A Review of Health Benefits of Cherries

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History of Cherry Human Research Studies

- Blau LW, 1950
- Jacob RJ, 2003
- Kelley DS, 2006
- Connolly DAJ, 2006
- 2009-2017, 25 more human studies

nutrients

MDPI

Review

A Review of the Health Benefits of Cherries

Darshan S. Kelley [1,2,*], Yuriko Adkins [1,2] and Kevin D. Laugero [1,2]

Major Nutrients in Cherries

- Polyphenols
- Carotenoids (beta carotene & lycopene)
- Vitamin C and others
- Tryptophan, Serotonin & Melatonin
- Fiber
- Potassium
- Low caloric content

Sweet versus Tart Cherries

- Tart cherries have higher concentration of total polyphenols than sweet, but sweet cherries have higher concentration of anthocyanins than tart.
- Vary with variety, growth stage & environments, part of fruit, storage & handling (ranging 1-20% of total phenols)
- Anthocyanins very sensitive to oxidation & need to be protected

Bioavailability of Anthocyanins

- Earlier studies blood concentration peaks at 2 hr., suggesting rapid elimination.
- recent studies using radio-labelled (13C) anthocyanins report peak at 10 hr. and detectable until 48 hr.
- only 12 % 13C recovered in breath, feces and urine in 48 hr.
- More sensitive analytical methods needed to detect different metabolites

Acute Effects of Cherries on Plasma Biomarkers

*Jacob R. et al. Consumption of cherries lowers plasma urate in healthy women. J Nutr. **2003**; 133:1826-1829*

Biomarker	Baseline	5 h
Urate (μmol/L)	214 ± 13	183 ± 15*
CRP (mg/L)	4.29 ± 2.18	3.59 ± 1.59
Nitric Oxide (μmol/L)	37.4 ± 5.2	31.6 ± 2.1

*Different from baseline, $P<0.05$

2006 WHNRC Cherry Study

Specific Aims

Determine the effects of cherry consumption on:

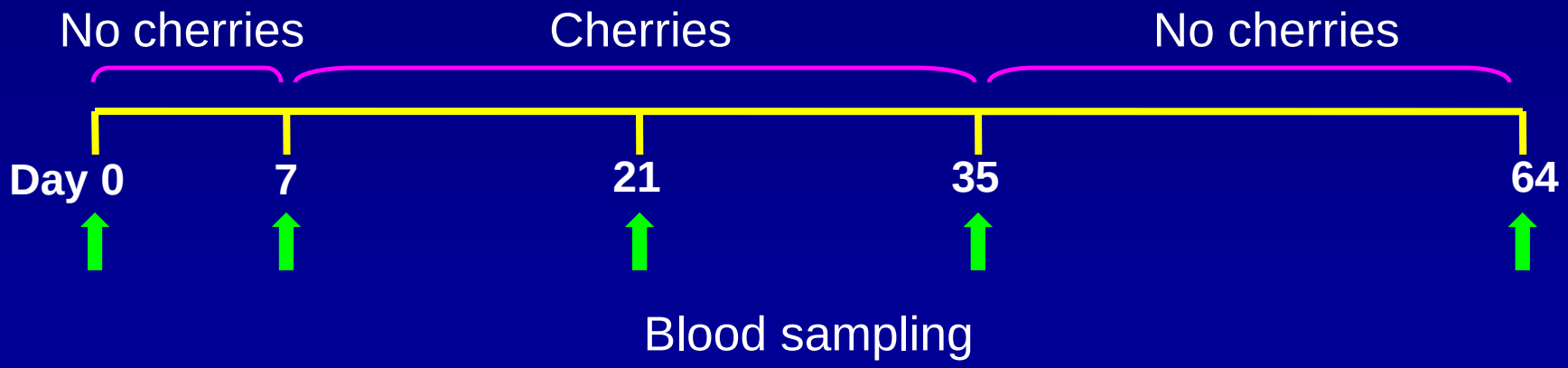
1. Serum concentration of markers of inflammation
2. Blood lipids, lipoproteins, particle size & number;
3. Hematology & clinical chemistry panels including insulin

Subject Characteristics and Study Design WHNRC 2006

2 men, 18 women

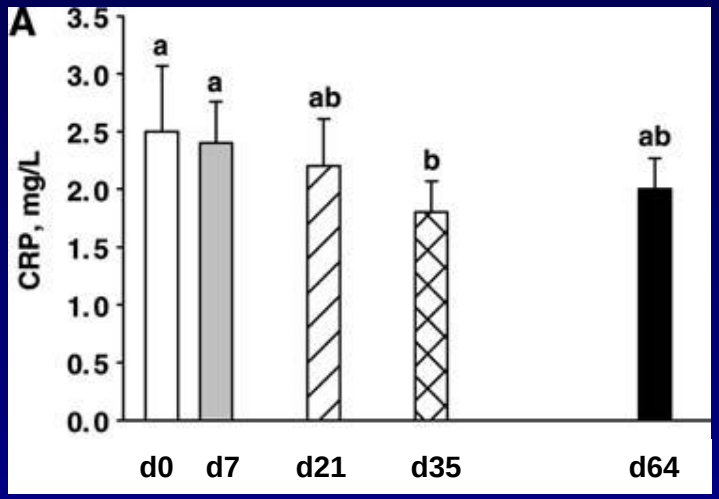
Variable	Min	Max	Mean	SEM
Age (yrs)	45	61	50	0.9
Weight (kg)	53.6	113.0	73.3	3.6
Height (cm)	150.5	186.0	166.3	2.2
BMI	19.6	30.4	26.3	0.9

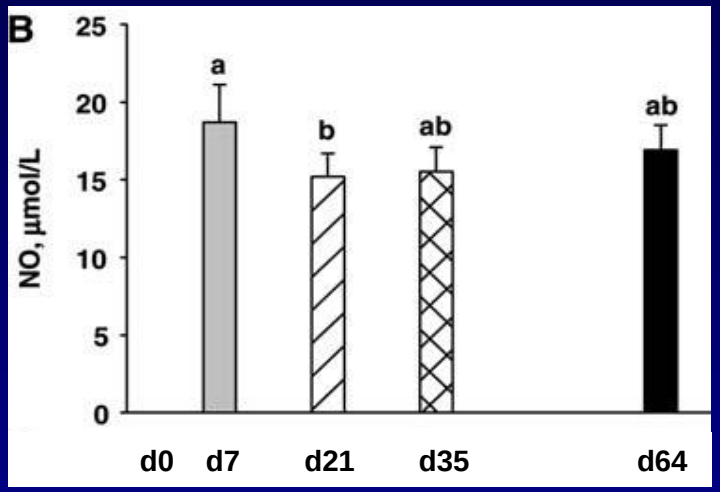
Intervention: 280 g cherries (~45 cherries)

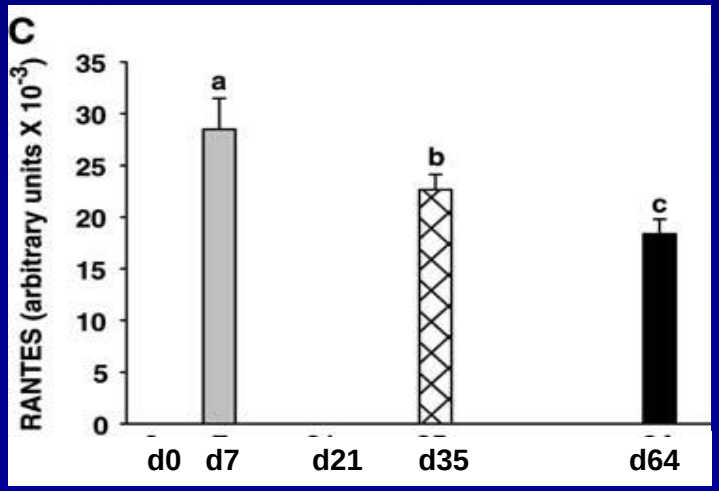


Effect Of Cherry Consumption On Circulating Markers Of Inflammation

Kelley et al. J Nut. 2006; 136:981-986







No changes in:

- IL-6
- ICAM-1
- TIMP-2
- Glucose
- Insulin
- Blood lipids
- Lipoprotein size and numbers
- Haematological and chemistry panels

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Consumption of Bing Sweet Cherries Lowers Circulating Concentrations of Inflammation Markers in Healthy Men and Women[1,2]

Darshan S. Kelley,*[3] Reuven Rasooly,* Robert A. Jacob,* Adel A. Kader,† and Bruce E. Mackey**

*U.S. Department of Agriculture/ARS, Western Human Nutrition Research Center, and Department of Nutrition, University of California, Davis, CA 95616; †Department of Plant Sciences, University of California, Davis, CA 95616; and **Western Regional Research Center, ARS, U.S. Department of Agriculture, Albany, CA 94710

J. Nutr. 2006; 136:981-986

Summary of Findings
Kelley DS et. al. 2013

- Changes in plasma concentrations of biomarkers in our human study caused by cherries suggest potential decreases in:
- Inflammation (CRP, ferritin, IL-18, TNFα, IL-1Ra, ET-1, EN-RAGE, PAI-1)
- Arthritis (CRP, TNFα, IL-18, IL-1Ra)
- Diabetes and CVD (CRP, Ferritin, ET-1, EN-RAGE, PAI-1, IL-18)
- Hypertension (ET-1)
- Cancer (EGF, ET-1)

JN THE JOURNAL OF NUTRITION

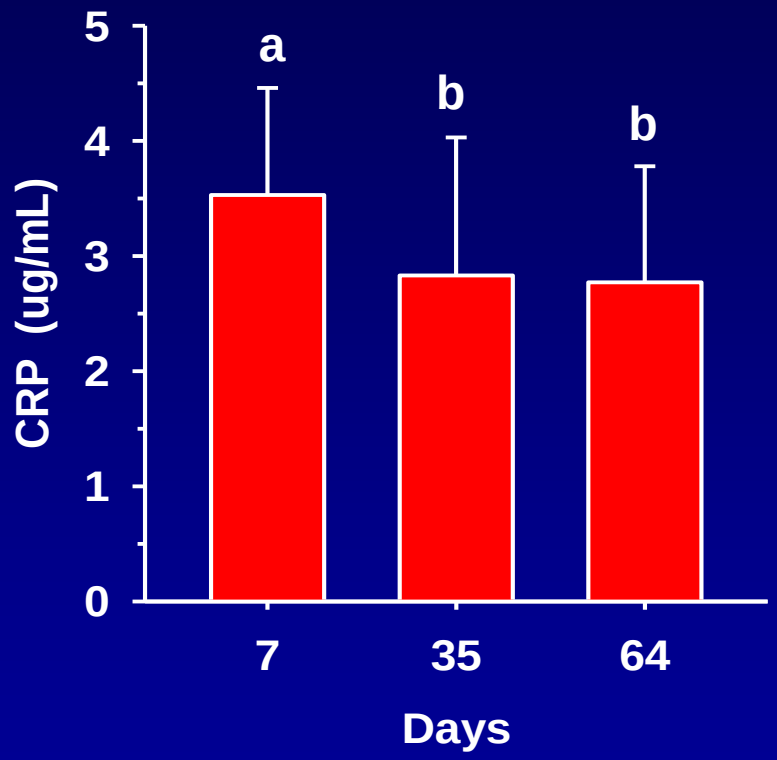
Sweet Bing Cherries Lower Circulating Concentrations of Markers for Chronic Inflammatory Diseases in Healthy Humans[1-4]

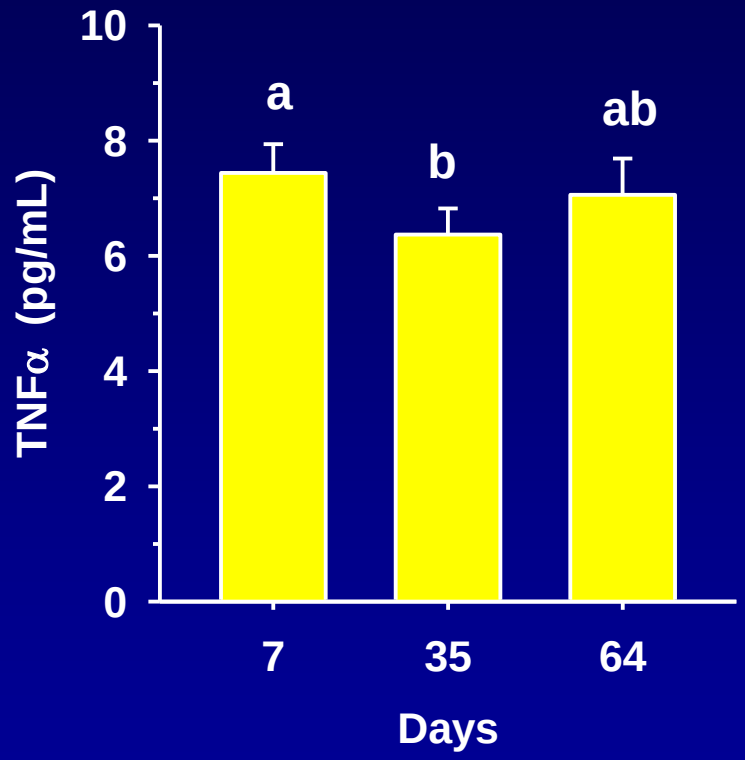
Darshan S. Kelley[5]*, Yuriko Adkins[5], Aurosis Reddy[5], Leslie R. Woodhouse[5], Bruce Mackey[6], and Kent L. Erickson[7]

[5]Western Human Nutrition Research Center, Agricultural Research Service, USDA, and Department of Nutrition, University of California, Davis, CA; [6]Western Regional Research Center, Agricultural Research Service, USDA, Albany, CA; and [7]Department of Cell Biology and Human Anatomy, School of Medicine, University of California, Davis, CA

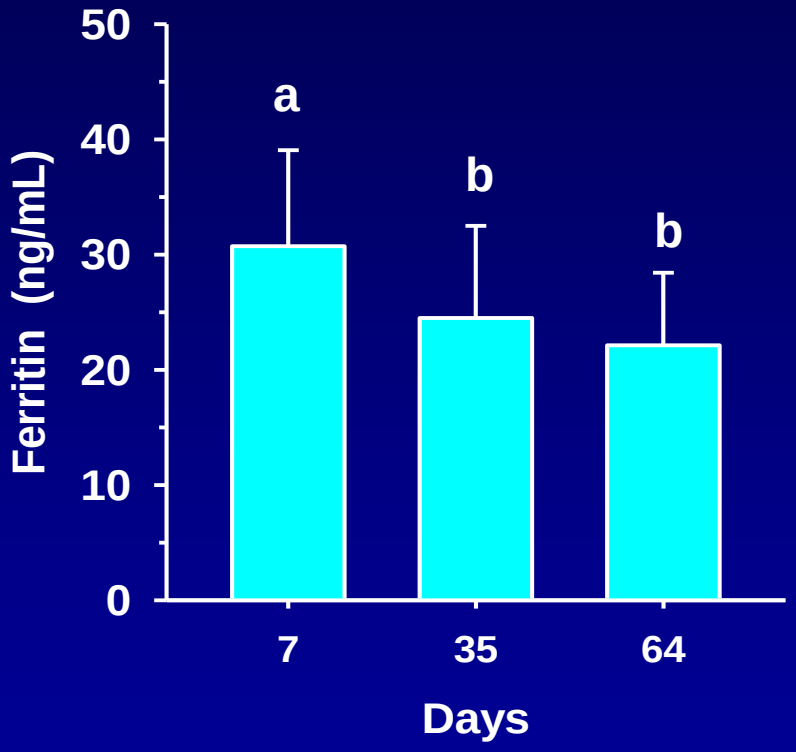
J. Nutr. 2013 (vol. 143)

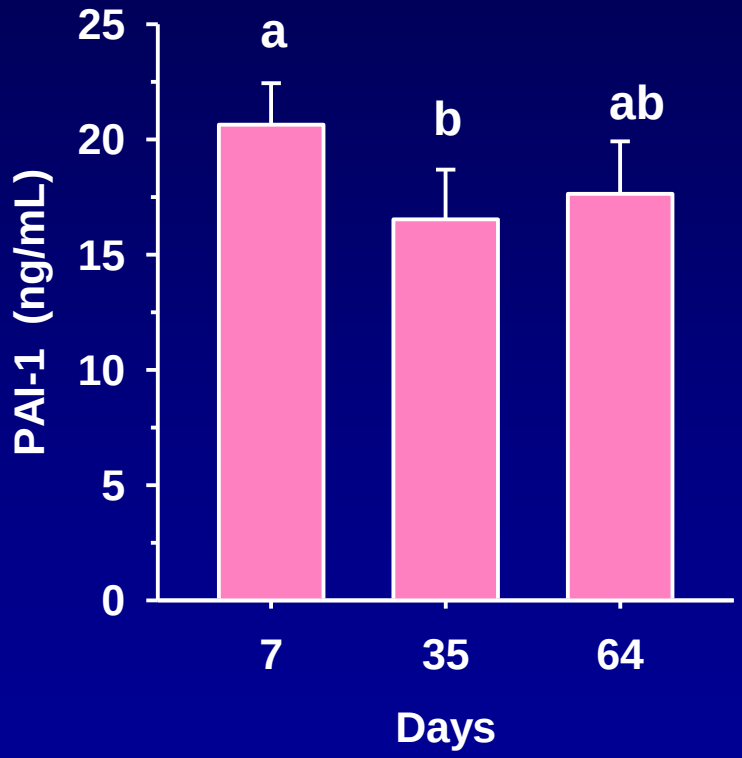
Effects of Bing Sweet Cherry Consumption on CRP and TNFα



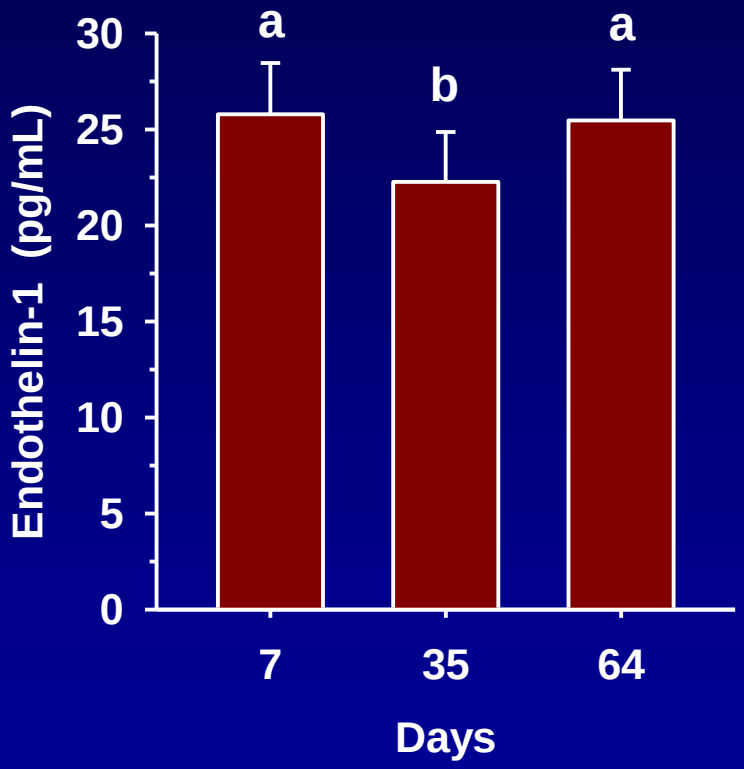


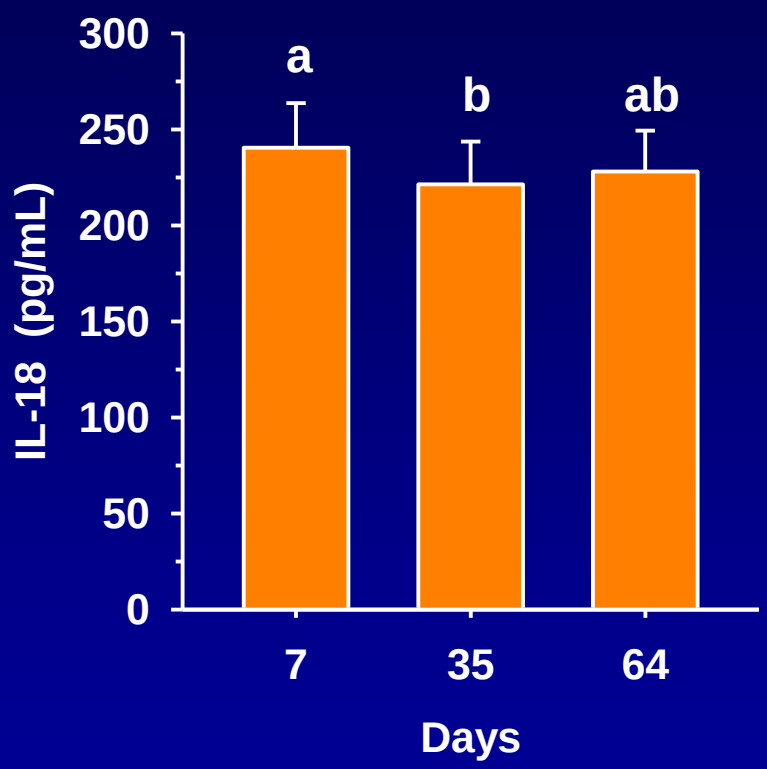
Effects of Bing Sweet Cherry Consumption on Ferritin and PAI-1



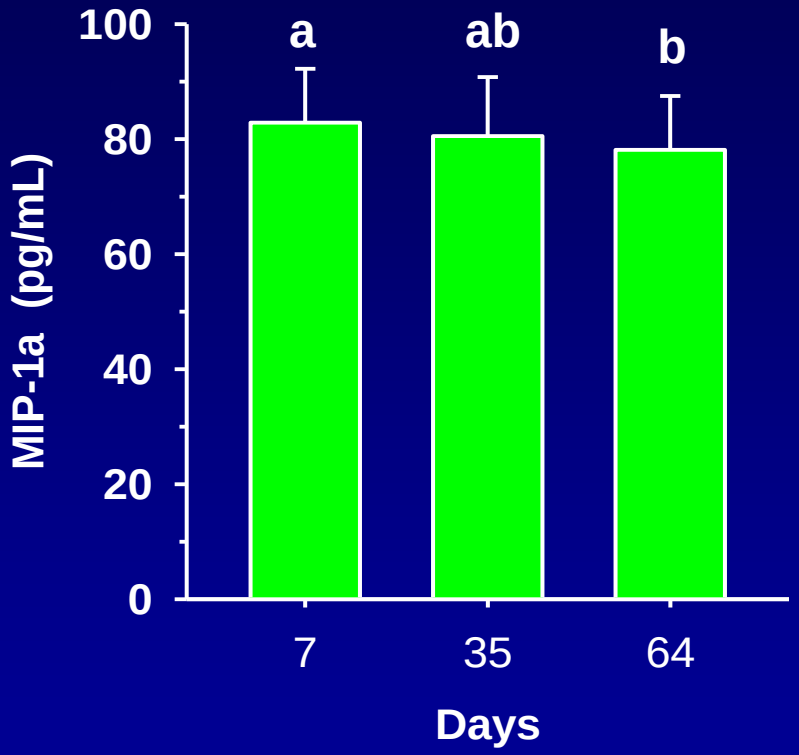


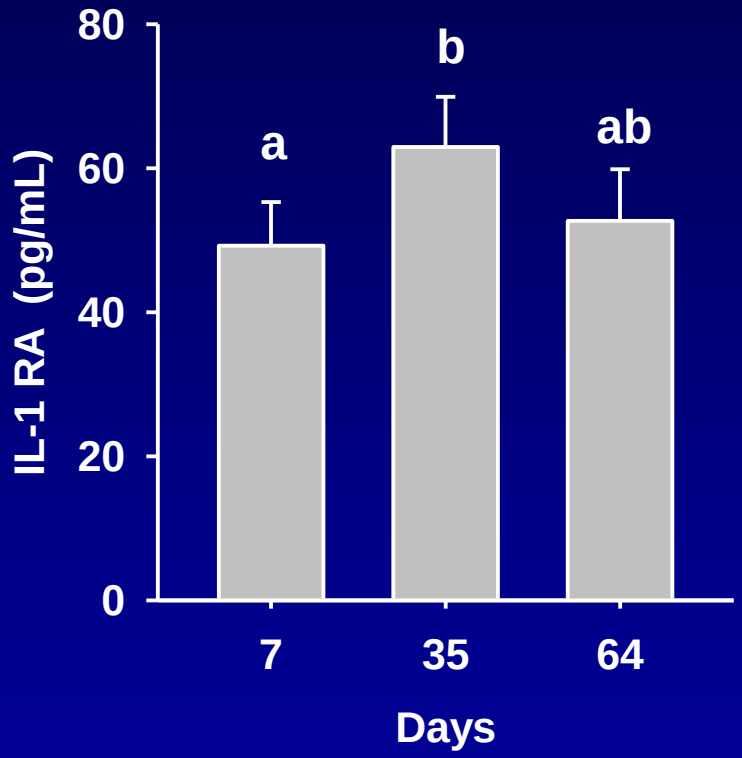
Effects of Bing Sweet Cherry Consumption on Endothelin-1 and IL-18



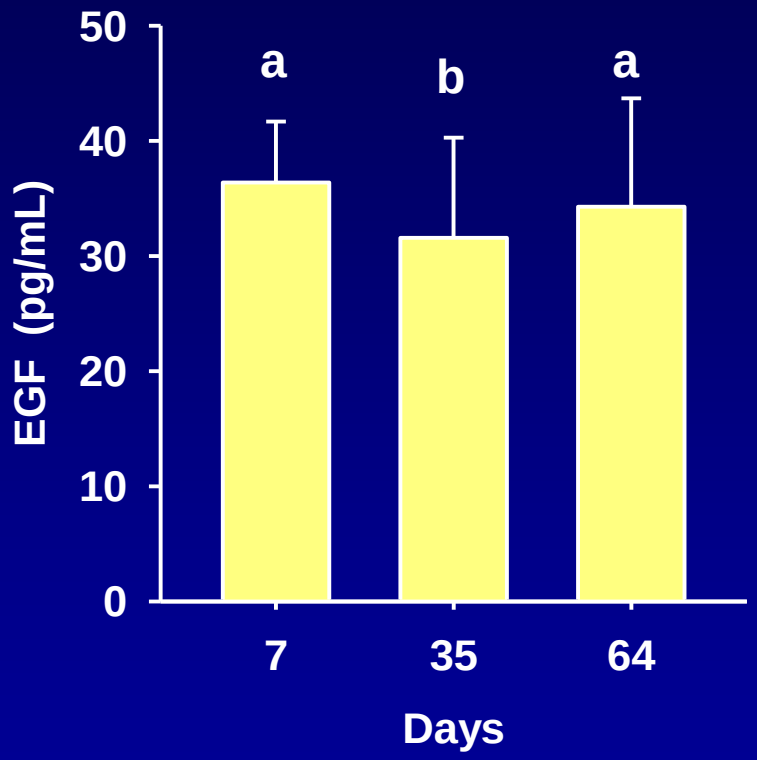


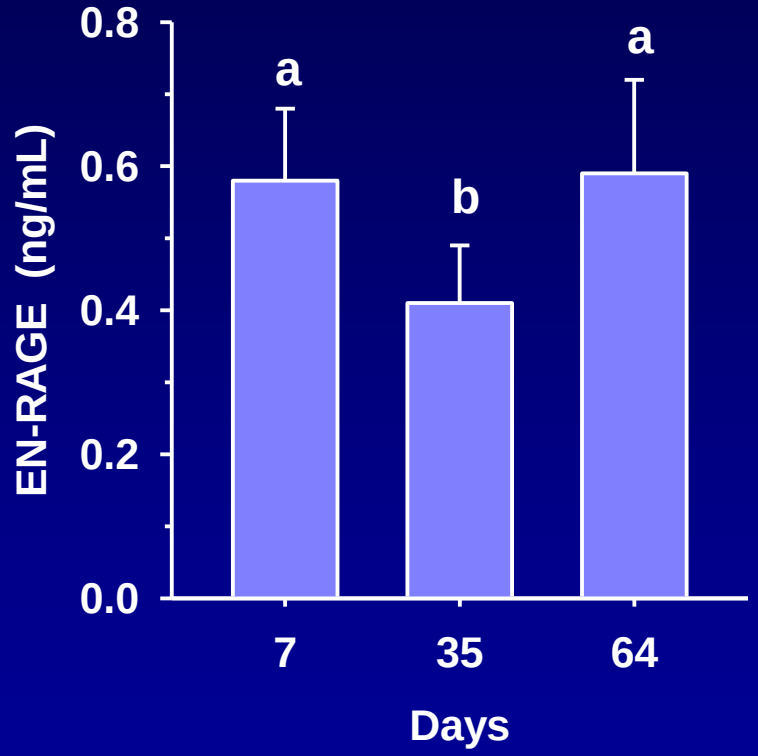
Effects of Bing Sweet Cherry Consumption on MIP-1α and IL-1RA





Effects of Bing Sweet Cherry Consumption on EGF and EN-RAGE





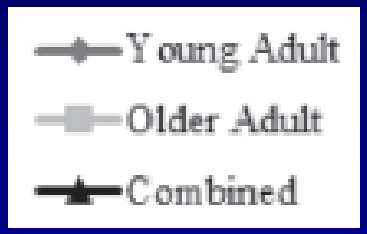
Summary of Human Cherry Studies

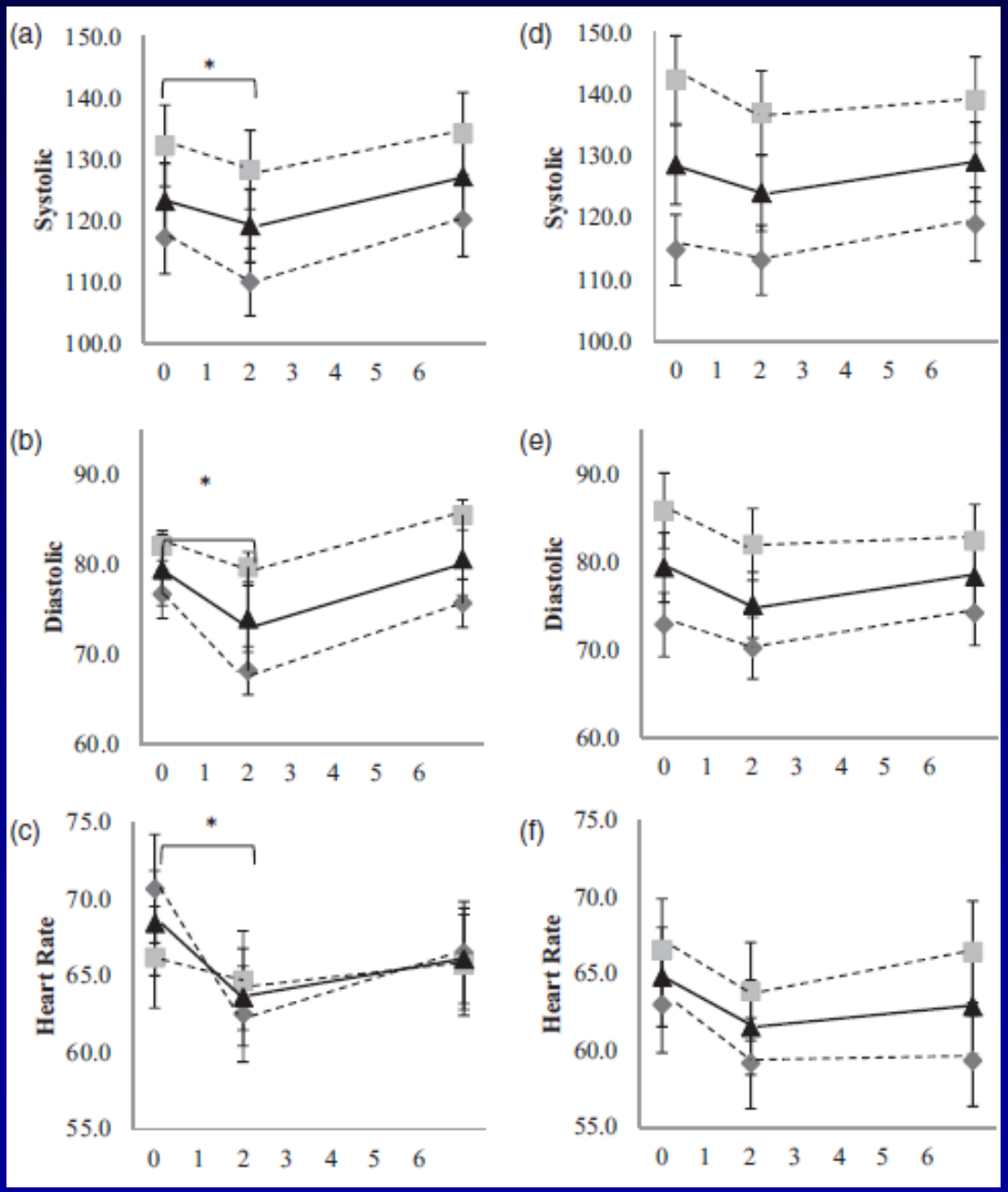
- 29 studies published; 20 with tart & 7 with sweet, 2 UK
- Oxidative stress 8/10
- Inflammation 11/16
- Exercise 8/9
- Arthritis 5/5
- Sleep 4/4
- Stress 2
- Diabetes/CVD, (HbA1c, EN-RAGE, FBG, BP, blood lipids) 9 studies

Risk Factors for Diabetes & Cardio Vascular Disease

- ↓ HbA1C 1in diabetics; ENRAGE 1; No change in fasting glucose & insulin in healthy subjs-2
- ↓ VLDL & TG/HDL in obese-1; no change in healthy subjects-2
- ↓ SBP in 4; Both SBP & DBP in 2; no change 1. Acute vs chronic effects

Acute Effects of Cherries on BP





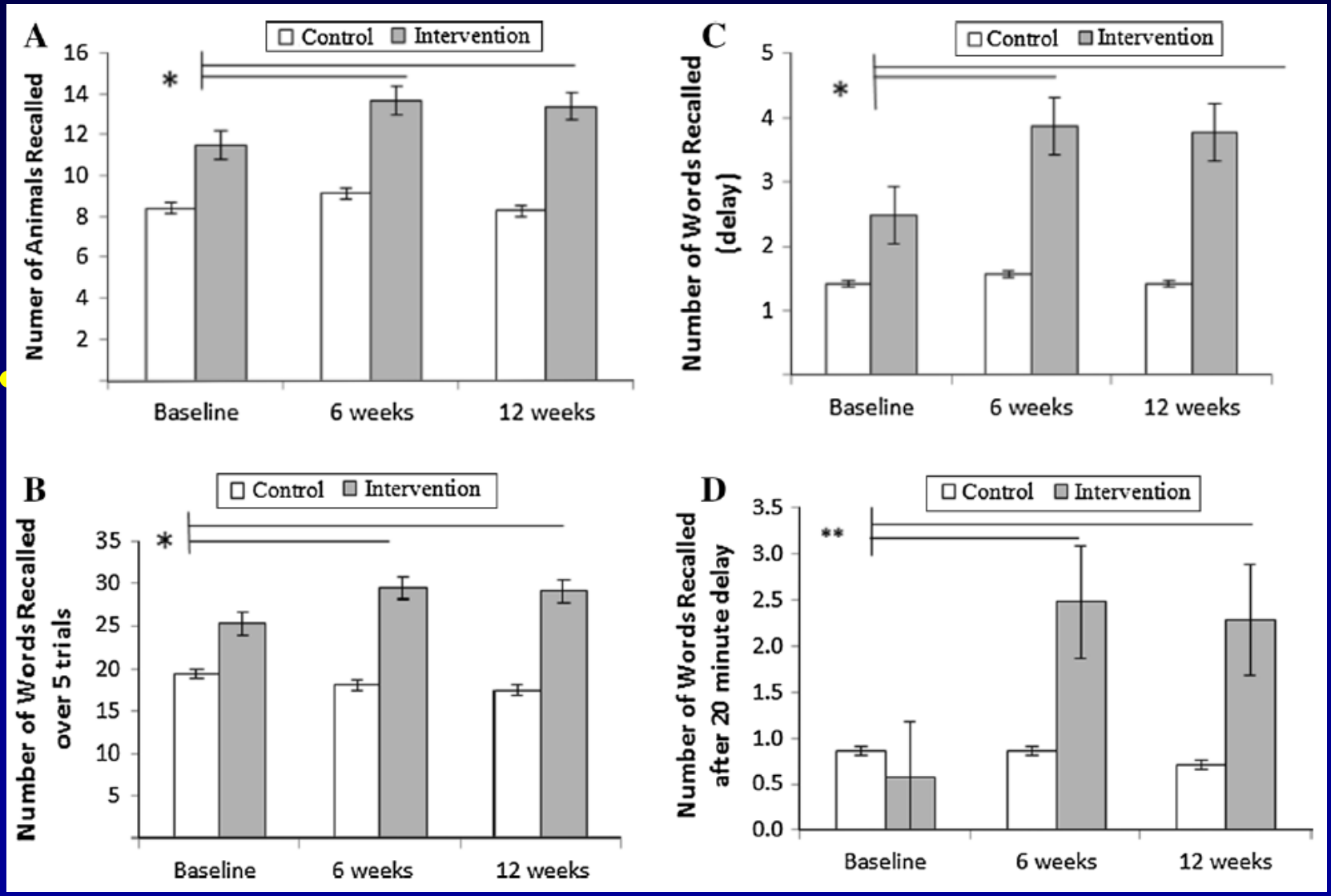
Kent K 2015, Int J Food Sci &Nutr 67:47

Cherries and Blood Pressure

	Control group			Intervention group		
	Baseline $n = 25$	6 weeks $n = 21$	12 weeks $n = 21$	Baseline $n = 24$	6 weeks $n = 21$	12 weeks $n = 21$
Systolic BP*	140 ± 19.7	138.5 ± 12.3	137.0 ± 10.1	138.2 ± 16.4	133.7 ± 9.9	130.5 ± 12.2
Diastolic BP	80.6 ± 9.8	81.0 ± 8.0	81.3 ± 11.6	78.6 ± 11.7	77.0 ± 9.9	77.0 ± 12.6
Heart Rate	70.2 ± 10.2	70.2 ± 11.1	74.2 ± 11.8	67.9 ± 10.7	66.0 ± 7.2	67.5 ± 7.9

Kent K, Eur. J Nutr., 56:333, 2017

Effect of Cherries on Memory



Kent K, Eur. J Nutr., 56:333, 2017

Effect of cherries on HbA1C, BP & Lipids

Variable	Week 0	Week 6
Body weight (kg)	72.8 ± 14.9	69.9 ± 13.6*
BMI (kg/m^2)	29.6 ± 4.3	28.7 ± 3.9*
FBS (mg/dl)	158.3 ± 43.4	145.3 ± 38.0
HbA1c (%)	7.9 ± 1.6	7.5 ± 1.2*
Systolic blood pressure (mmHg)	129.1 ± 15.7	123.1 ± 12.8**
Diastolic blood pressure (mmHg)	81.7 ± 8.1	76.3 ± 8.7**
Total cholesterol (mg/dl)	196.4 ± 29.7	184.9 ± 22.0
LDL-cholesterol (mg/dl)	105.2 ± 19.6	96.9 ± 15.0
HDL-cholesterol (mg/dl)	47.6 ± 7.1	48.2 ± 7.9
Triacylglycerol (mg/dl)	158.5 ± 43.2	145.5 ± 49.1

Notes: Significantly different from baseline (Wilcoxon signed test): *$p < 0.01$; **$p < 0.05$

Variable (mg/dl)	Week 0	Week 6
Total cholesterol	213.9 ± 27.0	193.2 ± 20.2[a]
LDL-cholesterol	118.4 ± 14.7	103.6 ± 13.5[a]
HDL-cholesterol	47.1 ± 5.1	46.3 ± 8.6
Triacylglycerol	161.4 ± 37.3	157.3 ± 48.9

Notes: [a]Significantly different from baseline, $p < 0.05$ (Wilcoxon signed test)

Ataie-Jafari A, Nutr. & Food Sci. 38:355, 2008

Sleep & Cognitive Functions

- ↑ quantity & quality of sleep in all 4 stds
- ↓ Urinary cortisol, stress & anxiety 2 stds
- improved memory, mood, and cognitive functions in 2 stds (Spanish patent # ES 2342 141 B1); sweet cherry based product to improve mood & insomnia

Summary, Health Benefits of Cherries

- Decrease oxidative stress & inflammation
- Decrease exercise induced pain, muscle damage & enhanced recovery
- Decrease risk for diabetes and CVD (blood pressure, HbA1C, lipids)
- Lower attacks of gout & osteoarthritis
- Decrease stress & anxiety; improve sleep, memory & cognitive functions
- Others (cancer, neuroprotection)

Future Needs

- Desperately need a cherry product that retains the nutrient composition and is stable for use throughout yr. Someone knowledgeable is needed to pursue it.
- Randomized, placebo controlled, blinded intervention studies with adequate control, power, and state of the art technology are needed
- Critical analysis of the available literature
- Health claims (inflammation, BP, glycemic index, sleep)
- Identification of bioactive compounds
- Mechanisms involved

Collaborators

- California Cherry Advisory Board
- Washington State Fruit Commission
- USDA, ARS, WHNRC
- Robert A. Jacob, PhD, WHNRC
- Adel A. Kader, PhD, UCD
- Bruce E. Mackey, PhD, WRRC
- Yuriko Adkins, PhD, WHNRC
- WHNRC colleagues (Kevin Laugero PhD, Brian Bennett PhD, Charles Stephenson PhD)

Dietary Supplements

- A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet.
- The "dietary ingredients" in these products may include: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites.

New Dietary Ingredient

- A "new dietary ingredient" meets the definition for a "dietary ingredient" and was not sold in the U.S. in a dietary supplement before October 15, 1994.

- Manufacturer (and distributor) must demonstrate to FDA why the ingredient is reasonably expected to be safe for use in a dietary supplement, unless it has been recognized as a food substance and is present in the food supply

Role of FDA in regulating dietary supplements

- A firm is responsible for determining that the dietary supplements it manufactures or distributes are safe and that any representations or claims made about them are substantiated by adequate evidence to show that they are not false or misleading.
- Dietary supplements do not need approval from FDA before they are marketed, but manufacturer needs to register with FDA.

Who is responsible to ensure the safety of dietary supplements

- By law (DSHEA), the manufacturer is responsible for ensuring that its dietary supplement products are safe before they are marketed

- there are no provisions in the law for FDA to "approve" dietary supplements for safety or effectiveness before they reach the consumer. Under DSHEA, once the product is marketed, FDA has the responsibility for showing that a dietary supplement is "unsafe," before it can take action to restrict the product's use or removal from the marketplace.

Types of claims for dietary supplements

- By law, manufacturers may make three types of claims for their dietary supplement products.
- **Health claims:** the link between a food substance and disease or a health-related condition

- **Structure/function claims:** intended benefits of using the product

- **Nutrient content claims:** the amount of a nutrient or dietary substance in a product.

Substantiation Standard for Claims, FDA

- Meaning of the claims being made
- Relationship of the evidence to the claim
- Quality of the evidence
- Totality of evidence

Information that May be Used

- **Intervention studies-** Randomized, blinded, placebo controlled; study duration & number of participants; inclusion/exclusion criteria; baseline values; outcome measures; quality of analytical methods, statistical analysis; dietary advice & assessment; compliance; attrition; provide **causal evidence** to substantiate the effect of supplement

- **Observational studies-** correlation between dietary intake & tissue concentration (blood, urine, hair, tissue) of a nutrient and biomarker for disease. Assessment of dietary intake, food or food component. **Do not provide causal evidence** but associations only.

Totality of Publically Available Evidence

- Number & type of studies
- Number of subjects in each group
- Methodological quality
- Outcomes- beneficial, no & adverse effects
- Size of effect
- Peer-reviewed publications
- **Critical Review of public information**
- Expert panels (NIH, CDC, NAS, AHA)
- Relevance to US population