficial association between higher levels of chocolate consumption and the risk of cardiometabolic disorders. The highest levels of chocolate consumption were associated with a 37% reduction in cardiometabolic disorders (risk ratio 0.63 (95% confidence interval 0.44 to 0.96) and a 20% reduction in stroke compared with the lowest levels.

**Conclusions:** Based on observational evidence, levels of chocolate consumption seem to be associated with a substantial reduction in the risk of cardiometabolic disorders. Further experimental studies are required to confirm a potentially beneficial effect of chocolate consumption.

**Introduction**  
According to the World Health Organization, by 2030 nearly 2.6 billion people will die from cardiovascular disorders.<sup>1</sup> Furthermore, about a fifth of the world's adult population are thought to have metabolic syndrome, a cluster of factors associated with an increased risk of type 2 diabetes and cardiovascular diseases.<sup>2</sup> This increase in cardiometabolic disorders evokes a great burden on people, health-care organisations, and society in general. However, cardiometabolic disorders are largely preventable, and a better understanding of the factors associated to their development and implementation of interventions to modify these factors will be critical to tackling the current epidemic.

One of the key lifestyle factors involved in the genesis, prevention, and control of cardiometabolic disorders is cocoa products containing flavanols have been shown to have an atheroprotective effect in hypercholesterolaemic subjects.<sup>3</sup> Several studies, both experimental and observational, have suggested that chocolate consumption has a positive influence on human health, with antioxidant, anti-inflammatory, anti-inflammatory, anti-atherogenic, and anti-oxidative effects as well as influence on endothelial function, vascular arterial function, and activation of stress, insulin.<sup>4</sup> These beneficial effects have been observed in recent reviews and meta-analyses, supporting the positive role of cocoa and cocoa

Correspondence to: O H Franco o.hfranco@hsph.harvard.edu  
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# 2013: Building & Gaining Credentials

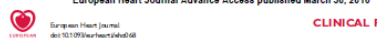
## Low vs. Higher-Dose Dark Chocolate and Blood Pressure in Cardiovascular High-Risk Patients

Steffen Desch<sup>1</sup>, Daniela Kobler<sup>1</sup>, Johanna Schmidt<sup>1</sup>, Melanie Sonnabend<sup>1</sup>, Volker Adams<sup>1</sup>, Mahdi Sareban<sup>1</sup>, Ingo Eitel<sup>1</sup>, Matthias Blüher<sup>2</sup>, Gerhard Schuler<sup>1</sup> and Holger Thiele<sup>1</sup>

European Heart Journal Advance Access published March 30, 2010

**BACKGROUND**  
Dark chocolate may be beneficial in cardiovascular disease. We conducted a prospective, randomized, controlled trial to study the effect of low vs. higher dose of dark chocolate on blood pressure in cardiovascular high-risk patients.

**METHODS**  
We enrolled a total of 100 patients with hypertension and/or diabetes mellitus. The primary outcome was the difference in 24-h ambulatory blood pressure between the two groups.



### Chocolate consumption in relation to blood pressure and risk of cardiovascular disease in German adults

Brian Buijsse<sup>\*</sup>, Cornelia Weikert, Dagmar Drogan, Manuela Bergmann, and Heiner Boeing

Department of Epidemiology, German Institute of Human Nutrition (DIfH) Potsdam-Nutrition, Arthur-Scheunert-Allee 114/116, 14558 Nuthetal, Germany  
Received 25 September 2009; revised 25 January 2010; accepted 7 February 2010

**Aims** To investigate the association of chocolate consumption with measured blood pressure (BP) and cardiovascular disease (CVD).

**Methods and results** Dietary intake, including chocolate, and BP were assessed at baseline (1994–98) in 19 357 participants from the European Prospective Investigation into Cancer and Nutrition. Incident cases of MI ( $n = 134$ ) were identified after a mean follow-up of 8 years. Mean systolic BP was 120 mmHg (95% CI: 116 to 124) and mean diastolic BP 73 mmHg (95% CI: 71 to 75) in the bottom quartile compared with the top quartile of chocolate consumption. The relative risk (RR) of MI and stroke for top vs. bottom quartile was 1.01 (95% CI: 0.64–1.60) and 1.00 (95% CI: 0.58–1.73), respectively. The inverse association was stronger for MI than for stroke. Further research is needed, in particular randomized trials.

**Conclusion** Chocolate consumption appears to lower CVD risk, in part through reducing BP. The inverse association was stronger for MI than for stroke. Further research is needed, in particular randomized trials.

**Keywords** Chocolate • Cocoa • Blood pressure • Myocardial infarction • Stroke • Epidemiology

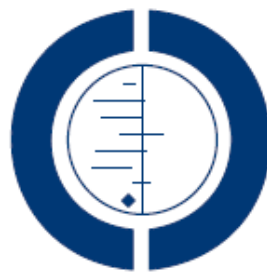
#### Introduction

Research on the health effects of cocoa and chocolate has accelerated during the last decade, in particular on cardiovascular health.<sup>1–4</sup> Although chocolate is considered typically as a food people should indulge in only occasionally, several short-term experimental studies suggest that chocolate, already in amounts of several grams per day, improves endothelial<sup>5,6</sup> and platelet function,<sup>6,7</sup> and reduces blood pressure (BP)<sup>8</sup> and markers of inflammation.<sup>9</sup> Research in cocoa and chocolate is thought to be responsible for these effects.<sup>10</sup> Despite this body of experimental evidence, observational studies on cocoa and the occurrence of cardiovascular disease (CVD) have only sparsely been published. Two European cohort studies have suggested an inverse relation between the consumption of cocoa or chocolate and CVD<sup>11,12</sup> whereas two studies in the USA showed absent<sup>13</sup> or statistically weaker relations<sup>14</sup> between chocolate consumption and CVD.

\*Corresponding author. Tel: +49 33068721; Fax: +49 33068721; Email: b.buijsse@dife.de  
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## Effect of cocoa on blood pressure (Review)

Ried K, Sullivan TR, Falder P, Frank OR, Stocks NP



THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2012, Issue 8

<http://www.thecochranelibrary.com>



Effect of cocoa on blood pressure (Review)  
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123-0864



### Chocolate and Blood Pressure in Elderly Individuals With Isolated Systolic Hypertension

Dirk Taubert, Reinhard Berkeles, Renate Roosen, et al.  
JAMA. 2003;290(6):1029-1030 (doi:10.1001/jama.290.6.1029)  
<http://jama.ama-assn.org/content/full/290/6/1029>

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**Cocoa and Cardiovascular Health**  
Cori, Andreas J; Flammer, Norman K; Hollenberg and Thomas F. Lüscher  
Circulation. 2009;119:1433-1441  
DOI: 10.1161/CIRCULATIONAHA.108.827022  
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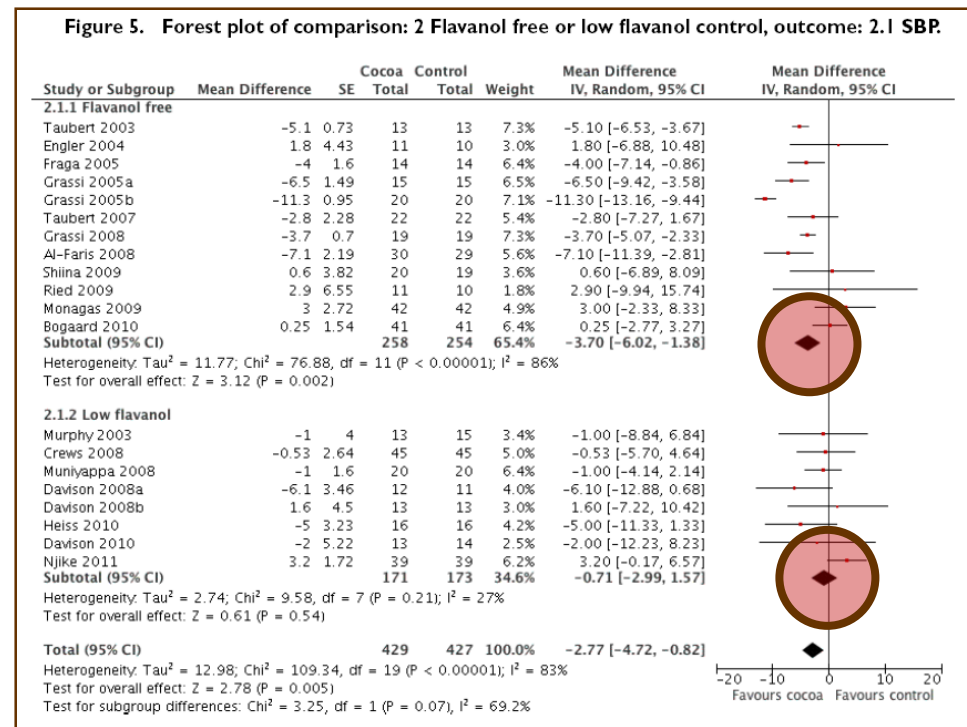
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# Cochrane Review: Effects of Cocoa on Blood Pressure

- A recent Cochrane Review assessed 20 human studies that looked at the effects of cocoa on blood pressure.
- The blood pressure lowering effect of cocoa has been attributed to the flavanol content of cocoa (1) and in all of the assessed studies, subjects consumed products of known flavanol content daily for 2-18 weeks.
- “Flavanol-rich chocolate and cocoa products may have a small but statistically significant effect in lowering blood pressure by 2-3 mm Hg in the short term.”(2)



(1) *Circulation*. 2009;119:1433-41. **Cocoa and cardiovascular health.** Corti R, Flamme AJ, Hollenberg NK, Lusher TF.  
 (2) *Cochrane Database Syst Rev*. 2012 Aug; 8: CD008393. **Effects of cocoa on blood pressure.** Ried K, Sullivan TR, Fakler P, Frank OR, Stocks NP.

# Epidemiological Evidence: Death

## ■ Individuals consuming chocolate may have reduced risk of morbidity & mortality



- Zutphen study (Netherlands) reported elderly men who consumed the highest tertile of cocoa-containing products had lower SBP and DBP and a 50% reduced risk of CVD death and a 47% reduced risk of all-cause mortality.
- Median cocoa intake was 2.11g/day

» Buijsse B et al. Arch Intern Med, 2006



# Incorporating Natural Cocoa into a Balanced Lifestyle

Incorporating moderate amounts of natural cocoa and dark chocolate as part of a healthy, balanced diet can provide cardiovascular health benefits. (1)



Report of the  
Dietary Guidelines  
Advisory Committee  
on the  
Dietary Guidelines for  
Americans, 2010

(1) Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans, 2010

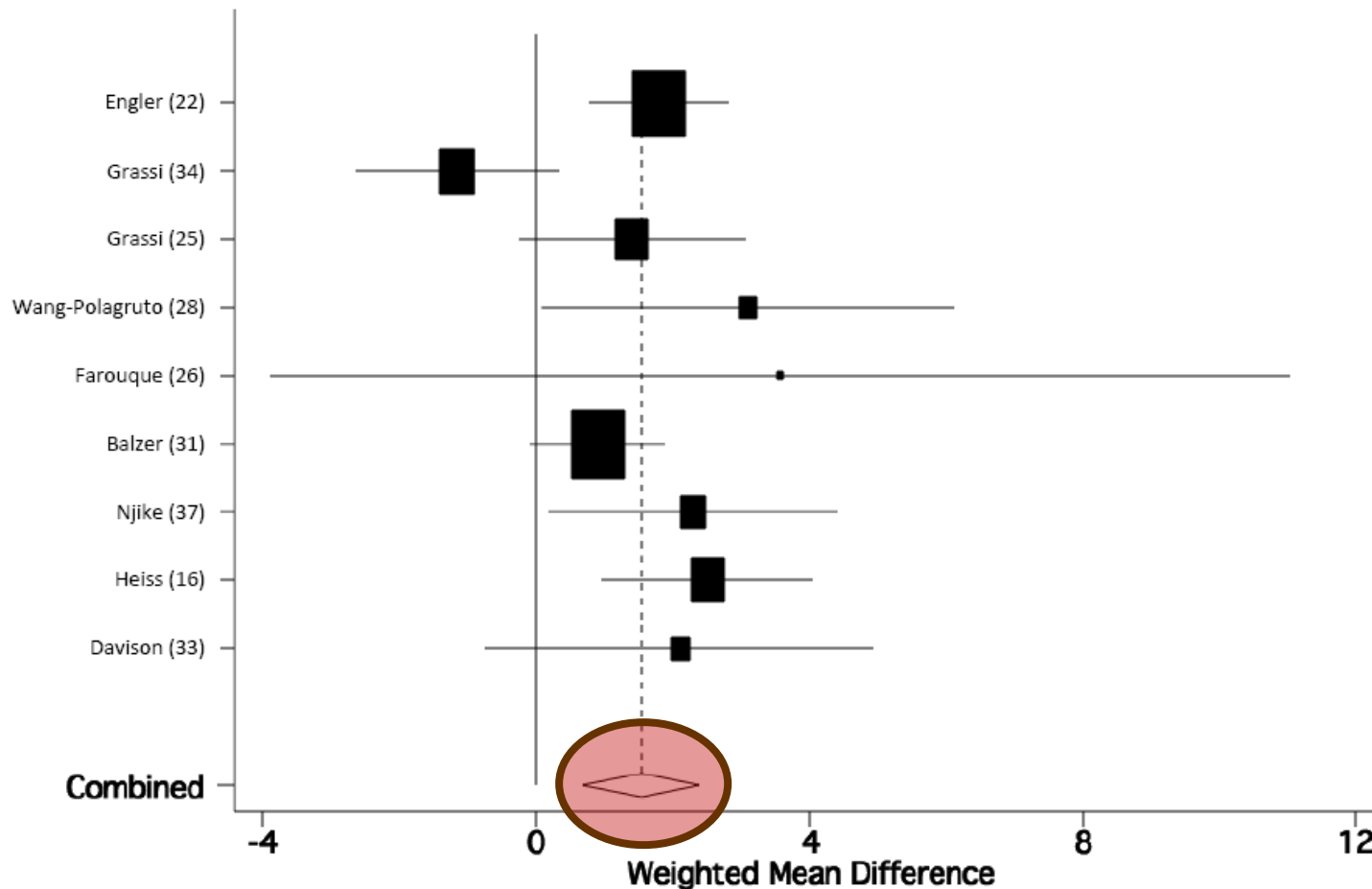




# 2011: First meta-analysis on cocoa to include flow-mediated dilation

## ■ Flavonoid-Rich Cocoa Consumption Affects Multiple Cardiovascular Risk Factors in a Meta-Analysis of Short-Term Studies

-Shrime et al., *J Nutr.* 2011;141(11):1982-8.



# EFSA Claim:

## Cocoa Flavanols & Endothelial Function

- EFSA – European Food Safety Authority
- Barry Callebaut = SUBMITTER
- Approved via EFSA process 2012

*Cocoa flavanols help maintain endothelium-dependent vasodilation which contributes to normal blood flow*

*In order to obtain the claimed effect, 200 mg of cocoa flavanols should be consumed daily*

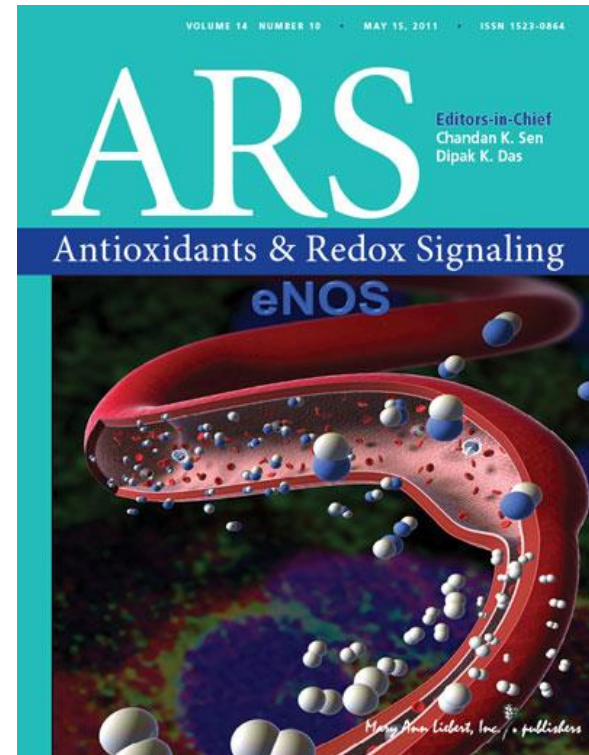


# Emerging Research



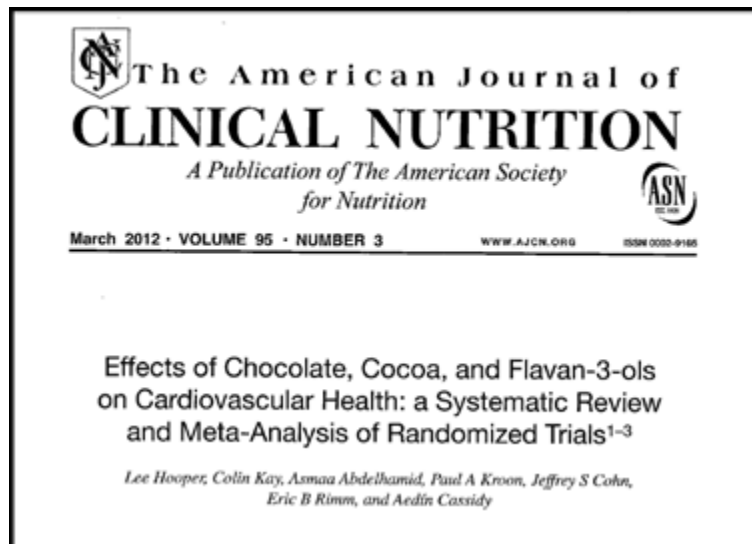
# Insulin Sensitivity

- ✓ There are plausible mechanisms for the antioxidant effects of cocoa polyphenols to influence insulin resistance
- ✓ Cocoa...
  - ❑ may induce pancreatic  $\beta$ -cell regeneration and stimulate insulin secretion
  - ❑ may have a hypoglycemic effect
  - ❑ may improve glucose tolerance
- ✓ Sustained consumption of cocoa over long periods of time may affect insulin resistance to a greater degree than single doses of cocoa products





# Latest Meta-Analysis of Cocoa & Chocolate finds additional Benefit for Insulin and Glucose Management



**Conclusions:** We found consistent acute and chronic benefits of chocolate or cocoa on FMD and previously unreported promising effects on insulin and HOMA-IR. Larger, longer-duration, and independently funded trials are required to confirm the potential cardiovascular benefits of cocoa flavan-3-ols. *Am J Clin Nutr* 2012;95:740–51.

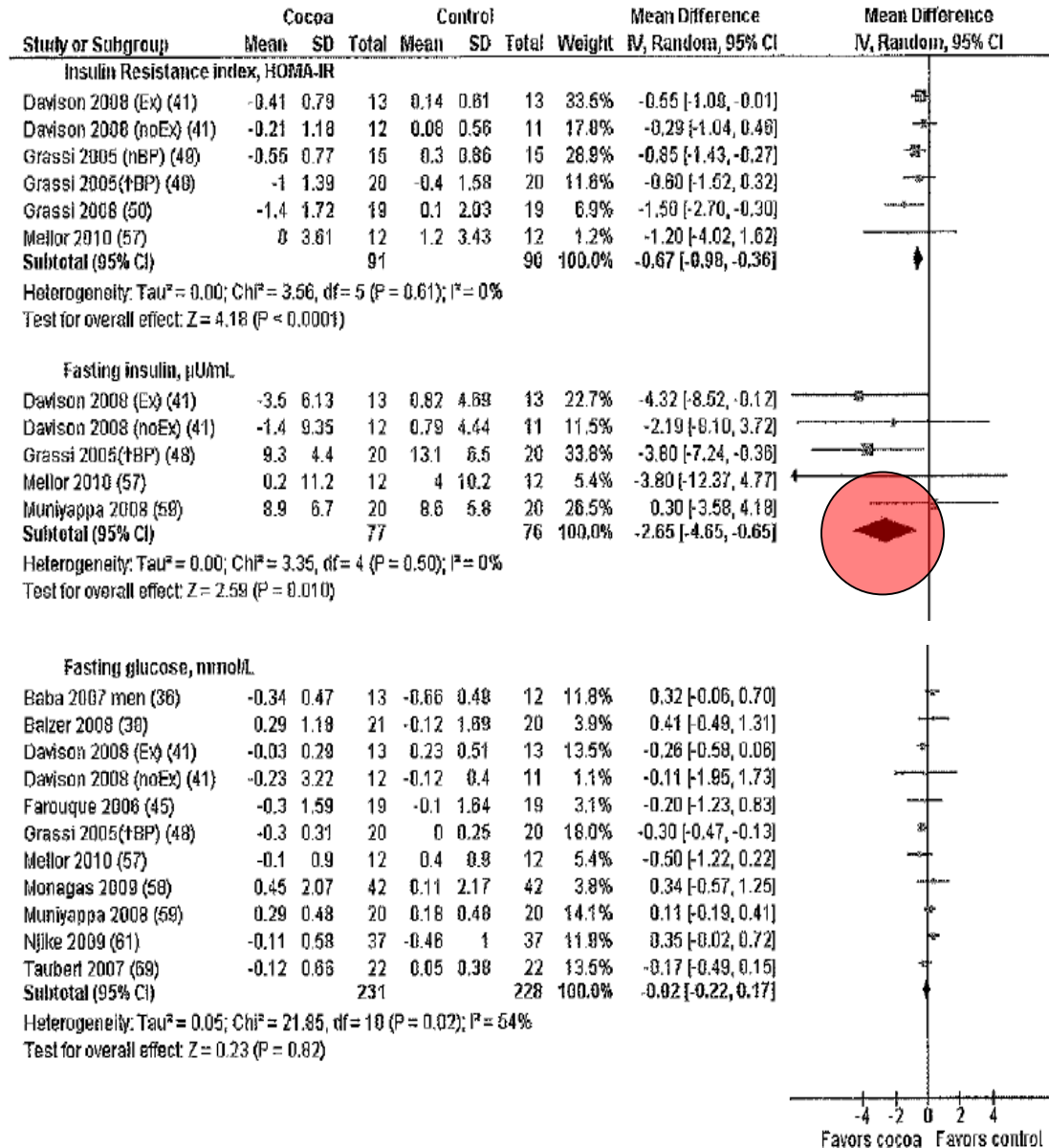


# Meta-Analysis Indicates Cocoa & Dark Chocolate Reduce Fasting Insulin

HOMA-IR

Fasting Insulin

Fasting Glucose



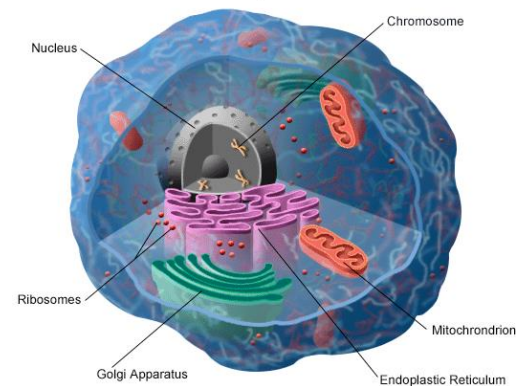
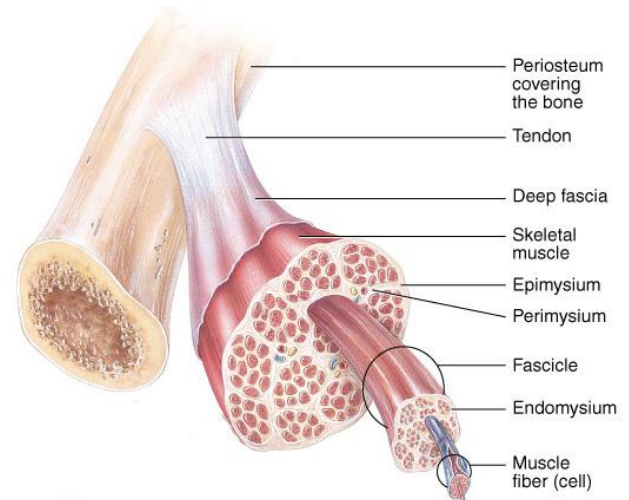
# Emerging Research: Mitochondrial Function

## Alterations in Skeletal Muscle Indicators of Mitochondrial Structure and Biogenesis in Patients with Type 2 Diabetes and Heart Failure: Effects of Epicatechin Rich Cocoa

Pam R. Taub, M.D.<sup>1,2</sup>, Israel Ramirez-Sanchez, Ph.D.<sup>1,3</sup>, Theodore P. Ciaraldi, Ph.D.<sup>1,2</sup>, Guy Perkins, Ph.D.<sup>1</sup>, Anne N. Murphy, Ph.D.<sup>1</sup>, Robert Naviaux, M.D., Ph.D.<sup>1</sup>, Michael Hogan, Ph.D.<sup>1</sup>, Alan S. Maisel, M.D.<sup>1,2</sup>, Robert R. Henry, M.D.<sup>1,2</sup>, Guillermo Ceballos, M.D., Ph.D.<sup>3</sup>, and Francisco Villarreal, M.D., Ph.D.<sup>1</sup>

### Abstract

(-)-Epicatechin (Epi), a flavanol in cacao stimulates mitochondrial volume and cristae density and protein markers of skeletal muscle (SkM) mitochondrial biogenesis in mice. Type 2 diabetes mellitus (DM2) and heart failure (HF) are diseases associated with defects in SkM mitochondrial structure/function. A study was implemented to assess perturbations and to determine the effects of Epi-rich cocoa in SkM mitochondrial structure and mediators of biogenesis. Five patients with DM2 and stage II/III HF consumed dark chocolate and a beverage containing approximately 100 mg of Epi per day for 3 months. We assessed changes in protein and/or activity levels of oxidative phosphorylation proteins, porin, mitofilin, nNOS, nitric oxide, cGMP, SIRT1, PGC1 $\alpha$ , Tfam, and mitochondria volume and cristae abundance by electron microscopy from SkM. Apparent major losses in normal mitochondria structure were observed before treatment. Epi-rich cocoa increased protein and/or activity of mediators of biogenesis and cristae abundance while not changing mitochondrial volume density. Epi-rich cocoa treatment improves SkM mitochondrial structure and in an orchestrated manner, increases molecular markers of mitochondrial biogenesis resulting in enhanced cristae density. Future controlled studies are warranted using Epi-rich cocoa (or pure Epi) to translate improved mitochondrial structure into enhanced cardiac and/or SkM muscle function. Clin Trans Sci 2012; Volume 5: 43-47





# Emerging Research: Weight Management

## Effects of Incorporating Dark Chocolate into a Weight-Loss Diet on Biomarkers of Inflammation, Oxidative Stress and Bone Metabolism

Sharon M. (Shelly) Nickols-Richardson, PhD, RD, Associate Professor  
Kathryn E. (Katy) Piehowski, RD, CDBT, Graduate Research Assistant

Department of Nutritional Sciences  
The Pennsylvania State University

PENNSSTATE





# Materials and Methods: Diet Intervention

## ■ Dark Chocolate Snack Group (N=26)

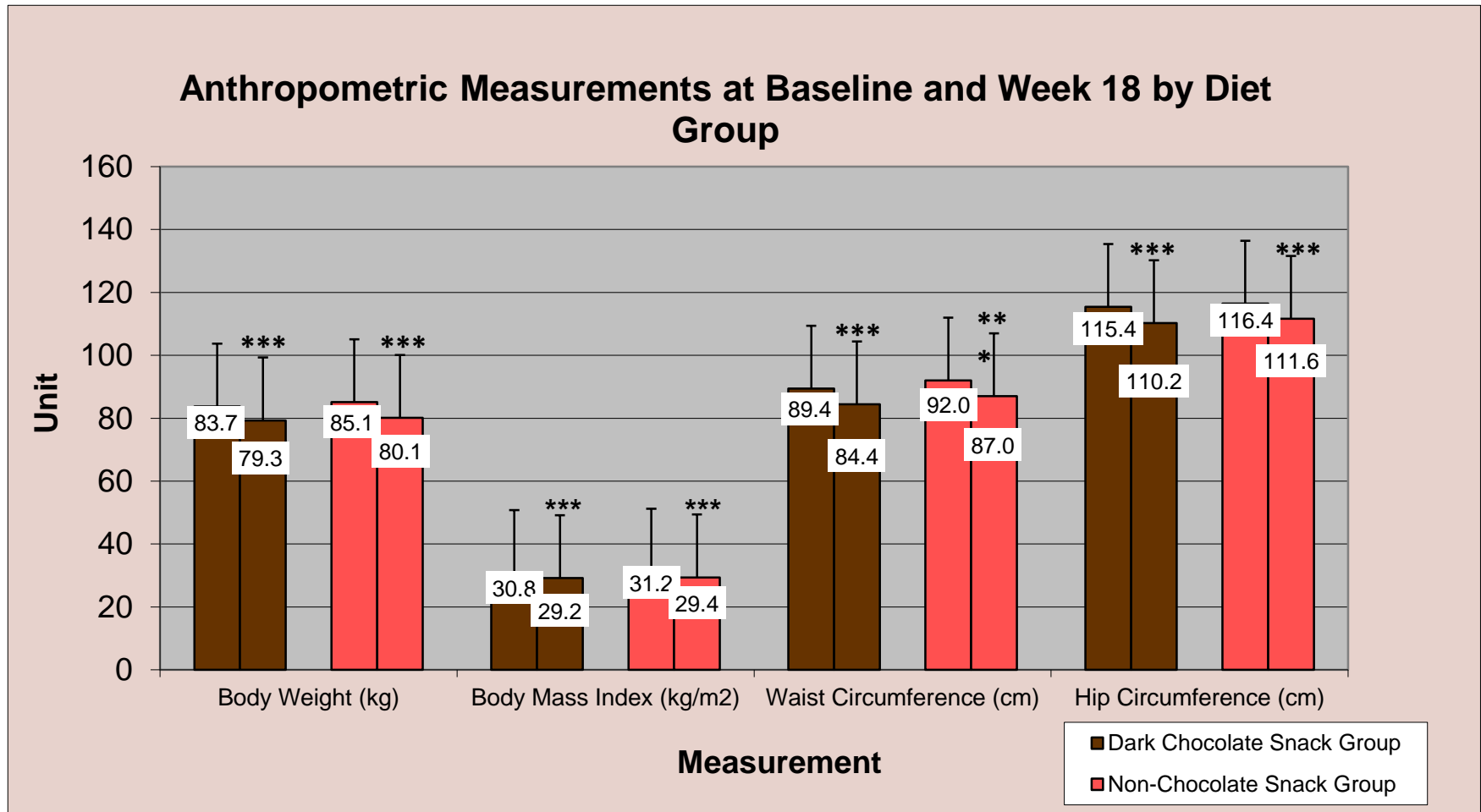
- Energy-restricted diet
- 50% Carbohydrate
- 30% Fat
- 20% Protein
- 1300 to 1800 kcal/d,  
individualized for 500 kcal  
deficit/d

## ■ Non-Chocolate Snack Group (N=25)

- Energy-restricted diet
- 50% Carbohydrate
- 30% Fat
- 20% Protein
- 1300 to 1800 kcal/d,  
individualized for 500 kcal  
deficit/d



Participants reduced body weight by ~6.6% (~10 pounds) and waist circumference by about 2 inches while including a sweet snack in an energy-restricted diet

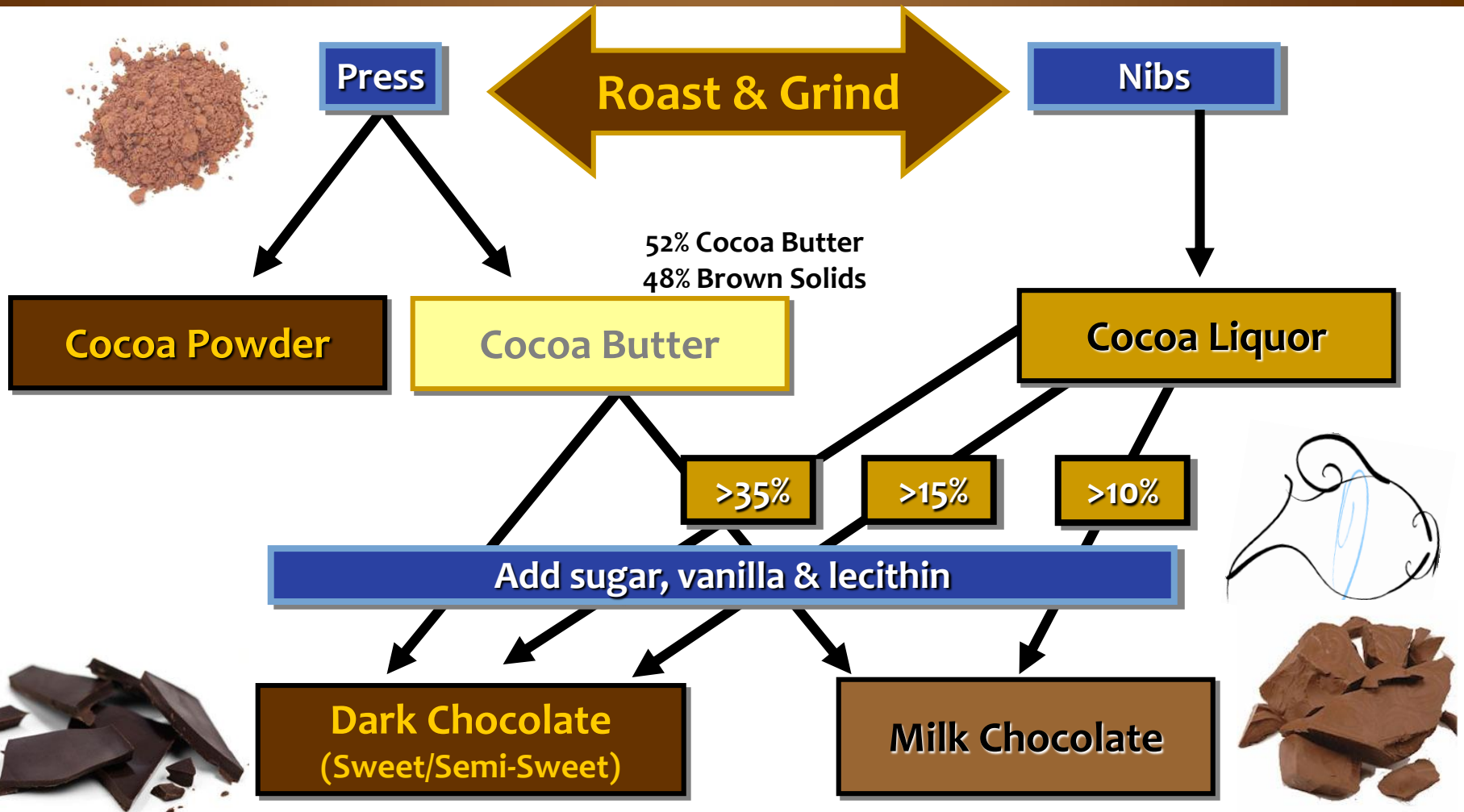


\* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ ;  $p$ -value analyzed using paired t-tests for change over time within group and independent t-tests for change over time between groups. Statistically significant differences between diet groups at baseline, week 18 or over time were not found.

# From the Science Bench to Clinical Practice



# From bean to bar...

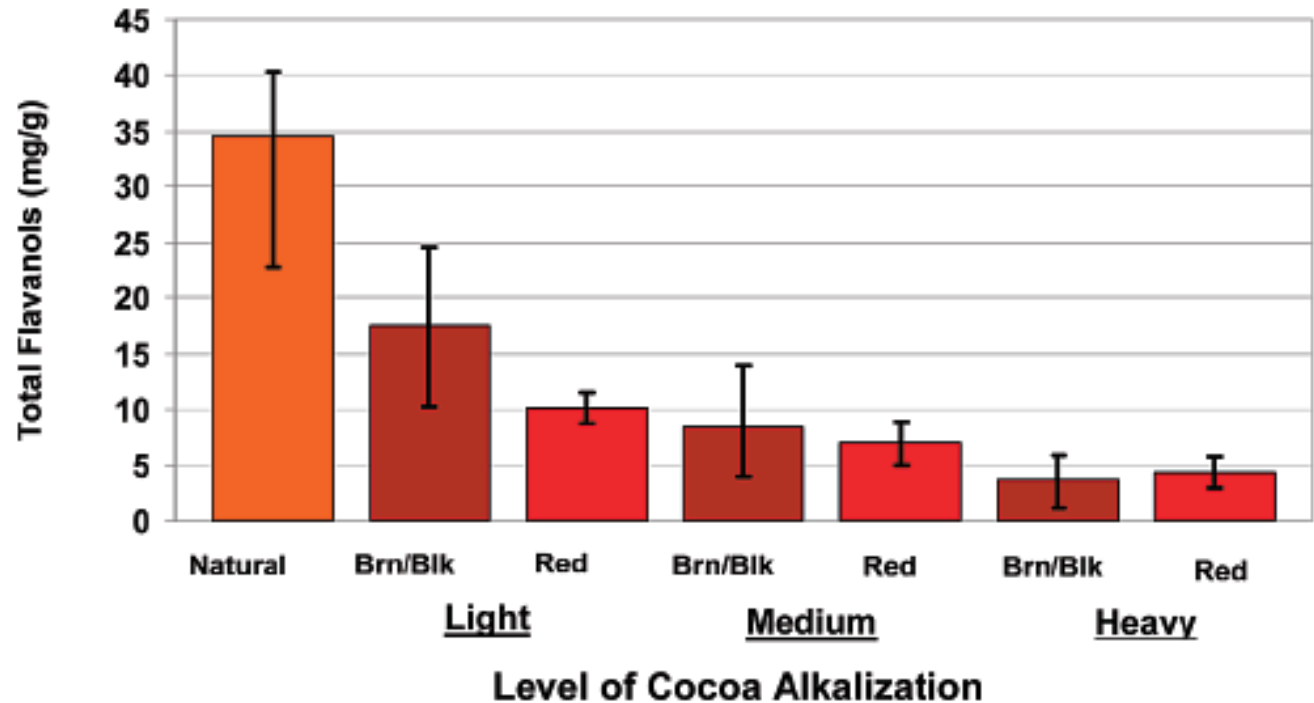




# Not all cocoa is created equal

Miller et al., *J. Agric. Food Chem* 2008.

- Most chocolate flavored beverages use alkalized or “dutched” cocoa
- Cocoa is alkalized to reduce bitterness and enhance the solubility of cocoa
- The alkalization process also reduces the flavanol content



# Types of Cocoa Powder



**Natural Unsweetened**

INGREDIENTS: Cocoa



**Mixed Natural & Dutched**

INGREDIENTS: Cocoa, Cocoa  
Processed with Alkali

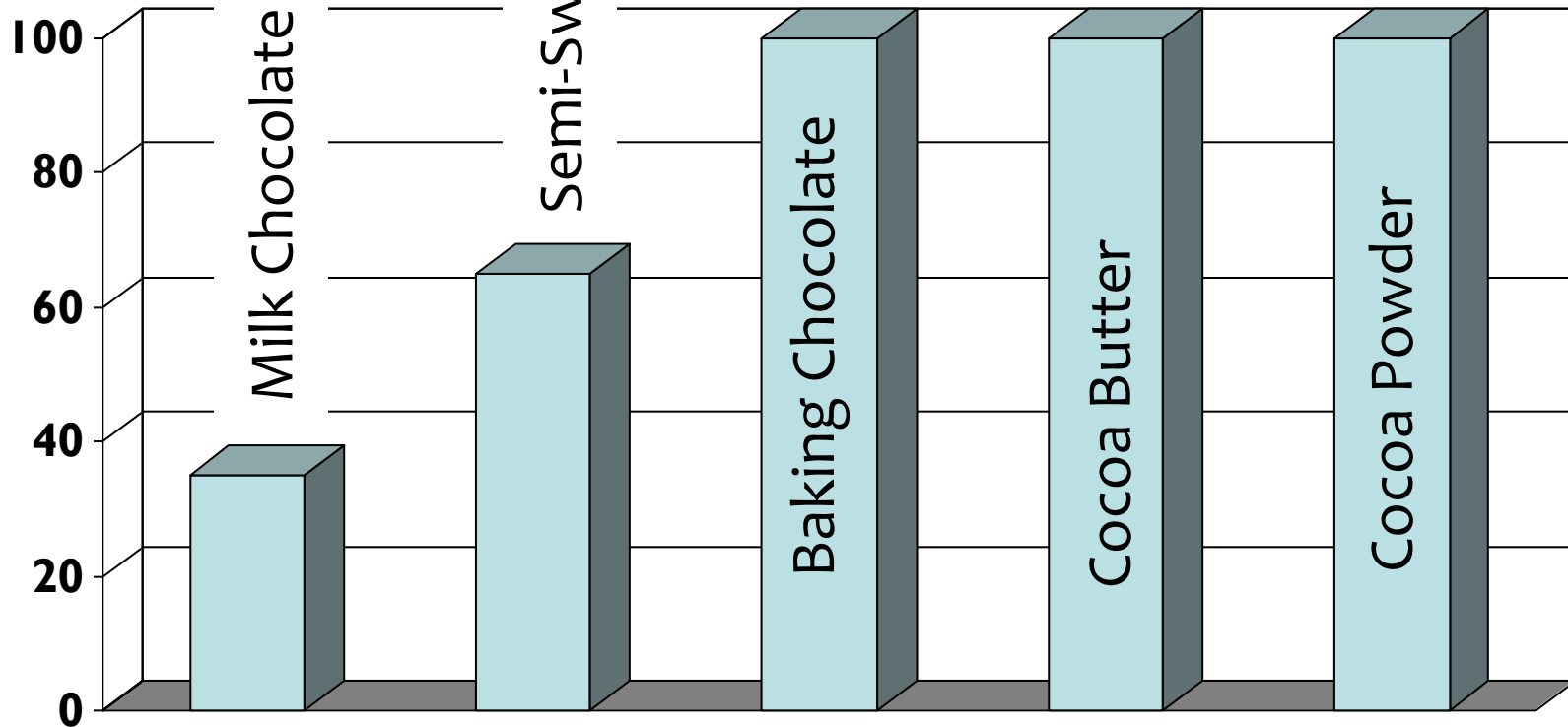


**Dutched (Alkalized) Cocoa**

INGREDIENTS: Cocoa  
Processed with Alkali



# % Cacao



52% Cocoa Butter

21% Carbohydrates

17% Protein

10% Polyphenols

Minerals

34% Oleic Acid  
33% Stearic Acid  
27% Palmitic Acid  
6% Other

~1% Sugar, 20% Fiber

Arginine, Glutamine, Leucine

2% Proanthocyanins

Fe, Mg, P, K, Cu





# Types of Chocolate



**50% Cacao**

## **Dark Chocolate**

**INGREDIENTS:** Sugar, Chocolate, Cocoa Butter, Nonfat Milk, Milk Fat, Cocoa Processed with Alkali, Soy Lecithin, Vanillin, Milk



**35% Cacao**

## **Milk Chocolate**

**INGREDIENTS:** Sugar, Cocoa Butter, Chocolate, Nonfat Milk, Milk, Lactose, Milk Fat, Cocoa Processed with Alkali, Soy Lecithin, Vanillin



**25% Cacao**

## **White Chocolate**

**INGREDIENTS:** Sugar, Cocoa Butter, Nonfat Milk, Milk, Lactose, Milk Fat, Lecithin, Tocopherols (to maintain freshness), Vanillin, Salt





# Chocolate in Moderation

## ■ Dark Chocolate:

- 6-10g (1 tasting square) over time can benefit blood pressure levels
- 3 small squares = ~100 kcal
- 2 larger squares = ~100 kcal



## ■ Natural Cocoa Powder:

- 1-2 TBSP = ~10-20 kcal



## ■ Treats in the Diet

- 50-100 kcal can be included in the diet per day or 500 per week



# Key Take Away Messages...

- ✓ Natural cocoa powder is extracted from the cocoa bean, a fruit rich in polyphenolic compounds called flavanols which support heart health. Cocoa has been an ancient remedy the Mayans recognized, only now supported by modern scientific research.
- ✓ More than 250 studies show that natural cocoa and dark chocolate may have properties that contribute to heart health.
- ✓ Many products contain alkalized or “dutched” cocoa powder to give it a darker color, smoother flavor and increased solubility. However, this process also depletes the flavanol content and reduces health benefits that can be derived from them.
- ✓ Enjoying one to two tablespoons of natural cocoa a day as an ingredient in beverages, meals or snacks or 20 grams of dark chocolate can contribute to positive heart health benefits.

