



ILSI

North America

# Nutrition Briefs

July 2016

## Cardiovascular Disease

### **L-Arginine Supplementation Alleviates Postprandial Endothelial Dysfunction When Baseline Fasting Plasma Arginine Concentration Is Low: A Randomized Controlled Trial in Healthy Overweight Adults With Cardiometabolic Risk Factors**

A. Deveaux, I. Pham, S.G. West, E. André, F. Lantoin-Adam, P. Bunouf, et al

*Journal of Nutrition*, Vol. 146, No. 7; pp. 1330–1340

doi: 10.3945/jn.115.227959

Link to full text: [Click here](#)

**Significance:** Supplementation with low-dose sustained release arginine alleviates postprandial endothelial dysfunction in healthy hypertriglyceridemic waist adults when the baseline plasma arginine concentration is relatively low.

This randomized, double-blind, 2-period crossover, placebo-controlled trial examined the effects of low dose sustained-release (SR) l-arginine supplement on postprandial endothelial function and investigated whether this effect may vary by baseline arginine status in 33 healthy overweight adults with cardiometabolic risk factors. Subjects with BMI 25 to >30 kg/m<sup>2</sup> and hypertriglyceridemic waist (HTW) phenotype [plasma triglycerides > 150 mg/dL; waist circumference > 94 cm (men) or > 80 cm (women)] were randomized to 1.5 g SR-l-arginine 3 times/d (4.5 g/d) or placebo. In the total population, the effects of SR-arginine supplementation on postprandial endothelial function were mixed and largely varied with baseline fasting arginine concentration. In the lower half of the population (below the median of 78.2 μmol arginine/L plasma), SR-arginine supplementation attenuated the postprandial decrease in both flow-mediated dilation (FMD) (29% decrease with SR-arginine compared with 50% decrease with placebo) and Framingham reactive hyperemia index (fRHI) (5% increase with SR-arginine compared with 49% decrease with placebo), resulting in significantly higher mean ± SEM values with SR-arginine (FMD: 4.0% ± 0.40%; fRHI: 0.41 ± 0.069) than placebo (FMD: 2.9% ± 0.31%; fRHI: 0.21 ± 0.060) at the end of the postprandial period (P < 0.05).

### **The Alternative Healthy Eating Index Is Associated With a Lower Risk of Fatal and Nonfatal Acute Myocardial Infarction in a Chinese Adult Population**

N. Neelakantan, N. Naidoo, W-P. Koh, J.-M. Yuan, R.M. van Dam

*Journal of Nutrition*, Vol. 146, No. 7; pp. 1379–1386

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**Significance:** Adherence to dietary recommendations as reflected in the Alternative Healthy Eating Index-2010 was associated with a substantially lower risk of fatal and nonfatal acute myocardial infarction in an Asian population, and independent of traditional cardiovascular risk factors.

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This nested case-control study investigated the association between the Alternative Healthy Eating Index (AHEI)-2010 and risk of acute myocardial infarction (AMI), and evaluated potential mediation by traditional cardiovascular risk factors (including glycated hemoglobin, high-sensitivity C-reactive protein, creatinine, plasma lipids [LDL and HDL cholesterol, triglycerides], and blood pressure) in 751 incident cases of AMI (564 nonfatal and 288 fatal) and 1443 matched controls within the prospective Singapore Chinese Health Study. Higher AHEI-2010 scores were associated with a lower risk of AMI (OR for the highest quartile compared with the lowest quartile: 0.62; 95% CI: 0.47, 0.81; P-trend < 0.001), with similar associations for fatal (OR: 0.60; 95% CI: 0.39, 0.94; P-trend = 0.009) and nonfatal (OR: 0.59; 95% CI: 0.43, 0.81; P-trend = 0.002) AMI. This association was only slightly attenuated after adjustment for potential biological intermediates (OR: 0.64; 95% CI: 0.48, 0.86; P-trend = 0.003).

### Dietary Intake and Adipose Tissue Content of $\alpha$ -Linolenic Acid and Risk of Myocardial Infarction: A Danish Cohort Study

C.S. Bork, M.U. Jakobsen, S. Lundbye-Christensen, A. Tjønneland, E.B. Schmidt, K. Overvad

*American Journal of Clinical Nutrition*, Vol. 104, No. 1; pp. 41–48

doi: 10.3945/ajcn.115.127019

Link to full text: [Click here](#)



**Significance:**  $\alpha$ -linolenic acid has no appreciable association with risk of incident myocardial infarction in either men or women.

The association between dietary intake of  $\alpha$ -linolenic acid (ALA), adipose tissue content of ALA, and risk of incident myocardial infarction (MI) were investigated in 57,053 participants, aged 50–64 y, who were enrolled in the prospective Danish cohort study Diet, Cancer and Health between 1993 and 1997. The adipose tissue content of ALA was determined in all incident MI cases and in a random sex-stratified sample of the total cohort (n = 3500). During a median of 17 y of follow-up, 2177 male and 912 female cases of MI were identified. After appropriate exclusions, 2124 men and 854 women were included for analyses of dietary intake of ALA, whereas 1994 men and 770 women were included in the analysis of the adipose tissue content of ALA. In multivariate analyses (adjusting for established CHD risk factors), weak positive associations in men and weak U-shaped associations in women were shown between both dietary intake and the adipose tissue content of ALA and risk of MI, but these associations were not statistically significant. Additional adjustments for dietary factors did not influence the observed associations numerically.

### Dietary Epicatechin Intake and 25-y Risk of Cardiovascular Mortality: The Zutphen Elderly Study

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*American Journal of Clinical Nutrition*, Vol. 104, No. 1; pp. 58–64

doi: 10.3945/ajcn.115.128819

Link to full text: [Click here](#)

**Significance:** Epicatechin intake is inversely related to coronary heart disease mortality in elderly men and to cardiovascular disease (CVD) mortality in prevalent cases of CVD.

The associations of dietary epicatechin intake with 25-y cardiovascular (CVD) mortality in elderly Dutch men were investigated. Data from the Zutphen Elderly



improved directly by diet, but paradoxically, some characteristics of vegetarian diets may promote a negative scenario that increases the risk of certain chronic diseases. Additionally, many benefits of a vegetarian diet are mediated by the gut microbiota, members of which not only have taxonomic and functional differences but also produce diverse, specific metabolites that vary according to whether the host consumes an omnivorous or a vegetarian diet.

### Cheese and Cardiovascular Disease Risk: A Review of the Evidence and Discussion of Possible Mechanisms

J. Hjerpsted, T. Tholstrup

*Critical Reviews in Food Science and Nutrition*, Vol. 56, No. 8; pp. 1389–1403

doi: 10.1080/10408398.2013.769197

Link to full text: [Click here](#)

**Significance:** The paper reviews the current evidence from studies investigating the intake of cheese and cardiovascular disease (CVD) risk or CVD risk markers in the form of cholesterol concentrations.



The purpose of this review is to give an overview of the existing literature regarding the effect of cheese intake and risk of cardiovascular disease (CVD). Studies included four human intervention studies, nine prospective studies, one prospective case-cohort study, one prospective nested case-control study, five case-control studies, five cross-sectional studies and three correlation studies. The possible mechanisms that may be of importance include calcium, protein, fermentation and the fatty acid composition of cheese. Results from four prospective studies reported no association between cheese intake and CVD risk, whereas one reported an increased risk, two reported a decreased risk and one reported no association in men but a decreased risk in women. In addition, results from four intervention studies indicated no harmful effect on cholesterol concentrations when comparing fat intake from cheese with fat from butter.

### Type 2 Diabetes

#### Plasma Alkylresorcinols, Biomarkers of Whole-Grain Wheat and Rye Intake, and Risk of Type 2 Diabetes in Scandinavian Men and Women

I. Biskup, C. Kyrø, M. Marklund, A. Olsen, R.M. van Dam, A. Tjønneland, et al.

*American Journal of Clinical Nutrition*, Vol. 104, No. 1; pp. 88–96

doi: 10.3945/ajcn.116.133496

Link to full text: [Click here](#)

**Significance:** Total whole-grain wheat and rye intake was not associated with a lower risk of type 2 diabetes (T2D) in those with high whole-grain intake; however, the proportion of whole-grain rye to whole-grain wheat intake, indicated by the plasma C17:0-to-C21:0 ratio, was inversely associated with T2D.

This nested case-control study examined the association between plasma total alkylresorcinols and the alkylresorcinol C17:0-to-C21:0 ratio, biomarkers of whole-grain wheat and rye intake and relative whole-grain rye over whole-grain wheat intake, respectively, and the risk of type 2 diabetes (T2D) among 931 case-control pairs of Scandinavian men and women. ORs for T2D were calculated for plasma total alkylresorcinol concentration or C17:0-to-C21:0 ratio in quartiles with the use of conditional logistic regression that was adjusted for potential confounders. The plasma total alkylresorcinol concentration was not associated with T2D risk (OR: 1.34; 95% CI: 0.95, 1.88) for the highest compared with the lowest quartiles in

multivariable adjusted models. However, the C17:0-to-C21:0 ratio was associated with a lower diabetes risk (OR: 0.54; 95% CI: 0.37, 0.78).

### Chromium Supplements for Glycemic Control in Type 2 Diabetes: Limited Evidence of Effectiveness

R.B. Costello, J.T. Dwyer, R.L. Bailey

*Nutrition Reviews*, Vol. 74, No. 7; pp. 455–468

doi: 10.1093/nutrit/nuw011

Link to full text: [Click here](#)

**Significance:** Chromium supplements have limited effectiveness, and there is little rationale to recommend their use for glycemic control in patients with existing type 2 diabetes.

This narrative review examines the efficacy of chromium supplements for improving glycemic control as measured by decreases in fasting plasma glucose (FPG) or hemoglobin A1c (HbA1c). Using systematic search criteria, 20 randomized controlled trials of chromium supplementation in type 2 diabetes mellitus (T2DM) patients were identified. Clinically meaningful treatment goals were defined as an FPG of  $\leq 7.2$  mmol/dL, a decline in HbA1c to  $\leq 7\%$ , or a decrease of  $\geq 0.5\%$  in HbA1c. In only a few randomized controlled trials did FPG (5 of 20), HbA1c (3 of 14), or both (1 of 14) reach the treatment goals with chromium supplementation. HbA1c declined by  $\geq 0.5\%$  in 5 of 14 studies. Future meta-analyses should include only high-quality studies with similar forms of chromium and comparable inclusion/exclusion criteria to provide scientifically sound recommendations for clinicians.

### Blood Pressure

#### Acute Effects of Quercetin-3-O-glucoside on Endothelial Function and Blood Pressure: A Randomized Dose-Response Study

N.P. Bondonno, C.P. Bondonno, L. Rich, E. Mas, S. Shinde, N.C. Ward, et al.

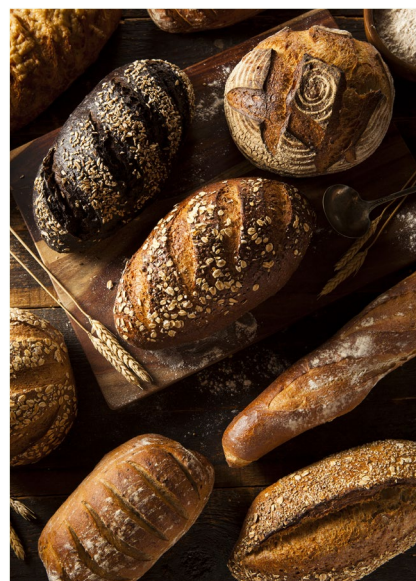
*American Journal of Clinical Nutrition*, Vol. 104, No. 1; pp. 97–103

doi: 10.3945/ajcn.116.131268

Link to full text: [Click here](#)

**Significance:** There are no acute changes in blood pressure or the nitric oxide-mediated endothelium-dependent relaxation of the brachial artery with doses of quercetin ranging from 50 to 400 mg in healthy men and women.

This randomized, controlled, crossover study determined whether acute administration of increasing doses of a common quercetin glycoside (quercetin-3-O-glucoside) improves endothelial function and reduces blood pressure (BP) in a dose-dependent manner. It also explored whether any effects were correlated with changes in plasma nitric oxide (NO) production. Subjects included 15 healthy volunteers who each completed 5 visits with a minimum washout period of 1 wk between testing days. Subjects received each of the following 5 interventions in a random order: 1) 0, 2) 50, 3) 100, 4) 200, or 5) 400 mg quercetin-3-O-glucoside. Although a significant correlation was observed between the dose of quercetin-3-O-glucoside and plasma concentrations of total quercetin ( $R^2 = 0.52$ ,  $P < 0.001$ ) and isorhamnetin ( $R^2 = 0.12$ ,  $P = 0.005$ ), no improvements in endothelial function or BP and no changes in NO production after any dose were found.



## Inflammation

### Postprandial Inflammatory Responses and Free Fatty Acids in Plasma of Adults Who Consumed a Moderately High-Fat Breakfast With and Without Blueberry Powder in a Randomized Placebo-Controlled Trial

*K.D. Ono-Moore, R.G. Snodgrass, S. Huang, S. Singh, T.L. Freytag, D.J. Burnett, et al.*

*Journal of Nutrition*, Vol. 146, No. 7; pp. 1411–1419

doi: 10.3945/jn.115.223909

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**Significance:** Plasma free-fatty acid concentration may be an important determinant affecting inflammatory cytokine production in blood.

This study determined whether plasma free fatty acids (FFAs), after a moderately high-fat (MHF, 40% kcal from fat) breakfast, modulate the inflammatory status of postprandial blood, and whether blueberry intake suppresses FFA-induced inflammatory responses in 23 healthy volunteers. Subjects with mean  $\pm$  SEM age ( $30 \pm 3$  y) and BMI ( $21.9 \pm 0.4$  kg/m<sup>2</sup>) consumed a MHF breakfast with either a placebo powder or 2 or 4 servings of blueberry powder in a randomized cross-over design. The median concentrations of FFAs and cytokines [tumor necrosis factor- $\alpha$ , interleukin (IL)-6 and IL-8] in postprandial plasma (3.5 h) decreased compared with fasting plasma regardless of the blueberry intake ( $P < 0.001$  for FFAs and  $P < 0.05$  for cytokines). However, concentrations of FFAs and cytokines including IL-1 $\beta$  increased in lipoprotein lipase (LPL)-treated whole blood compared with untreated blood samples from participants who consumed the placebo powder. Blueberry intake suppressed IL-1 $\beta$  and IL-6 production in LPL-treated postprandial blood compared with the placebo control when fasting changes were used as a covariate.



## Lipids

### The Increasing Use of Interesterified Lipids in the Food Supply and Their Effects on Health Parameters

*R.P. Mensink, T.A. Sanders, D.J. Baer, K.C. Hayes, P.N. Howles, A. Marangoni*

*Advances in Nutrition*, Vol. 7, No. 4; pp. 719–729

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**Significance:** This paper reports on the workshop sponsored by the Technical Committee on Dietary Lipids of ILSI North America that addressed the health effects of interesterified fats, identified research needs, and outlined considerations for the design of future studies.

A variety of modified fats that provide different functionalities are used in processed foods to optimize product characteristics and nutrient composition. Partial hydrogenation results in the formation of trans FAs (TFAs) and was one of the most widely used modification processes of fats and oils. However, the negative effects of commercially produced TFAs on serum lipoproteins and risk for cardiovascular disease resulted in the Institute of Medicine and the 2010 US Dietary Guidelines for Americans both recommending that TFA intake be as low as possible. After its tentative 2013 determination that use of partially hydrogenated oils is not generally regarded as safe, the FDA released its final determination of

the same in 2015. Many food technologists have turned to interesterified fat as a replacement. Interesterification rearranges FAs within and between a triglyceride molecule by use of either a chemical catalyst or an enzyme. Although there is clear utility of interesterified fats for retaining functional properties of food, the nutrition and health implications of long-term interesterified fat consumption are less well understood. The consensus from the workshop was that although interesterified fat production is a feasible and economically viable solution for replacing dietary TFAs, outstanding questions must be answered regarding the effects of interesterification on modifying certain aspects of lipid and glucose metabolism, inflammatory responses, hemostatic parameters, and satiety.

## Special Report

### Creating the Future of Evidence-Based Nutrition Recommendations: Case Studies From Lipid Research

J.T. Dwyer, K.H. Rubin, K.L. Fritsche, T.L. Psota, D.J. Liska, W.S. Harris, et al.

*Advances in Nutrition*, Vol. 7, No. 4; pp. 747–755

doi: 10.3945/an.115.010926

Link to full text: [Click here](#)

**Significance:** This article reports on the symposium sponsored by the American Society for Nutrition and ILSI North America, which provides specific recommendations to help increase the impact of nutrition research on future dietary guidance, policy, and regulatory issues, particularly in the area of lipids.

Strategic translational research is designed to address research gaps that answer specific guidance questions. It provides translational value with respect to nutrition guidance and regulatory and public policy. The relevance and the quality of evidence both matter in translational research. The process used in systematic reviews, developed by the USDA for its Nutrition Evidence Library, is described in this paper. An eating pattern and cardiovascular disease (CVD) evidence review is provided as an example, and factors that differentiated the studies considered relevant and included in that evidence base from those that were excluded are noted. Case studies on  $\omega$ -3 (n-3) fatty acids (FAs) and industrial trans-FAs illustrate key factors vital to relevance and translational impact, including choice of a relevant population; dose and form of the intervention; use of relevant comparators; and measures for both exposure and outcomes.

## About Us

*The North American branch of the International Life Sciences Institute (ILSI North America) is a public, non-profit scientific foundation that advances the understanding and application of science related to the nutritional quality and safety of the food supply.*

ILSI North America carries out its mission by sponsoring research programs, professional and educational programs and workshops, seminars, and publications, as well as providing a neutral forum for government, academic, and industry scientists to discuss and resolve scientific issues of common concern for the well-being of the general public. ILSI North America's programs are supported primarily by its industry membership.



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