
COMPLIMENTARY 1-CEU WEBINAR PRESENTATION
Strawberries and Cardiometabolic Health: Current and Future Directions for Research
EARN 1 CEU
PRESENTED BY
Arpita Basu, PhD, RD/LD
Britt Burton-Freeman, PhD
November 16, 2022, 2-3pm ET
*I ON FOOD is approved by the CDR to offer 1.0 CPEU for this webinar.
CALIFORNIA STRAWBERRIES

Learning Objectives

1. Analyze the current research demonstrating the potential role of strawberries and their bioactive components in cardiometabolic health.
2. Identify the bioactives in strawberries that may contribute to their positive impact on cardiometabolic health.
3. Describe future direction of research on strawberries and other fruits and their relationship to and impact on cardiometabolic health.

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What We'll Cover: Specifics

- Dietary exposure: strawberries' phytochemical and nutritional composition
- Health outcomes: cardiometabolic health, metabolic syndrome, and vascular dysfunction (risks)
- Relationship: how do dietary strawberries effect vascular dysfunction in high-risk adults?
  - Systematic review and meta-analyses
  - Clinical trials
- Summary and practical applications

Potential Health Benefits of Strawberries

- Anti-Metabolic Syndrome
- Anti-Inflammatory Effects
- Anti-Diabetic Effects
- Antioxidant Effects
- Anti-Cardiovascular Disease

Afrin et al. J Agric Food Chem 2016

Nutritional/Bioactive Composition of Strawberries (Selected)

Bioactive Compounds	Specific to Strawberries
Flavonoids	
Anthocyanins	Pelargonidin
Flavonols	Quercetin
Flavanols	Catechin
Phenolic acids	
Hydroxycinnamic acid	Caffeic acid
Hydroxybenzoic acid	Gallic acid
Hydrolyzable tannins	Ellagitannins

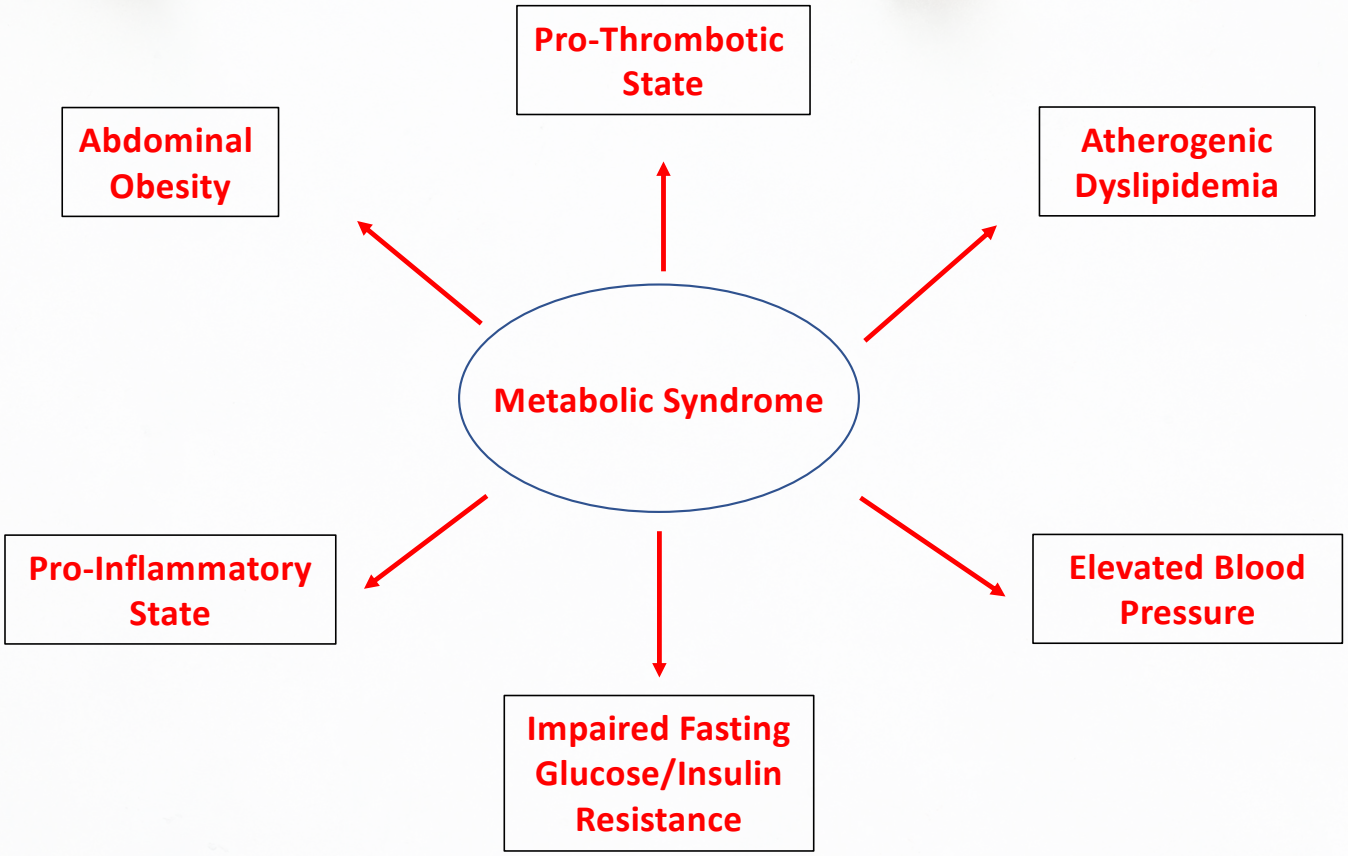
Nutrients	Amount/100g Fresh Weight
Water	91g
Energy	32kcal
Carbohydrates	7.7g
Dietary fiber	2g
Potassium	153mg
Sodium	1mg
Vitamin C	59mg
Folate	24mg
Thiamin	0.024
Riboflavin	0.022
Niacin	0.38

Afrin et al. J Agric Food Chem 2016

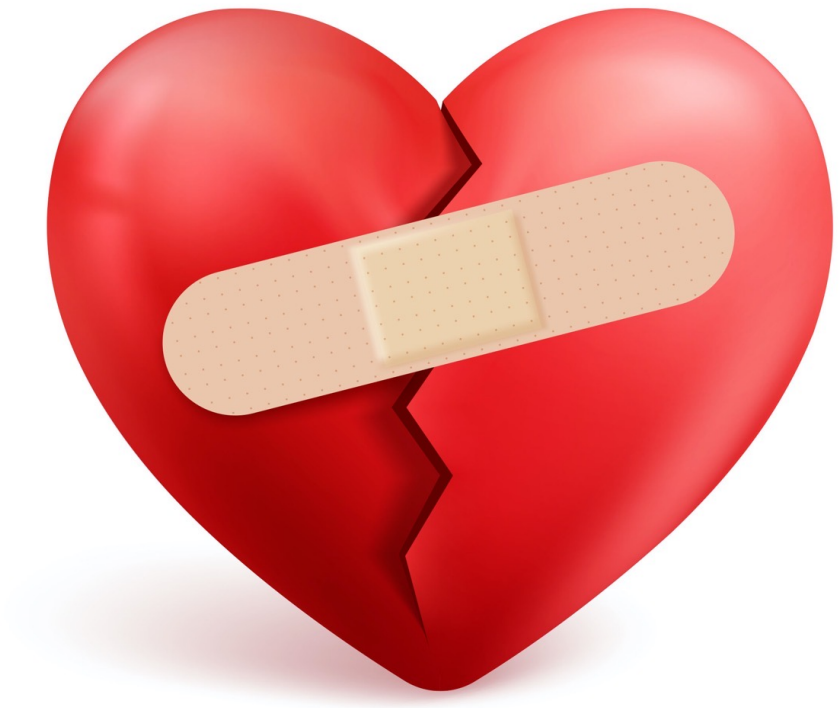
Cardiometabolic Health

- The normal functioning of the cardiovascular and metabolic systems, typically reflected by:
  - Body weight/adiposity
  - Blood glucose and lipids
  - Blood pressure and hormonal control
  - Blood coagulation
  - Inflammation markers
- Cardiometabolic diseases include:
  - Obesity
  - Diabetes
  - Atherosclerotic cardiovascular disease
  - Hypertension
  - Chronic kidney disease
  - Heart failure

Eckel et al. Lancet 2005



Adapted from Eckel et al. Lancet 2005



Poor Cardiometabolic Health in the US

- Metabolic syndrome represents poor cardiometabolic health
- According to CDC data, 88 million adults (1 in) have prediabetes or metabolic syndrome (including impaired glucose metabolism/insulin resistance)
- Health disparities in prediabetes/metabolic syndrome
  - Higher prevalence in Hispanics vs. non-Hispanic Whites
- Role of specific foods in metabolic syndrome must be explored, as changing the entire diet can be challenging for many!
- Role of strawberries in metabolic syndrome?

Lichtenstein et al. Circulation 2021

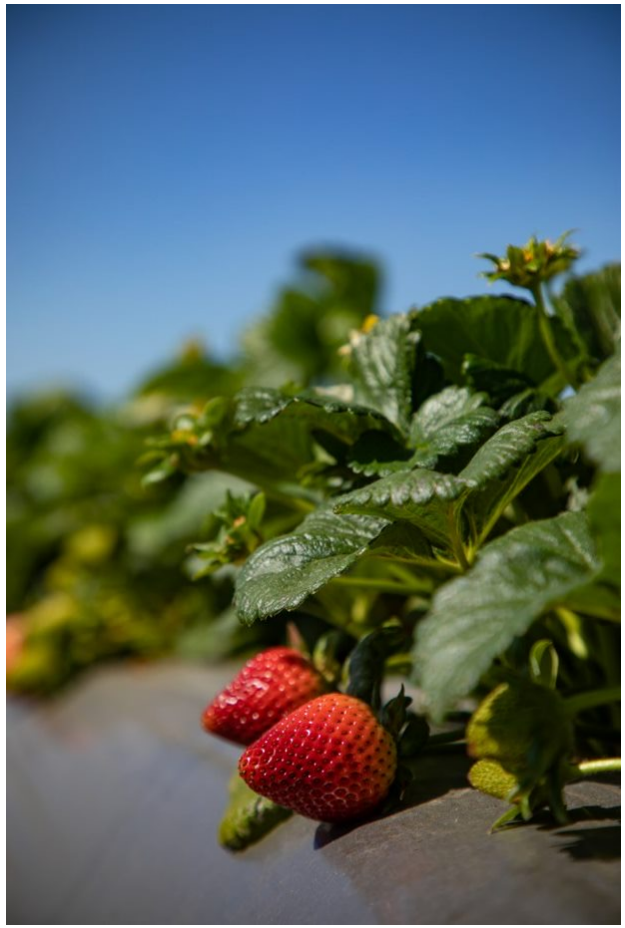
Prediabetes/Metabolic Syndrome: A Risk Factor of Vascular and Metabolic Dysfunction

- Hyperglycemia
- Lipids and lipoproteins
  - LDL-C, small, and medium lipid particles
  - Dyslipidemia (high TG, low HDL)
- Oxidative stress
  - Oxidized lipids play an important role in endothelial dysfunction and atherosclerosis
- Inflammation
  - Adhesion molecules, cytokines, and C-reactive protein shown to promote endothelial dysfunction (IL-6, TNF, MMP, CRP)
- Diet and lifestyle factors
  - High fat and low fiber diets
  - Physical inactivity
  - Smoking

Xu, et. al.. Pharmacol Rev. 2021

Epidemiological Evidence

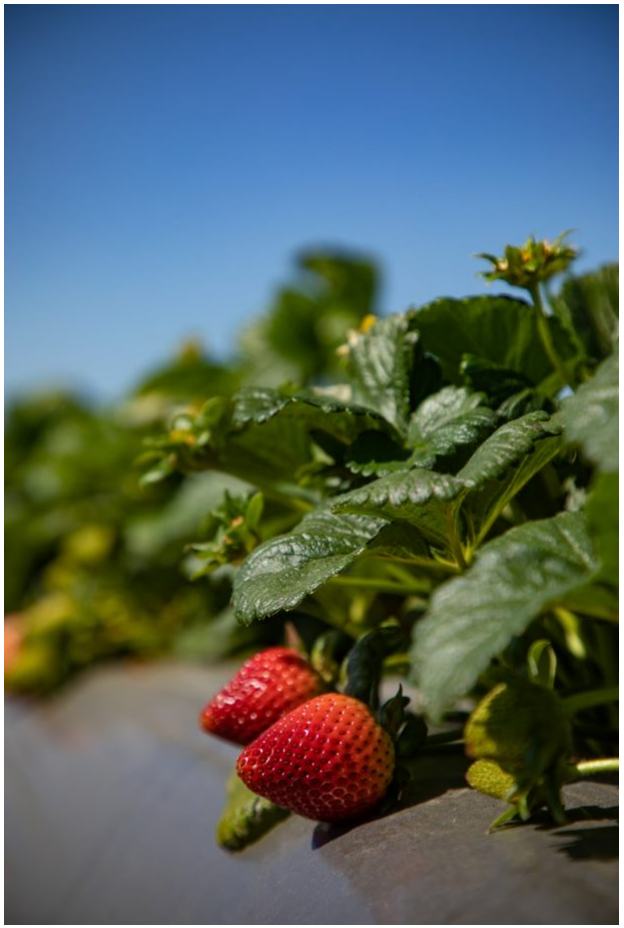
- Blueberries and strawberries – prevent hypertension?
- Prospective cohort:
  - Nurses' Health Study (NHS) II: n=87,242
  - NHS I: n=46,672
  - Health Professionals Follow-Up Study (HPFS): n=23,043
  - 14y follow-up
- Highest quintile of anthocyanin intake (~18-25mg/d) (predominantly from **blueberries and strawberries**) associated with an **8% reduction in risk for HTN** compared with the lowest quintile of anthocyanin intake (5-7mg/day)
- Adjusted pooled analyses



Cassidy et al. Am J Clin Nutr 2011

Epidemiological Evidence

- Blueberries and strawberries – reduce inflammation?
- Cross-sectional cohort:
  - n=2375
  - Framingham Heart Study Offspring Cohort
    - Highest quintile of apples, pears, red wine and strawberries associated with a **significantly lower inflammatory score** compared with the lowest quintile of these food intakes
    - Adjusted pooled analyses



Cassidy et al. Am J Clin Nutr 2011

The Effect of Berry-Based Food Intervention on Markers of Cardiovascular and Metabolic Health: A Systematic Review of Randomized Controlled Trials

Berry interventions of significance (adults with cardiometabolic risks):

1. **Blood pressure as an outcome**
   Chokeberry juice - 300mL for 8 weeks
   Blueberry beverage - 480mL for 8 weeks
   Cranberry juice - 480mL for 8 weeks
   Mixed berry puree/juice - 300g for 4 weeks
2. **Endothelial function and arterial stiffness as outcomes**
   Blueberry beverage - 480-680mL for 6 and 8 weeks
   Blackcurrant juice - 1000mL for 6 weeks
   Cranberry juice - 250mL for 4 weeks
3. **Adhesion molecules (ICAM, VCAM) as markers of endothelial dysfunction-**
   Strawberry beverage (powder) - 50g for 8 weeks
4. **Blood glucose and insulin as outcomes**
   Cranberry juice - 240-480mL for 8 and 12 weeks
   Blueberry beverage (powder) - 45g for 6 weeks
5. **Blood lipids as outcomes**
   Cranberry juice - 480mL for 8 weeks
   Strawberry beverage (powder) - 30-50g for 8 and 12 weeks or 6h postprandial
   Berry mix (fresh and puree) - 300g for 4 weeks

Mol. Nutr. Food Res. 2018, 62, 1700645

Strawberries and CVD: Meta-analysis of RTCs

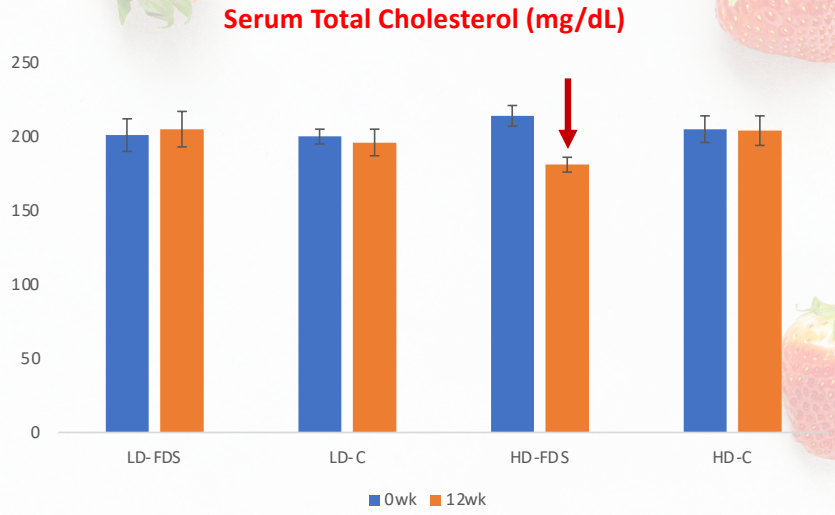
- 11 RCTs included in the analysis
- Fresh and freeze-dried strawberries used as intervention
- Six RCTs showed a **significant decrease in C-reactive protein** as a biomarker of inflammation following strawberry intervention
- Three RCTs of adults with elevated total-cholesterol and four RCTs of adults with elevated LDL-cholesterol revealed **improvements in lipid profiles** following strawberry intervention

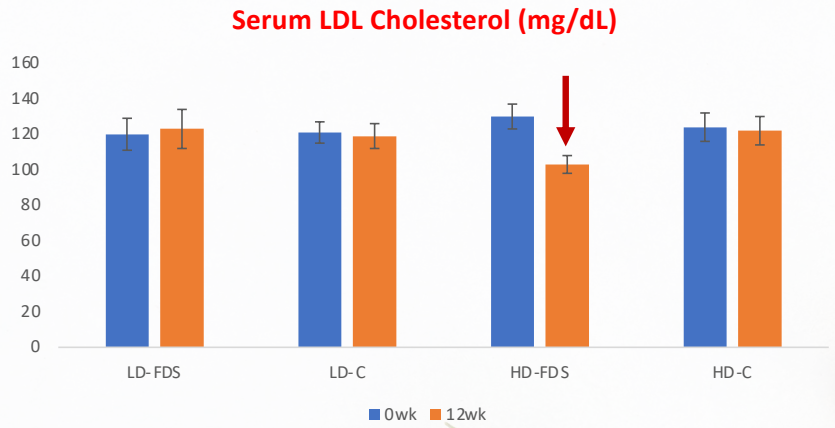
Gao et al. B J Nutr 2020

Effects of Strawberries on Cholesterol

Nutrient/Bioactive Compound	Strawberry Powder (LD-FDS)	Strawberry Powder (HD-FDS)
Total calories, Kcal	75	150
Total polyphenols, mg	1001	2005
Total anthocyanins, mg	78	155
Dietary fiber, g	4	8
Vitamin c, mg	55	109
Phytosterols, mg	23	50

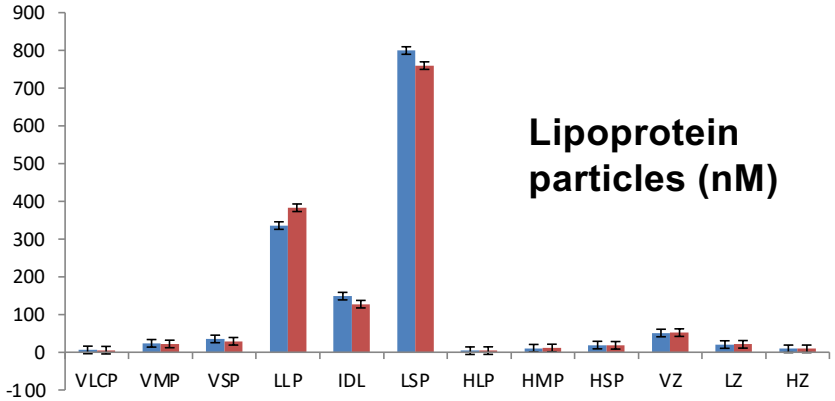
LD-FDS: low dose strawberry 25g/day for 12 weeks
HD-FDS: high dose strawberry 50g/day for 12 weeks
Control groups matched for fiber and calories

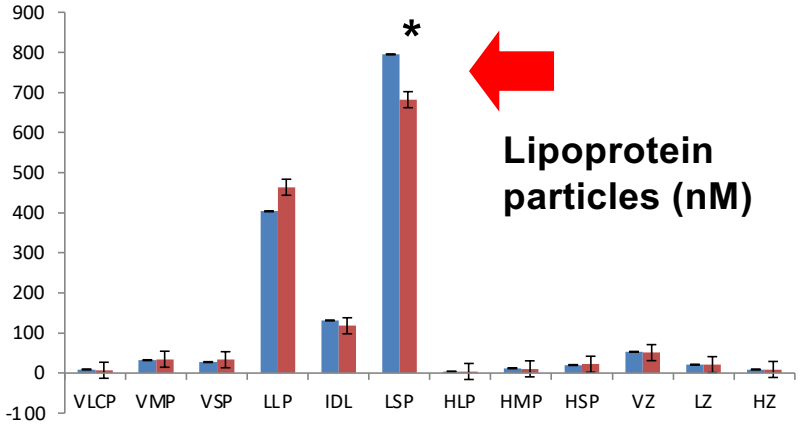


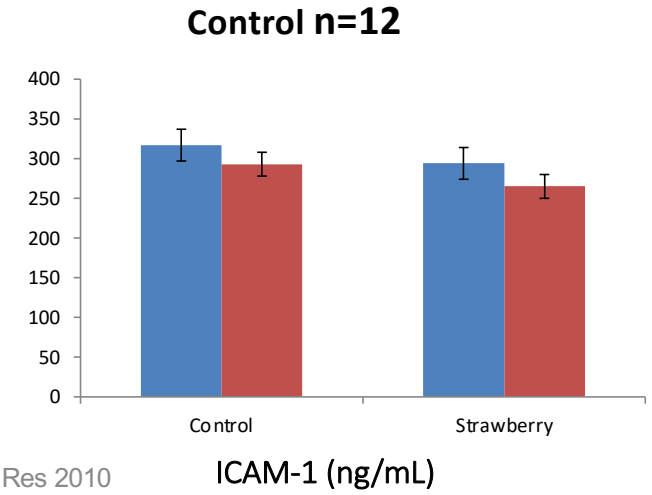


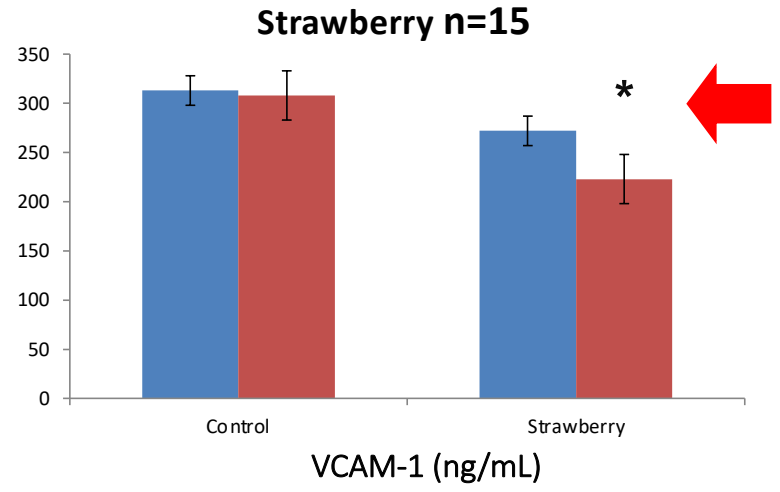
Adapted from Basu et al. J Nutr 2014

Strawberries Improve Lipid Particle Size and Adhesion Molecules in Adults with Metabolic Syndrome



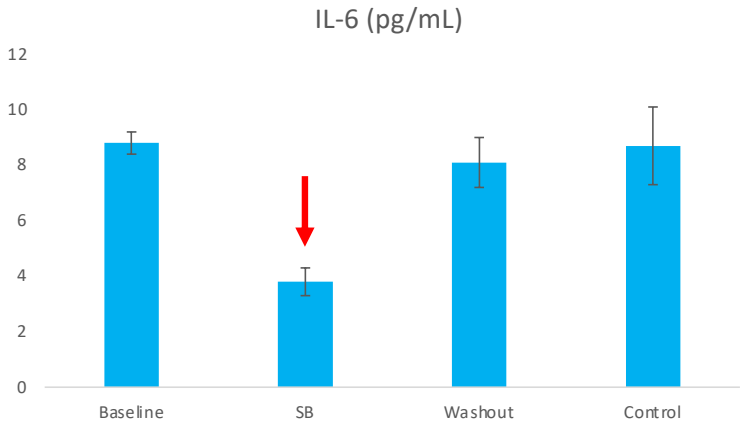


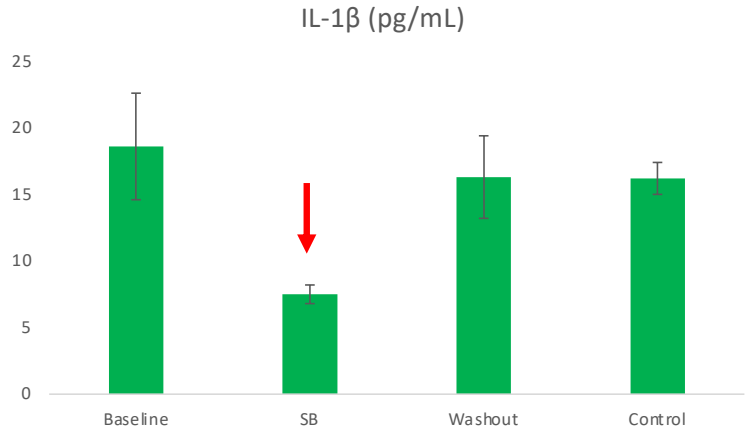


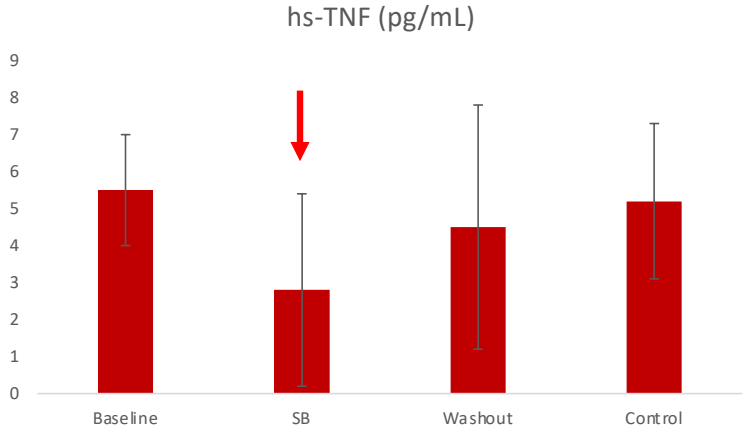


Basu et al. Nutr Res 2010

Decreased Inflammatory Markers in Adults with Metabolic Syndrome and Knee Osteoarthritis (OA) After 12-week Strawberry Supplementation (50g/day)







*SB = Strawberry

Basu et al. Food Function 2018; Basu et al. Nutrients 2017

Strawberries Improve Insulin Resistance in Adults with Metabolic Syndrome

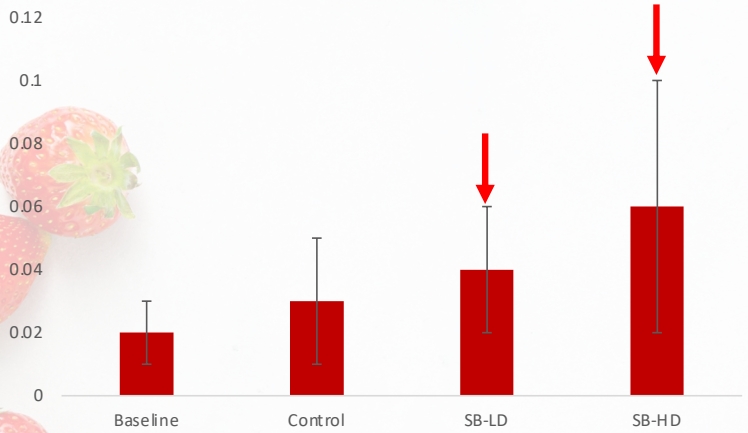
Variable	Baseline	Control (4-Week)	Strawberry (LD) (4-Week)	Strawberry (HD) (4-Week)	p-Value (Treatment)
Serum Fasting Glucose, mg/dL	93 ± 13	93 ± 12	94 ± 11	93 ± 15	0.97
Serum HbA1c, %	5.5 ± 0.3	5.5 ± 0.3	5.5 ± 0.3	5.5 ± 0.2	0.95
Serum Insulin, µIU/mL	15.4 ± 6.6	15.2 ± 6.4	14.0 ± 8.2	9.1 ± 3.1	**0.0002**
Serum HOMA-IR	3.6 ± 1.5	3.5 ± 1.4	3.3 ± 2.0	2.1 ± 0.5	**0.0003**
Serum hs-CRP, mg/L	4.3 ± 3.2	4.4 ± 3.5	4.3 ± 3.1	3.8 ± 2.9	0.85
Serum adiponectin, µg/mL	9.3 ± 5.7	10.5 ± 6.2	11.4 ± 5.2	11.7 ± 7.2	0.84

Effects of freeze-dried strawberries on glycemic control and insulin resistance in a 14-week crossover RCT of 4 weeks each (n=33 in each phase). LD: low-dose strawberries (1 serving/day); HD: high-dose strawberries (2.5 servings/day)

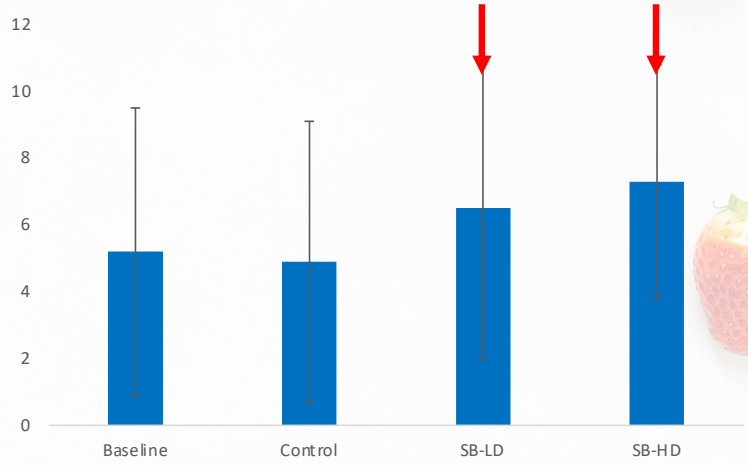
Basu et al. Nutrients 2021

Strawberries Improve Antioxidant Status in Adults with Metabolic Syndrome

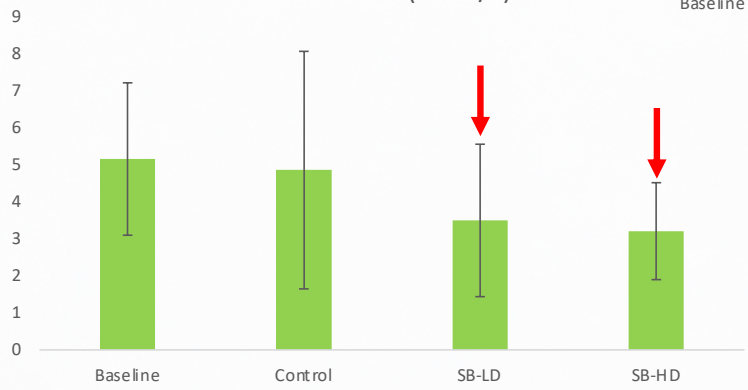
Serum SOD (U/mL)



Serum antioxidant capacity (µmol/L)



Serum MDA (nmol/L)



SB-LD: Strawberry low-dose (1 serving/day)
SB-HD: Strawberry high-dose (2.5 servings/day)

Basu et al. Antioxidants 2021

Practical Applications

- Strawberries exert significant anti-diabetic effects by decreasing insulin resistance and blood lipid peroxides
- Strawberries exert significant **anti-inflammatory** effects by decreasing blood cytokines that are associated with diabetes-related atherosclerosis
- Strawberries have been shown (in adults) to be **beneficial in reducing lipids** and **small LDL lipid particles** that lead to vascular complications in diabetes

Strawberries and Cardio-Metabolic Health: Current and Future Directions for Research

Britt Burton-Freeman, PhD
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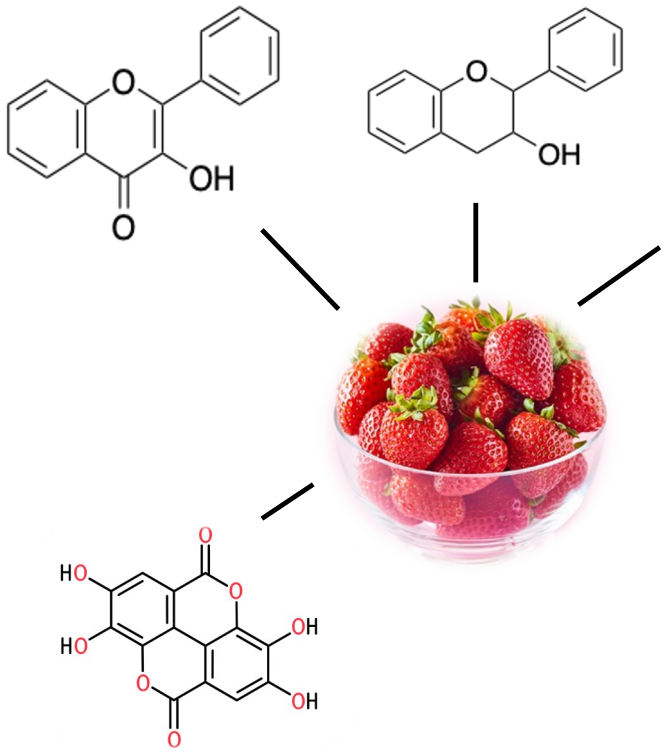
Image used with permission.

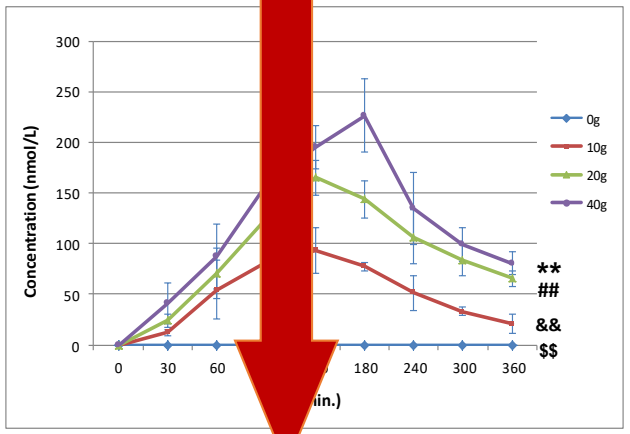
Outline

- **Strawberry Nutrition/Chemistry – unique attributes**
- **Unique components**
  - Absorbed?
  - Does eating more strawberries matter?
- **Functional Benefits**
  - What effects do strawberries have in the body?
- **Practical Implications**
- **Future Directions for Research**

Nutritional Bio- Chemistry



Blood



Park et al MNFR 2016

HEALTH ENDPOINT

Park et al MNFR 2016
Chemical structures used with permission from Y. Huang

Health Promoting Constituents

Vitamins

Minerals

Fiber

Phenolic acids

Anthocyanins

Flavan-3-ols

Hydrolysable and Condensed Tannins

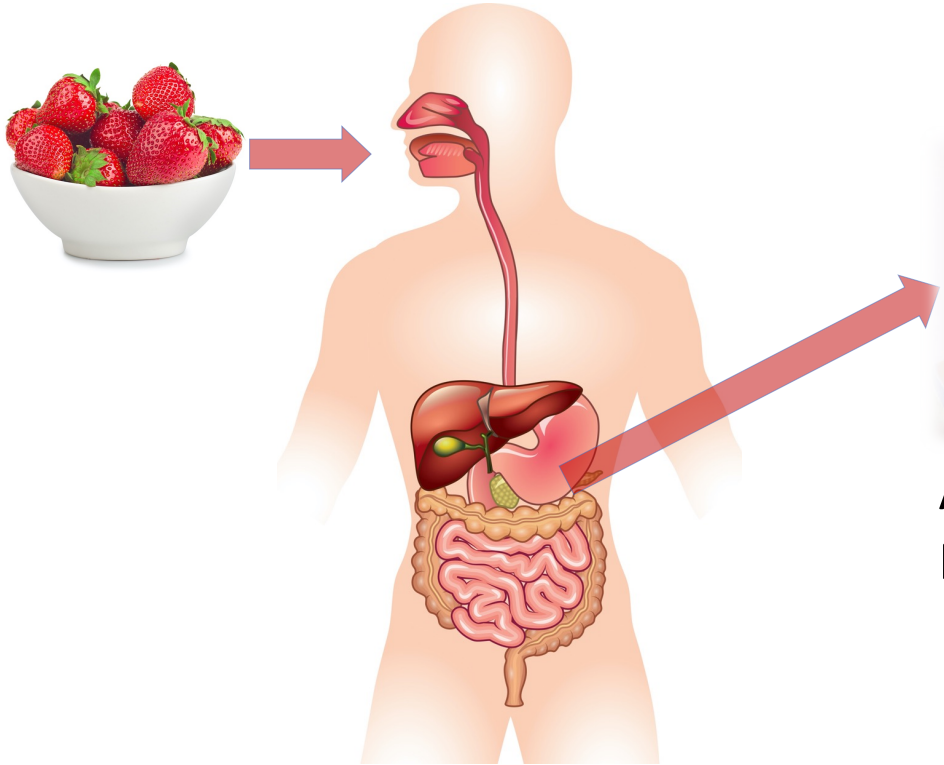
Hydroxybenzoic acids
P-hydrobenzoic acid
Protocatechuic acid
Vanillic acid
Syringic acid
Gallic acid

Hydroxycinnamic acids
Coumaric acid
Caffeic acid
Ferrulic acid
Sinapic acid
Caffeoylquinic acid

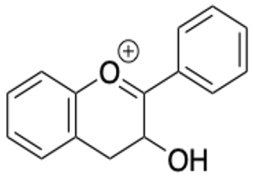
Sandhu et al 2018, Huang et al 2021

Bioavailability

Are the components in strawberries absorbed?



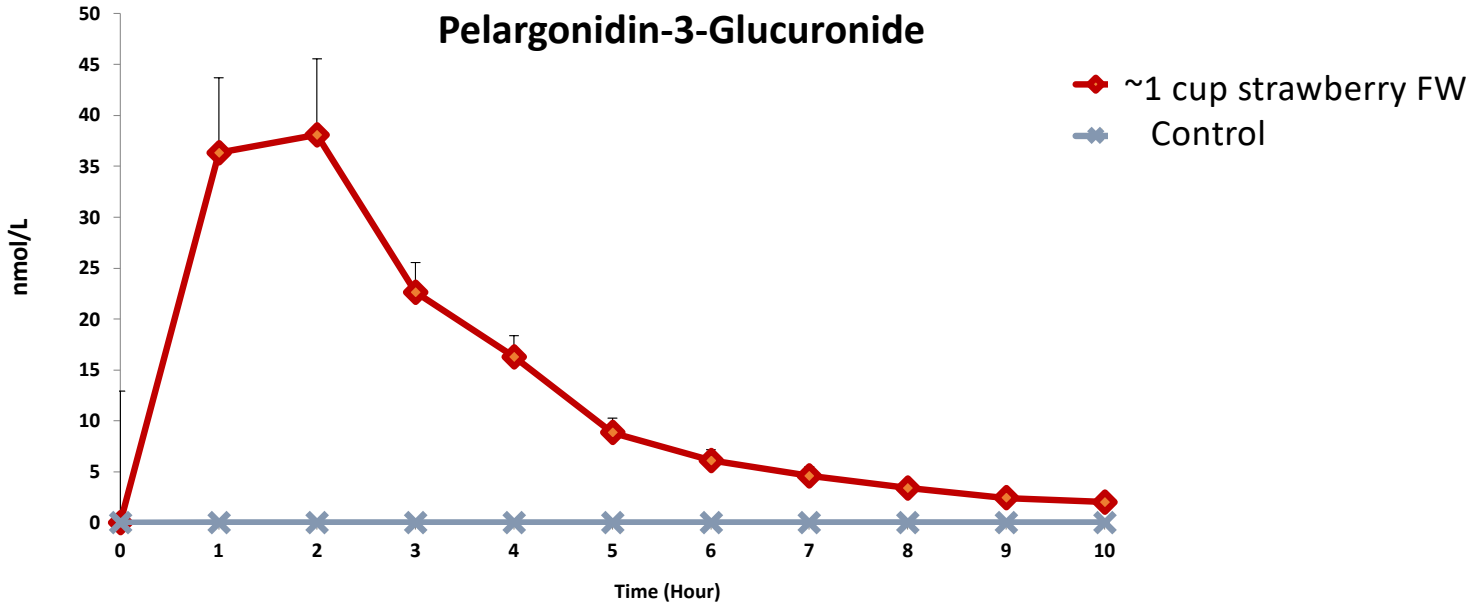
Anthocyanins absorbed and
Peak in blood in ~ 2 h



Chemical structures used with permission from Y. Huang

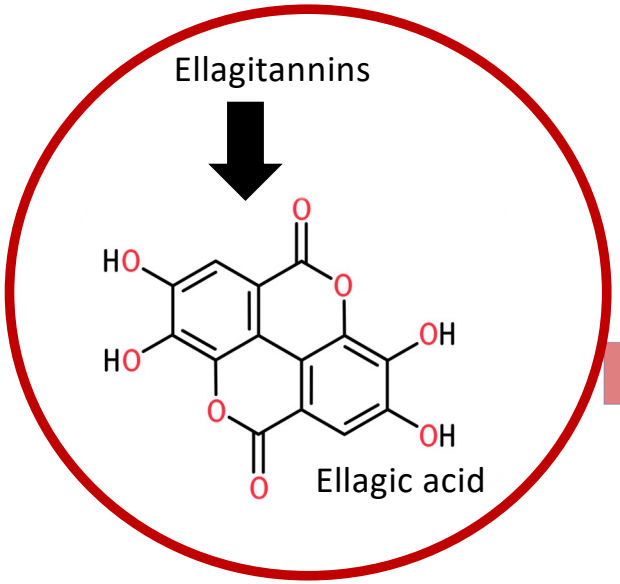
Anthocyanins from Strawberries Peak within 1-3 h

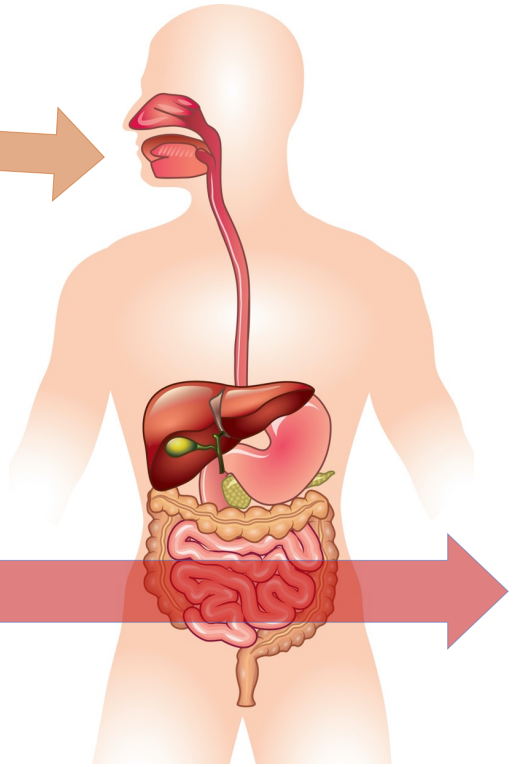
Early phase



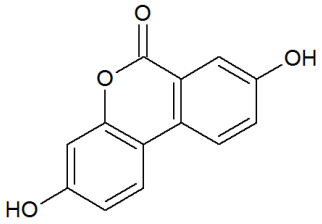
Sandhu et al JAFC 2016

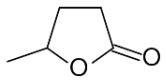
Absorption Patterns of Larger-Sized Tannin Components

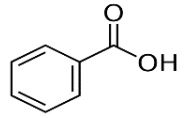




Phenolic acid metabolites and **Urolithins** are absorbed from the ileum and large intestine

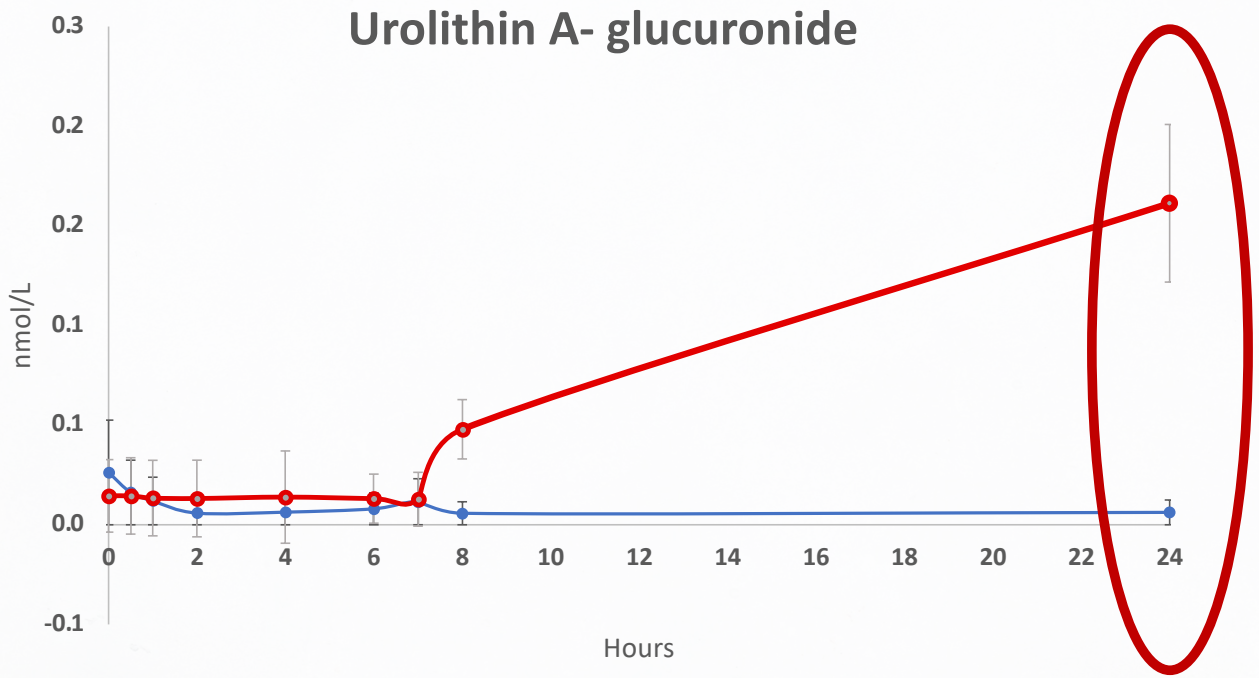






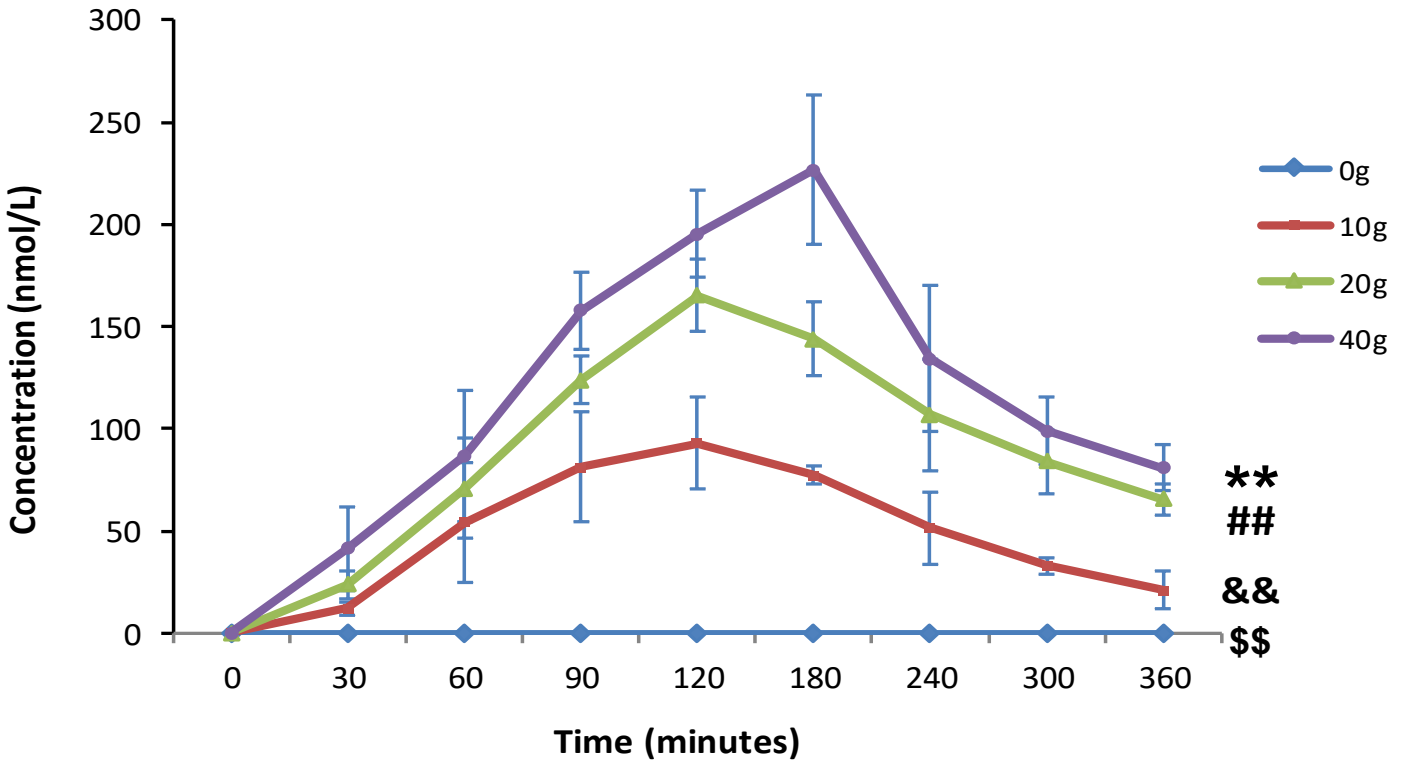
Burton-Freeman Lab

Ellagitannin Metabolites - Late Phase



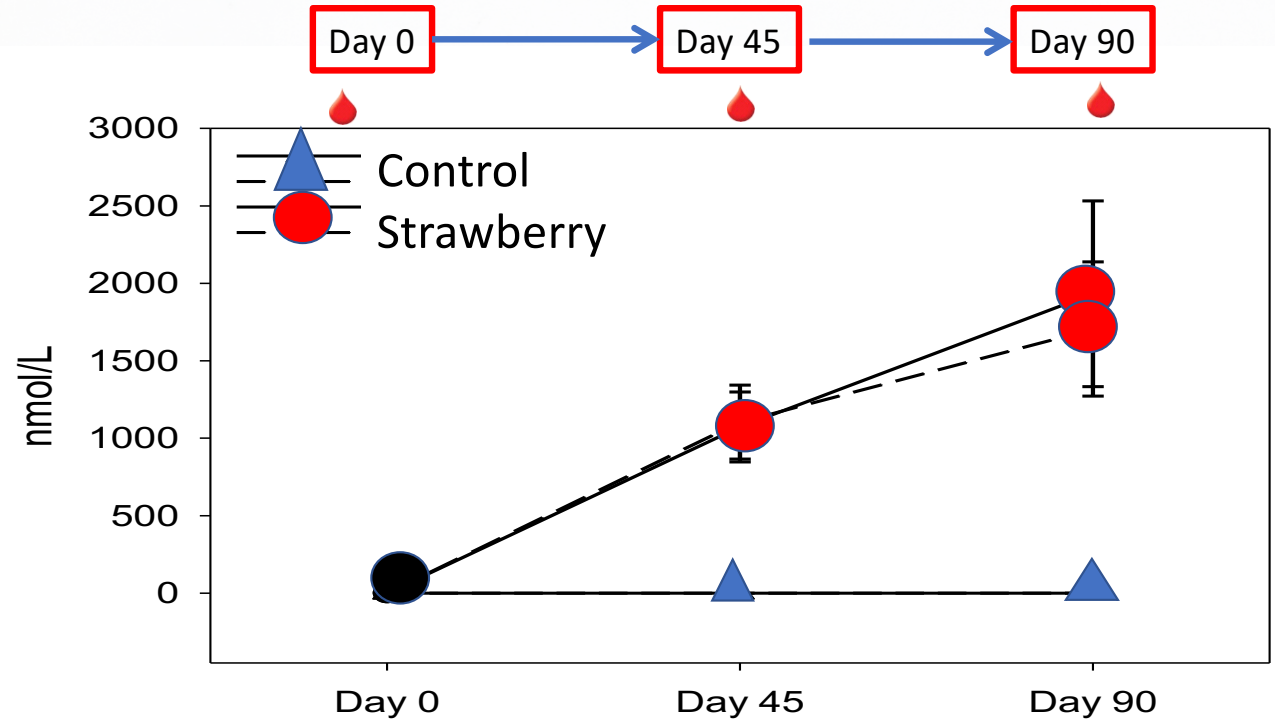
Zhang et al Food Func 2018

Dose-Response → Strawberry Anthocyanins



Park et al MNFR 2016

Strawberry Ellagitannin Metabolites (Urolithins) Increase in the Blood with Daily Intake



Sandhu et al Food Func 2018

24 g/day of freeze-dried strawberry powder vs control

The Story So Far…

- **Strawberry signature compounds**

  → **Anthocyanins and Ellagitannins**

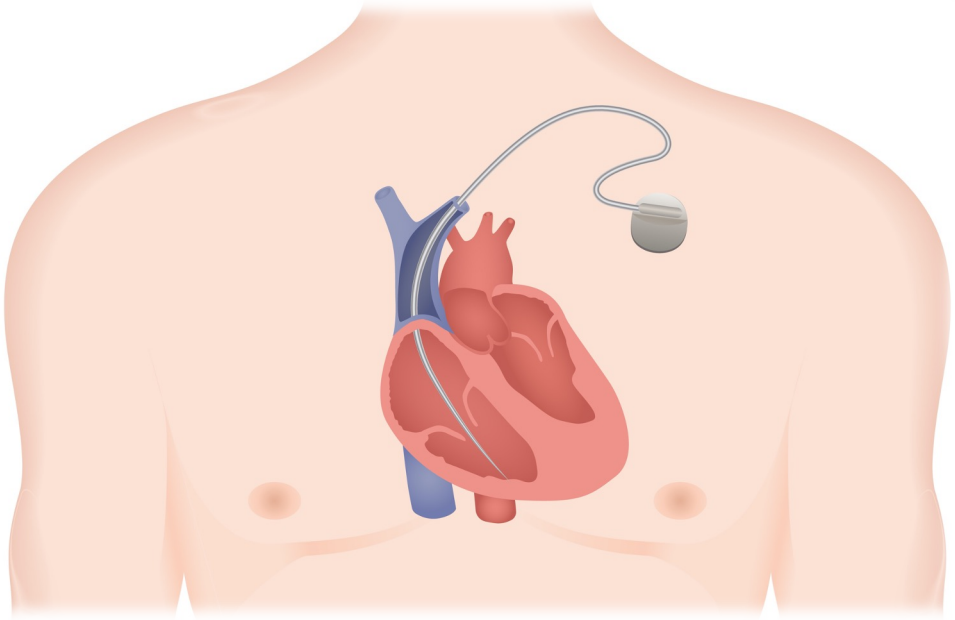
- **They are absorbed and metabolized by the human body**

- **INCREASE in blood with amount of strawberry consumed and with regular consumption**

Outline

- Strawberry Nutrition / Chemistry – Unique attributes
- Unique components
  - Absorbed?
  - Does eating more strawberries matter?
- **Functional Benefits**
  - What effects do strawberries have in the body?
- **Practical Implications**
- **Future Directions for Research**

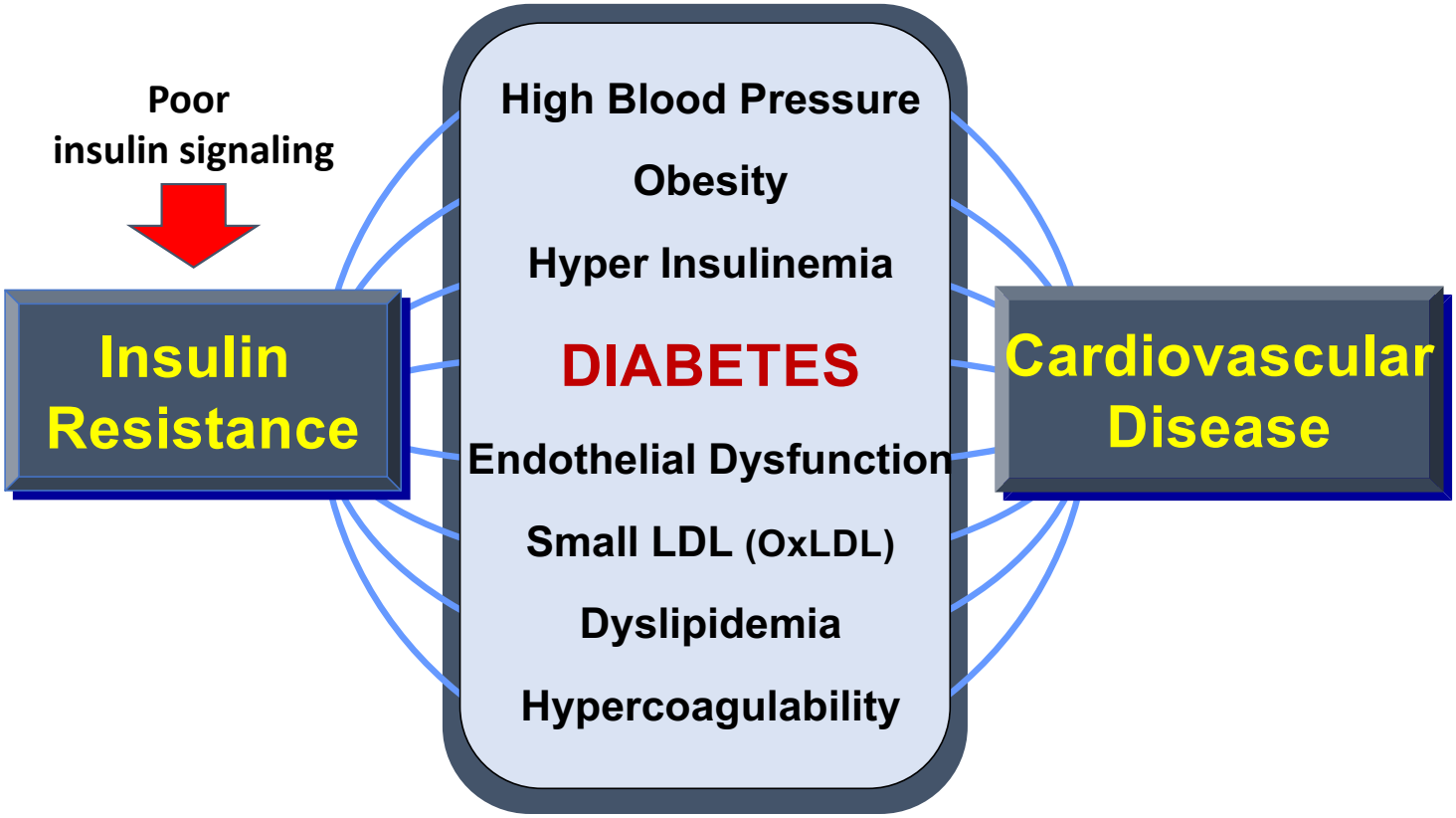
Cardiometabolic Disease Risk



Insulin Resistance/Sensitivity

Endothelial Function and Vascular Flexibility

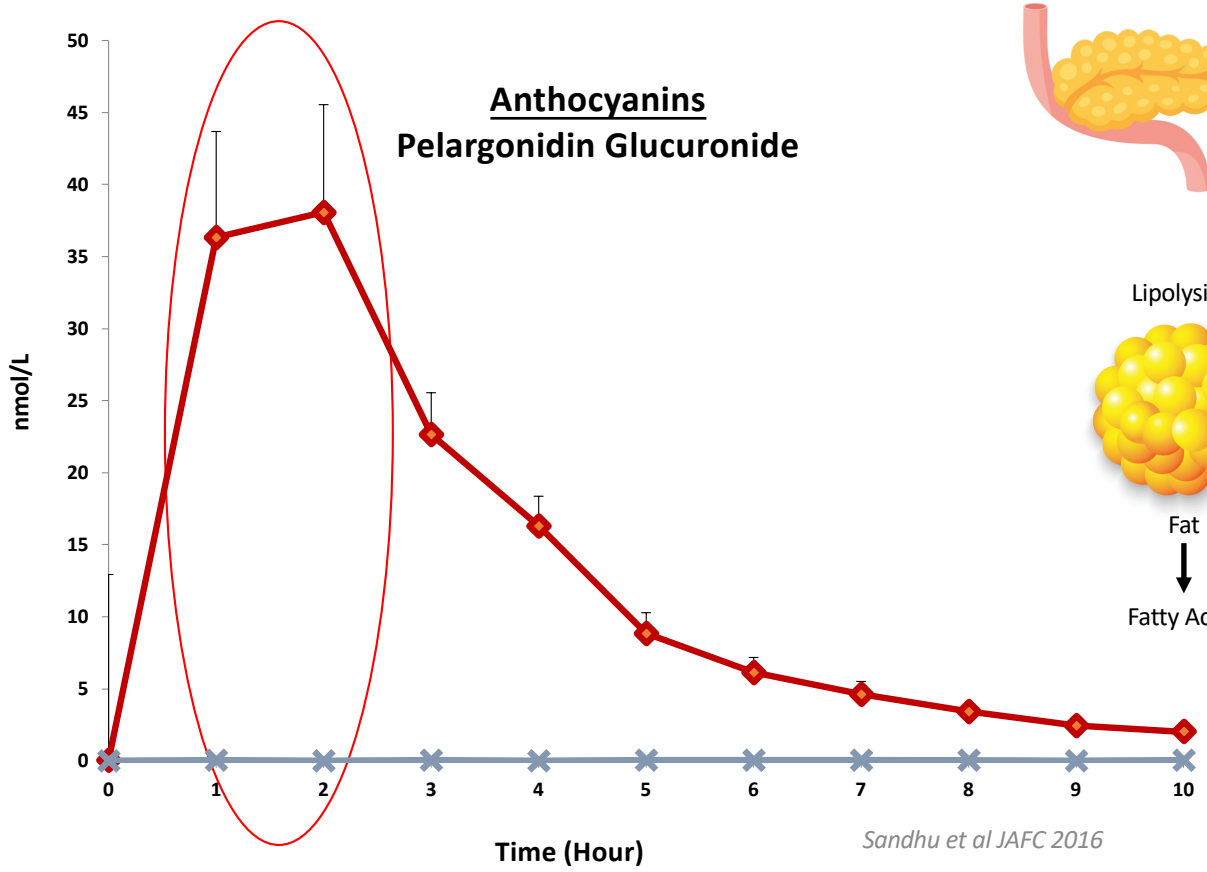
Many of the Risk Factors for CVDs are Precipitated by Insulin Resistance



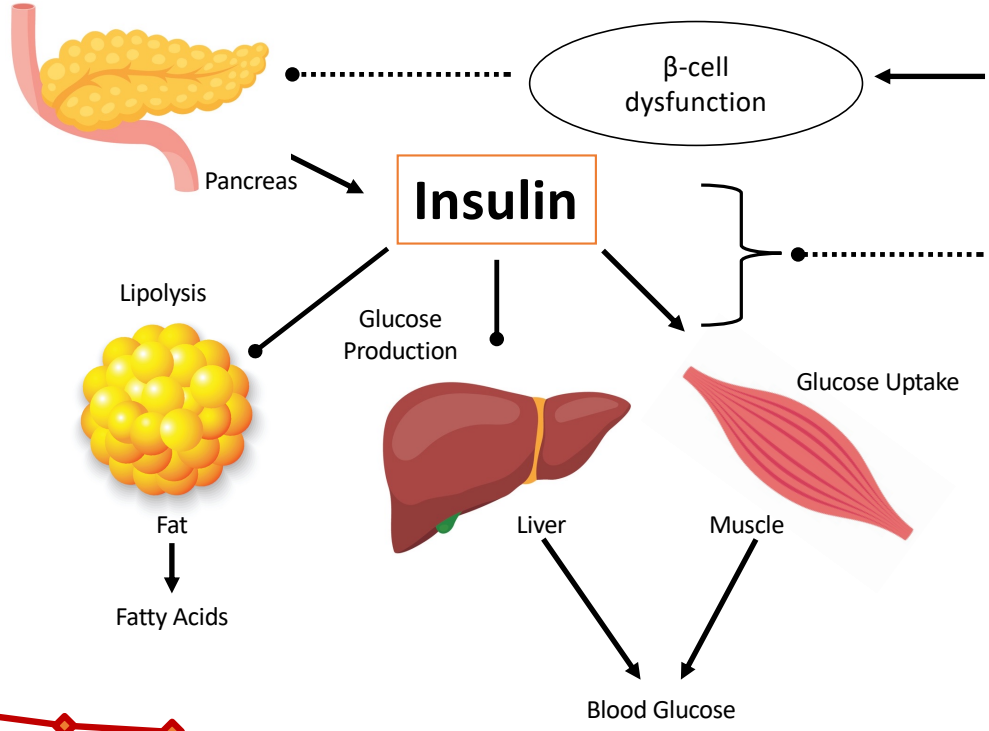
Diabetes increases risk of heart attack and stroke by 2 to 4 times

Adapted from Ginsberg HN. Insulin resistance and cardiovascular disease. J Clin Invest. 2000;106(4):453-458; and Adeva-Andany MM, Martínez-Rodríguez J, González-Lucán M, Fernández-Fernández C, Castro-Quintela E. Insulin resistance is a cardiovascular risk factor in humans. Diabetes Metab Syndr. 2019;13(2):1449-1455.

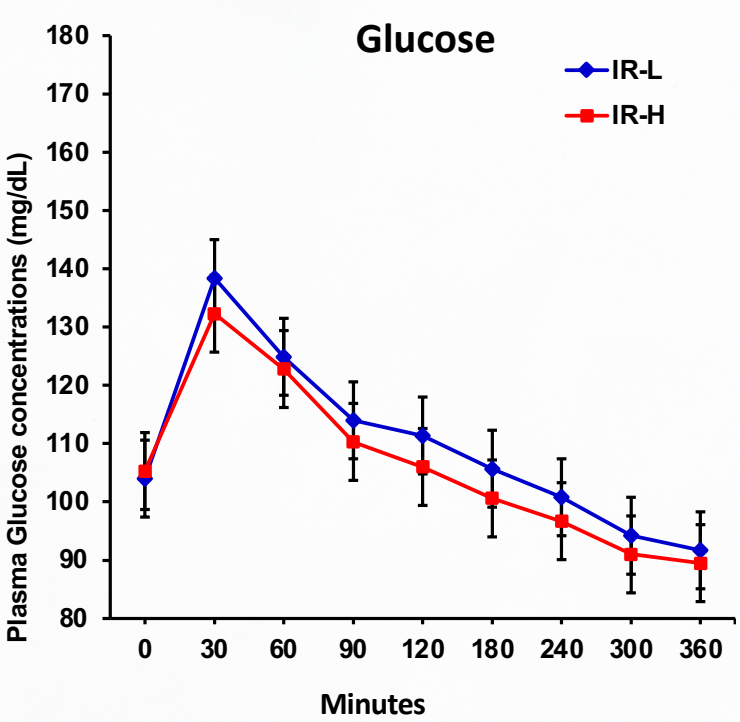
Early Phase Metabolites and Post-Meal Fuel Metabolism

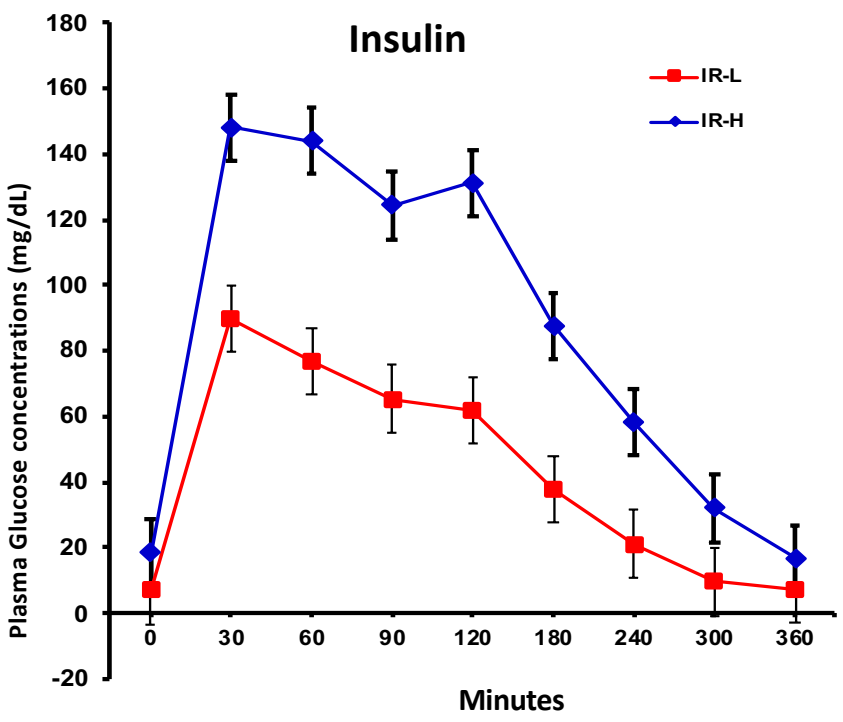


Sandhu et al JAFC 2016



Insulin Resistance Status Responses to Typical Western Style Meal





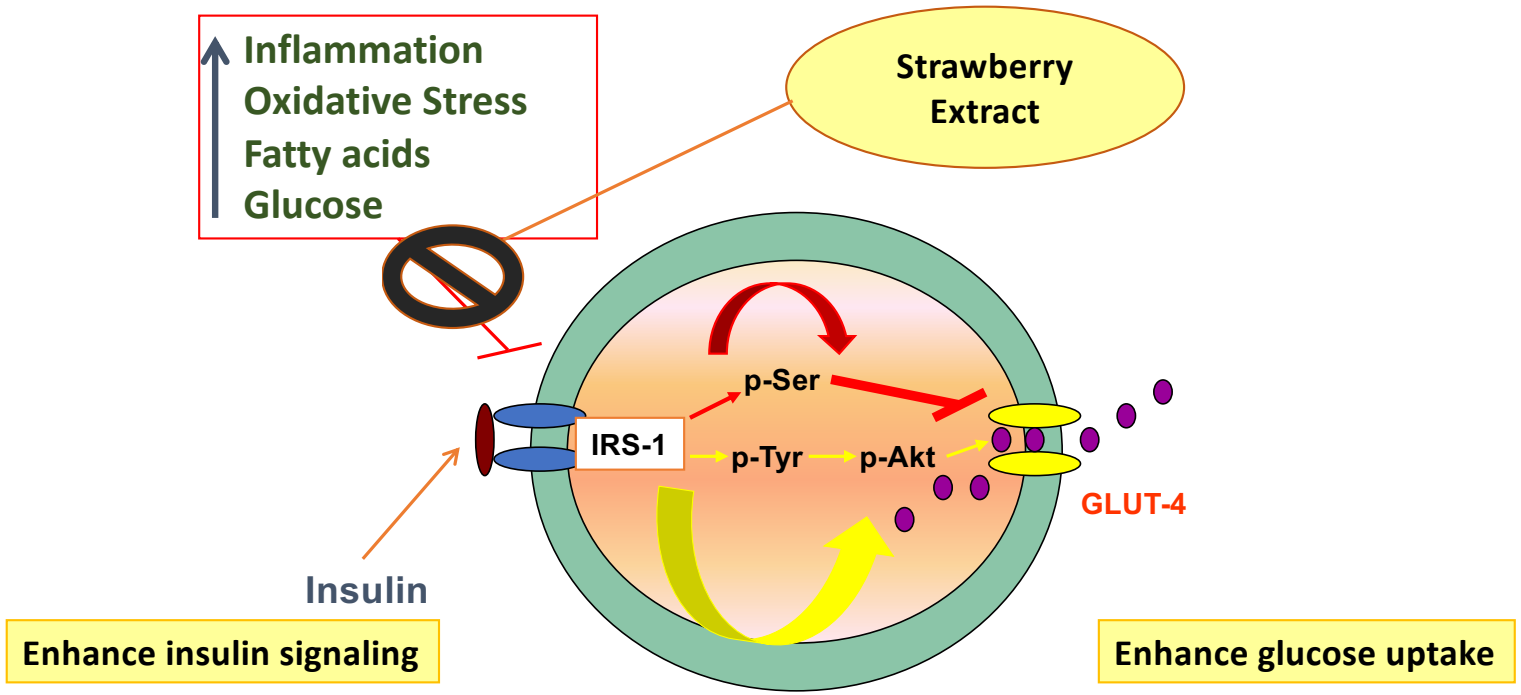
Greater the insulin resistance, greater the insulin demand for glucose control

-Hyperinsulinemia-

Burton-Freeman Lab, Park et al MNFR 2016

Insulin Resistance (IR); IR-H, HOMA-IR > 2.5; IR-L, HOMA-IR: 1-2.5

Insulin Signaling (Muscle Cells)



Insulin-Responsive Cells

High Carb/High Fat Breakfast Meal

+ Control beverage

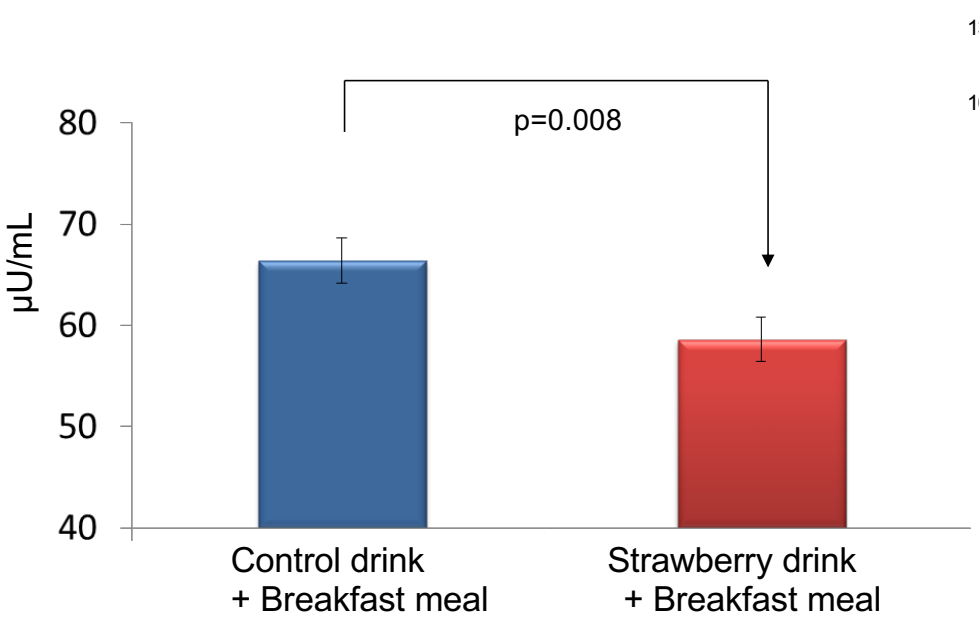
vs

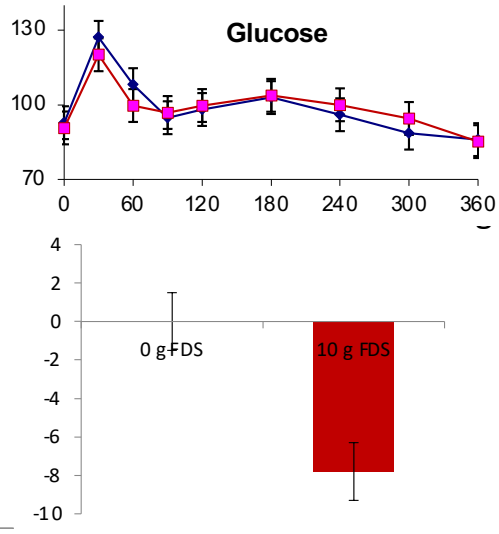
+ Strawberry beverage

~ 1 cup fresh fruit

Edirisinghe et al. BJN 2011

Strawberry (~1 cup or 110 g Fresh) vs Control Drink with a Meal Reduced the Amount of Insulin Needed for Glucose Control in Overweight Men and Women





~12% decrease in Insulin

Edirisinghe et al. BJN 2011

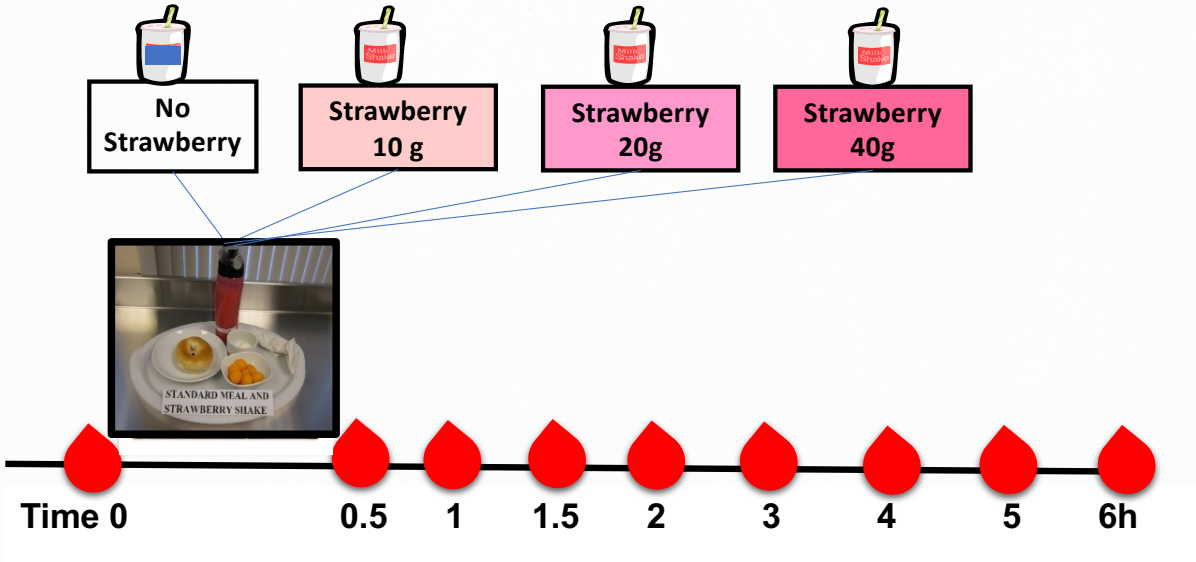
Insulin Resistance and Strawberries

Could strawberries help improve insulin action in people who are insulin resistant?

Implications:

- Reverse insulin resistance
- Prevent the transition to diabetes

Acute Challenge Meal Study



Blood Sampling

Randomized 4 treatment crossover

Park et al. MNFR 2016

Beverage Nutrient Composition

Insulin Resistance Dose-Response Study

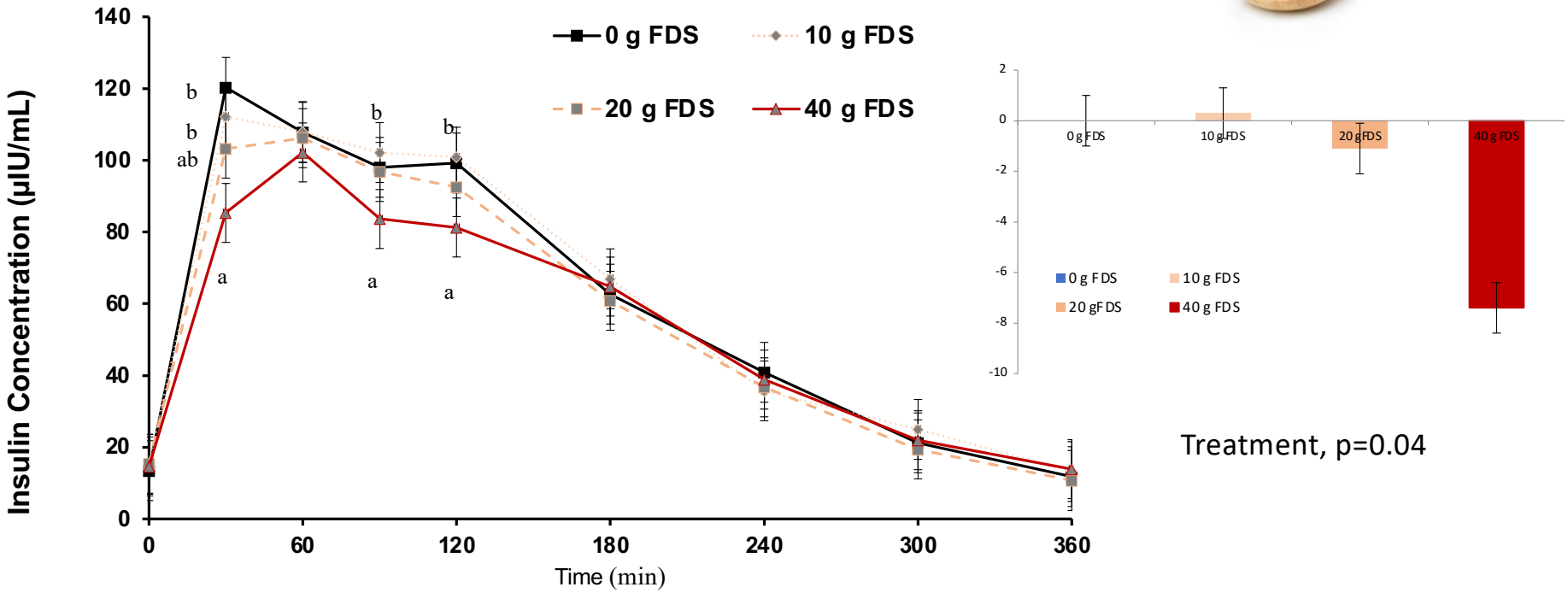
	0 g FDS Control Beverage	10 g FDS Strawberry Beverage	20 g FDS Strawberry Beverage	40 g FDS Strawberry Beverage
Calories (kcal)	324	313	310	333
Protein (g)	10	9	9	11
Carbohydrate (g)	67	67	68	73
Fiber (g)	8.5	8.3	8.2	8.7
Sugar (g)	63	62	60	61
Fat (g)	1.6	1.4	1.5	2.0
Vitamin C* (mg)	22	27	38	59
Total ANCY (mg)	0.0	42.2	87.9	154.5
Plg-3-Glc (mg)	0.0	35.2	72.3	123.8

Park et al. MNFR 2016

Less Insulin Needed

When Eating a Meal with a Strawberry Drink

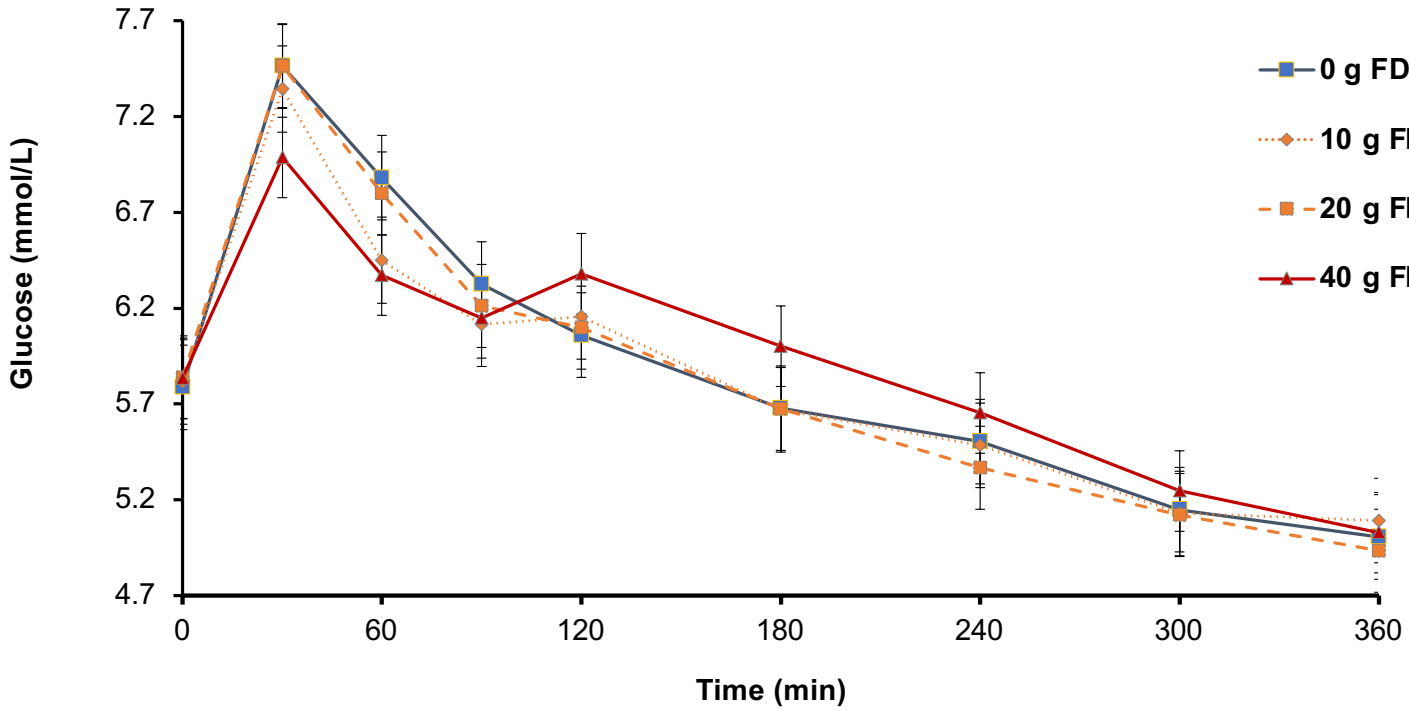
Age 40 year
BMI 40
N=21



Treatment, p=0.04

Park et al Molec Nutr Food Res. 2016

Plasma Glucose
Adults with Abdominal Obesity and Insulin Resistance



	0 g	10 g	20 g	40 g	
Insulin:Glucose Ratio	**10.5 ± 0.9^{a}**	**10.5 ± 0.9^{a}**	**9.7 ± 0.9^{ab}**	**9.0 ± 0.9^{b}**	**p= 0.008**

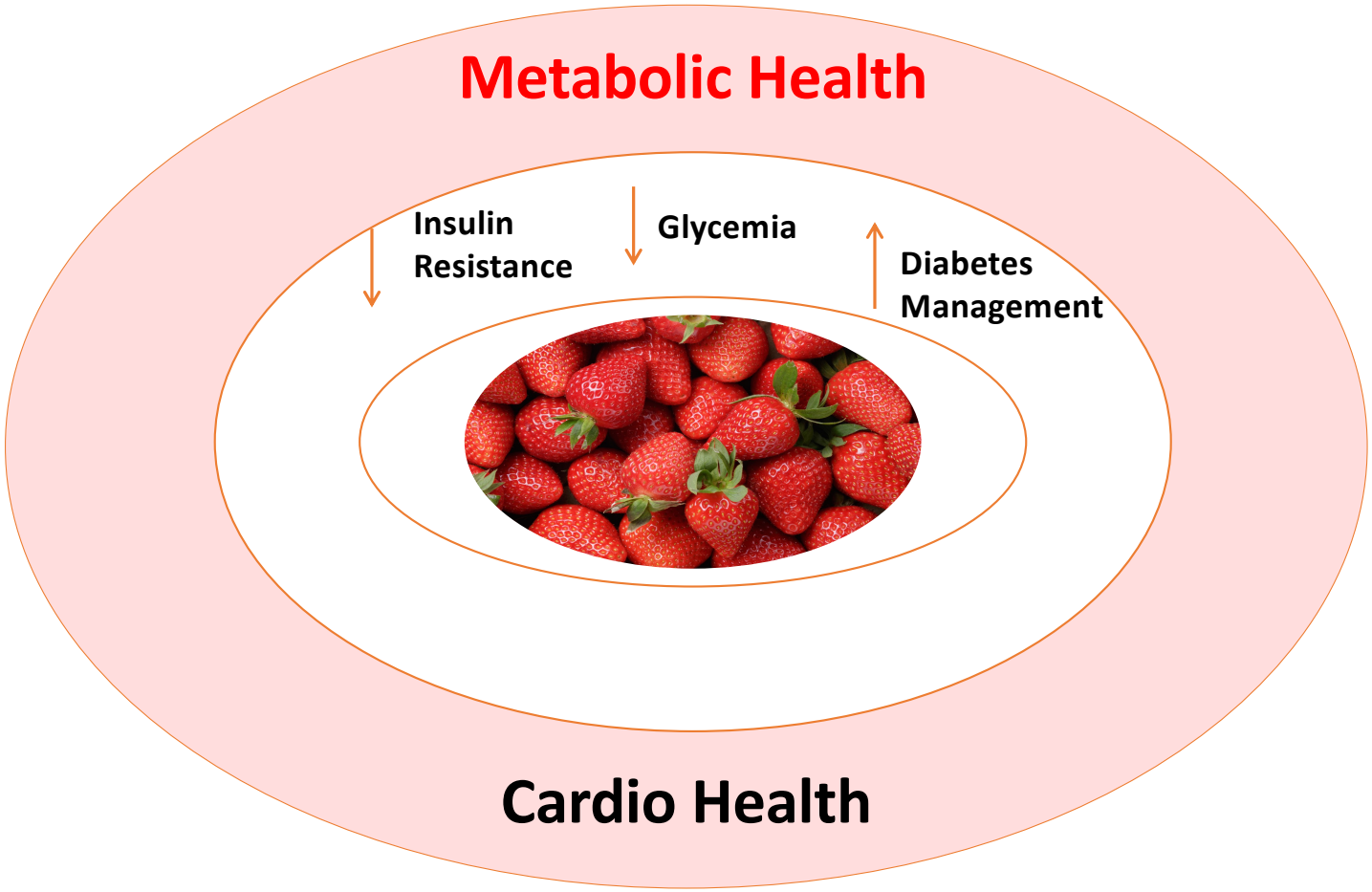
Park et al. MNFR 2016

Type 2 DM: Strawberry Intake for 6 Weeks (50g per day) Improves Glucose Control (HbA1c), Reduces Lipid Oxidation, Decreases Inflammation (hsCRP)

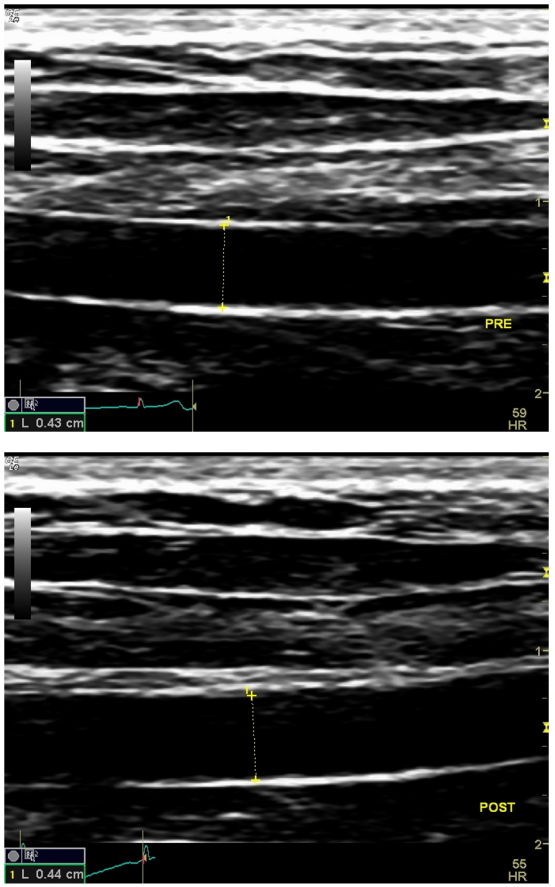
Type 2 DM: Purified Anthocyanin Supplementation for 24 weeks (160 mg bid) Reduces Dyslipidemia, Enhances Antioxidant Capacity, Improves Glycemic, Insulin Resistance, and Inflammation Status

Moezen et al 2013

Strawberries' Benefits … the Story So Far



Vessel Health - Flow Mediated Vasodilation



1% increase in diameter = 10% decrease CVD risk

Burton-Freeman Lab

Variables	Total Subjects (n=34)
Age (year)	53 ± 1
Male: Female	17 : 17
BMI (kg/m^2)	30.6 ± 0.6
SBP (mmHg)	120.3 ± 2.1
DBP (mmHg)	78.4 ± 1.6
TC (mg/dL)	203.8 ± 3.7
LDL (mg/dL)	132.9 ± 3.0
Glucose (mg/dL)	104.8 ± 1.5

Randomized, Blinded, Cross-over Design

4 weeks Strawberry intake (freeze-dried powder, 2 x 25 g/d, ~ 170 kcal)

vs

4 weeks Control Powder (packets, 2 x 25 g/d, ~ 170 kcal)

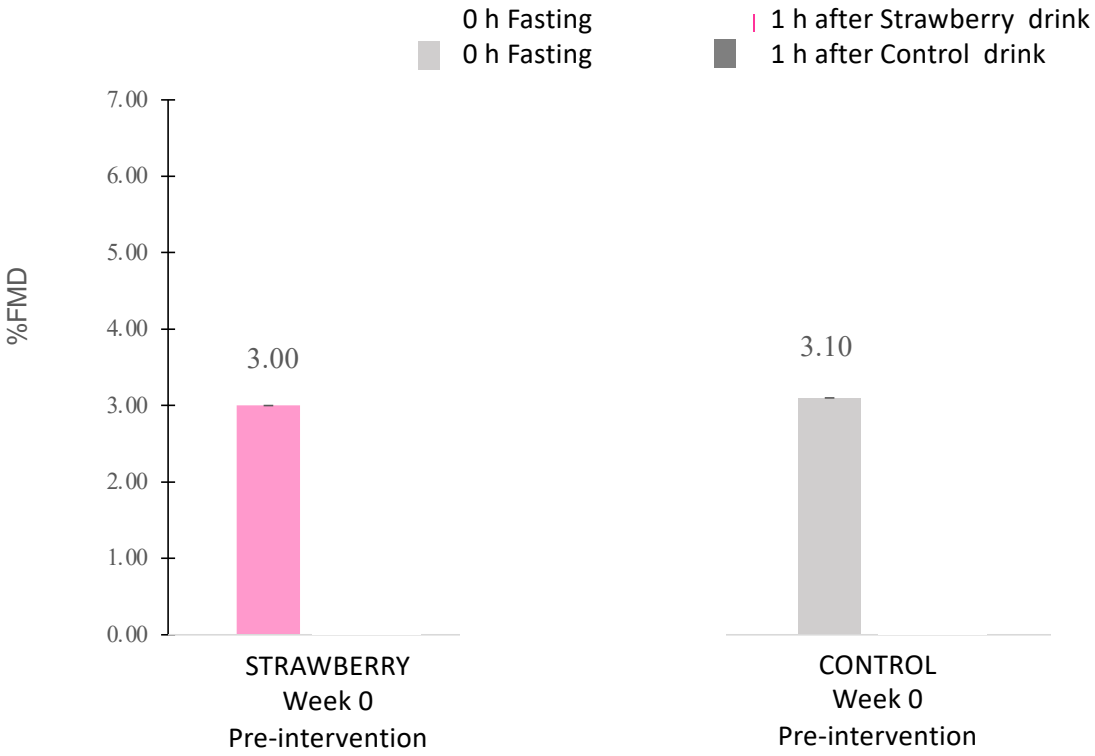
Fasting blood samples (0 h)

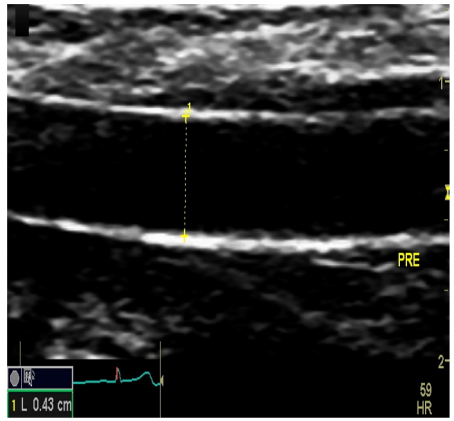
Flow mediated vasodilation (0 h and 1 h after assigned drink)

Blood Pressure (0 h, 1 h, 2 h after assigned drink)

Huang et al J Nutr 2021

Strawberry and Endothelial Function: FMD Vessel Relaxation Tone Improves





*** P < 0.05**

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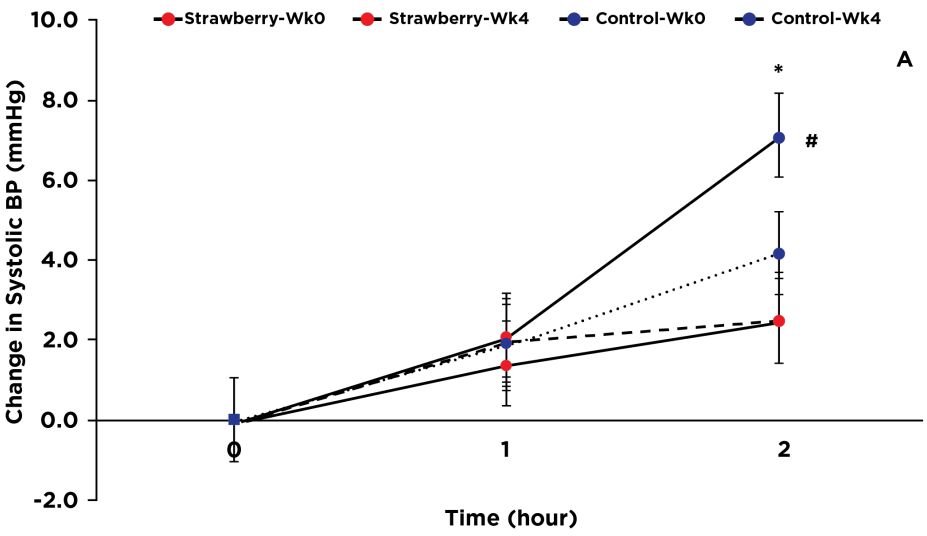
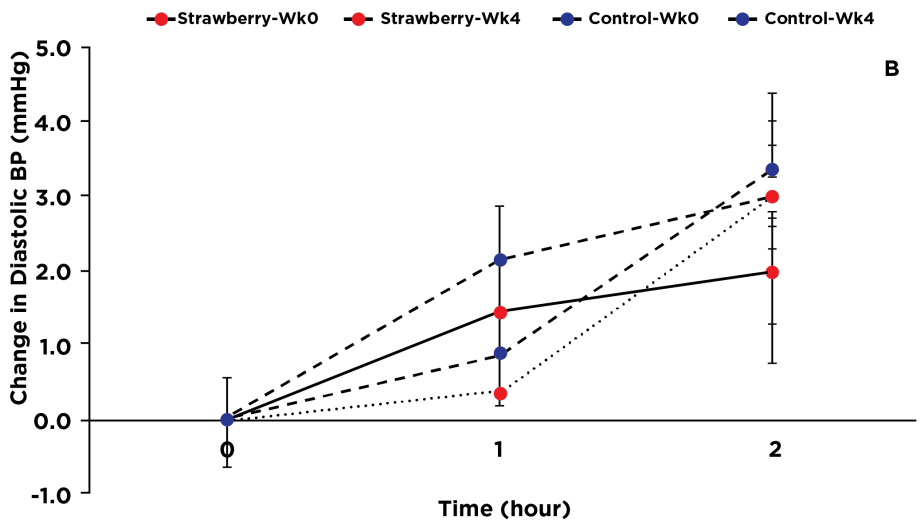
2h Systolic BP Attenuated After 4-Week Daily Strawberry Intake Compared to Energy Matched Control

SYSTOLIC



DIASTOLIC



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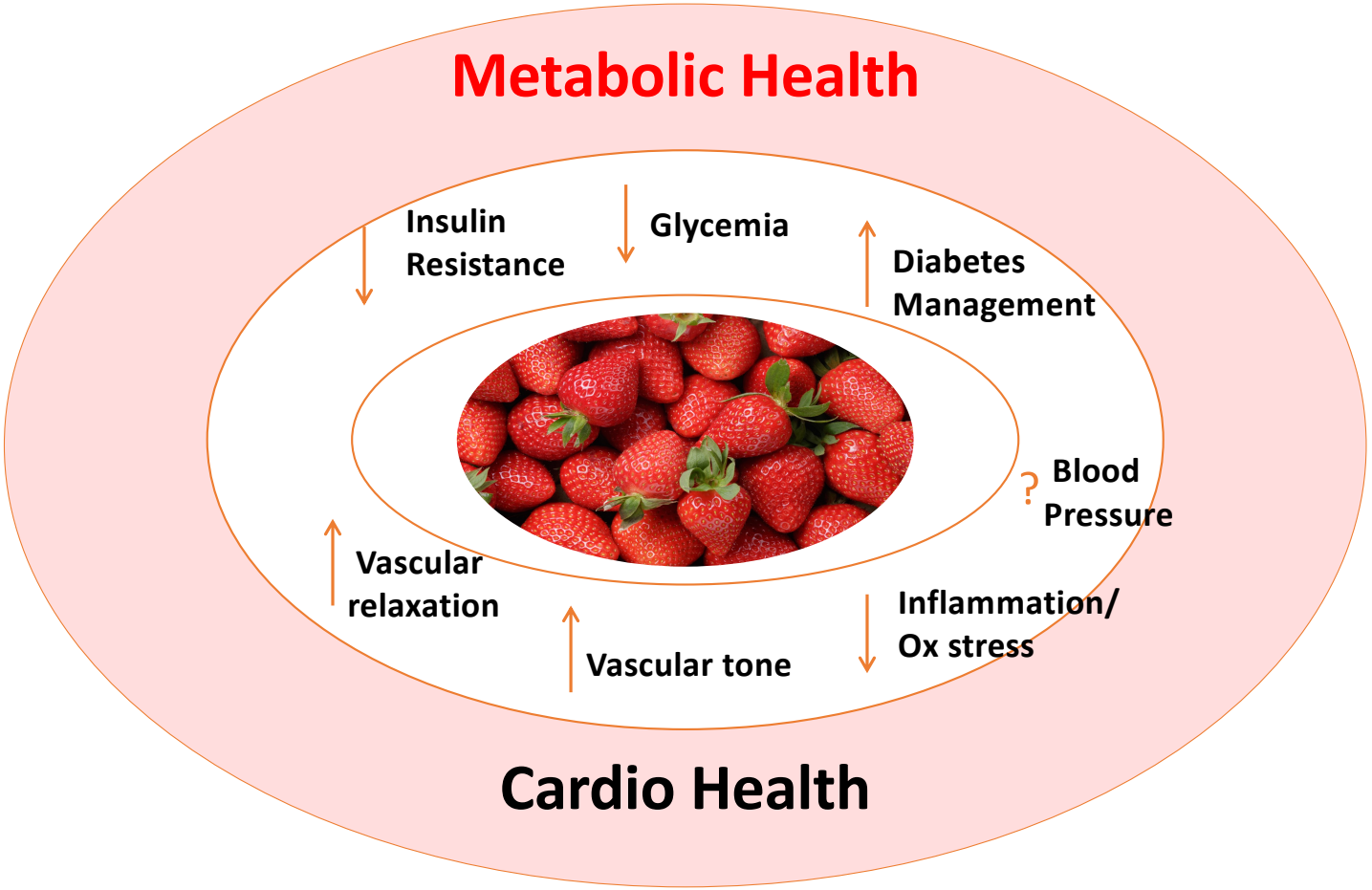
Strawberries' Benefits



Practical Implications

Addressing the Fruit Gap

Including strawberries in the diet regularly

Increases AMOUNT of total fruit consumed

Increases DIVERSITY of nutrients and phytochemical “bioactives” in the diet

Practical Implications

- Global Burden of Disease (GBD) study tells us a **DIET LOW in FRUIT** is among the **TOP 3 dietary risk factors for CVD and diabetes**

- **Increasing fruit variety lowers risk of developing diabetes**

- Evidence is required to develop policy, set recommendations, and inform people of **what foods/fruits and how much to eat to optimize health**

As little as 1 cup per day of strawberries shows beneficial effects

Future Directions in Research

- Precision nutrition for health
- Individualizing recommendations

Our Team

Our Team
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Thank You

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