



# Carotenoid & Retinoid News

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## From the editor:

*"The most valuable of all talents is that of never  
using two words when one will do."  
(Thomas Jefferson, 1743-1826)*

The great American statesman, Thomas Jefferson, was also one of the best writers and linguists, as illustrated by his skill in writing the Declaration of Independence. As you know, CARIG, the name of our organization now refers to carotenoids and retinoids. The Steering Committee has decided to include "retinoids" in the title of our newsletter. One could argue that the term "carotenoids" includes retinoids, since they are metabolites of carotenoids in animal organisms. However, the importance of retinoids in animal physiology is so great that they deserve more recognition and we want retinoid researchers to feel even more welcomed in CARIG activities. Hopefully, this newsletter brings useful information about upcoming meetings and important publications in the field of carotenoid and retinoid research.

Maria S. Sapuntzakis (Chicago, IL)

## CARIG Travel Awards

CARIG will award at least two monetary prizes, based on a poster competition to be held in conjunction with the CARIG Reception at Experimental Biology 2016 on Friday, April 1, 2016. Graduate students and postdoctoral trainees are eligible. Posters must address carotenoid and/or vitamin A research. For those assigned an oral presentation rather than a poster at EB'2016, printed copies of your slides with a print copy of your abstract and a small banner may be used for the CARIG poster competition. No advance registration is required to participate in the poster competition. Contact: Lisa Jahns ([Lisa.Jahns@ars.usda.gov](mailto:Lisa.Jahns@ars.usda.gov)) or Sherry Tanumihardjo ([sherry@nutrisci.wisc.edu](mailto:sherry@nutrisci.wisc.edu)).

## UPCOMING EVENTS

**April 1, 2016**

**CARIG Annual Conference, San Diego, CA.** Contact: Sherry Tanumihardjo, CARIG RIS Chair, **E-mail:** [sherry@nutrisci.wisc.edu](mailto:sherry@nutrisci.wisc.edu) [more information below].

**April 2-6, 2016**

**Experimental Biology 2016, San Diego, CA.** Contact: EB2016, FASEB Office of Scientific Meetings & Conferences, 950 Rockville Pike, Bethesda, MD 20814-3998, **e-mail:** [eb@faseb.org](mailto:eb@faseb.org), **website:** [www.experimentalbiology.org](http://www.experimentalbiology.org)

**May 4-6, 2016**

**Oxygen Club of California 2016 World Congress, Davis, CA.** Redox Medicine and Nutrition. Contact: <http://oxyclubcalifornia.org/OCC2016>

**May 22-27, 2016**

**The Gordon Conference on Carotenoids, Lucca, Italy.** Preceded by Gordon Research Seminar on Carotenoids on May 21, 2016. **Website:** [www.grc.org/programs.asp?id=12309](http://www.grc.org/programs.asp?id=12309)

**June 19-24, 2016**

**3<sup>rd</sup> International Conference on Retinoids, West Palm Beach, FL.** Contact: FASEB Office of Scientific Meetings & Conferences, 950 Rockville Pike, Bethesda, MD 20814-3998, **website:** [www.faseb.org/src](http://www.faseb.org/src)

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## CARIG Events at Experimental Biology 2016

**Friday, April 1, 1:00-5:00 pm**

### **CARIG Annual Symposium: Carotenoids and Retinoids during Inflammation**

Location: Hilton Bayfront Hotel – Aqua AB

Chair: Sherry A. Tanumihardjo

Co-Chair: Zeina Jouni

Registration 1:00-1:15 PM

Informal networking: 1:15-1:30 PM

**1:30 PM James Allen Olson Memorial Lecture:** "Inflammation effects on vitamin A and carotenoids in infants" Lewis Rubin, Texas Tech University Health Science Center, El Paso, TX

**2:15 PM Carotenoid and retinoid metabolism during inflammation.** Charles Stephensen, USDA Western Human Nutrition Research Center, Davis, CA

**2:45 PM Acute inflammation effects on vitamin A metabolism and immune function.** A. Catherine Ross, Pennsylvania State University, University Park, PA

**3:20 PM Break**

**4:00 PM Assessment of vitamin A status during inflammation.** Sherry A. Tanumihardjo, University of Wisconsin-Madison, Madison, WI

**4:30 PM Inflammation effects on carotenoid assessment, bioavailability and metabolism.** Torsten Bohn, Luxembourg Institute of Health, Luxembourg

**5:15 PM Steering Committee meeting**

**6:30-8:30 PM CARIG Poster Competition and Reception, Aqua C**

**Saturday, April 2, 2016**

San Diego Convention Center, Room 30A

**Minisymposium: Carotenoids and Retinoids: Molecular mechanisms of actions.**

Chair: Elizabeth Johnson, Co-Chair: Lisa Jahns

**Poster sessions:**

**Sunday, April 3**

**CARIG: Bioavailability and Metabolism of Carotenoids and Vitamin A**

**Monday, April 4**

**CARIG: Biofortification of Staple Crops with Micronutrients**

**CARIG: Carotenoids and Health**

## **FORTHCOMING / RECENT PUBLICATIONS**

**SIGHT AND LIFE Magazine 29 (2) 2015 .** PO Box 2116, 4002 Basel, Switzerland, tel: 41-61-815-8756, website: [www.sightandlife.org](http://www.sightandlife.org). See especially:

Arts RJW, Benn CH. Vitamin A induces long-term epigenetic modifications in the innate immune system, pp 17-20.

West KP, Vitamin A and epigenetic modifications. 1. Observations by Keith P. West, Jr. pp 21-22.

Stephensen CB, Vitamin A and epigenetic modifications. 2. Observations by Charles B. Stephensen, pp 22-23.

Harrison EH, **Conversion of dietary carotenoids and vitamin A into bioactive retinoids: exploring trails blazed by Jim Olson**, pp 24-31.

Solomons NW. **Carotenoids Research Interaction Group (CARIG) 2015 Conference**, pp 95-98.

**Carotenoids: Nutrition, Analysis and Technology**, eds. Kaczor A, Baranska M, J Wiley & Sons 2016.

**Lutein and brain function.** Erdman JW, Smith JW, Kuchan MJ, et al. *Foods* 2015, 4 (open access review) doi: 10.3390/foods4040547

**Green extraction methods and environmental applications of carotenoids: a review.** Singh A, Ahmad S, Ahmad A, *Cheminform* 46(37) August 2015, doi: 10.1002/chin.201537298

**Lutein, zeaxanthin and meso-zeaxanthin: The basic and clinical science underlying carotenoid-based nutritional interventions against ocular disease.** Bernstein PS, Li B, Vacholi PP et al. *Prog Retin Eye Res* 50:34-66, 2016.

**Potential of Dietary Non-Provitamin A Carotenoids in the Prevention and Treatment of Diabetic Microvascular Complications.** Murillo AG, Fernandez ML, *Adv Nutr* 7:14-24 2016.

**Alphabetical Listing of Recent Publications** may be found at [www.carotenoidsociety.org/articles-books-and-databases](http://www.carotenoidsociety.org/articles-books-and-databases). It is prepared by Dr. Harold Furr, Department of Nutritional Sciences, University of Wisconsin, Madison.

## **TECHNICAL NOTES**

### **New lutein-phospholipid complex boosts lutein absorption**

Lutein ester from enriched egg yolk has been reported to have superior absorption than lutein from vegetable or supplement sources, and this raises the possibility that the phospholipids in egg yolk may be contributing to this enhanced availability. Therefore a new solid-lipid particle (SLP) complex of lutein and phospholipids was formulated by Verdure Sciences and tested by Dr DiSilvestro from Columbus Nutraceutical Formulations LLC. The volunteers (6 men and 6 women, 52 - 65 years old) were randomly assigned to receive supplements with 10 mg of lutein in the form of lutein ester or SLP-lutein complex for 10 days. Plasma lutein values increased by 88% for the conventional lutein ester and by 563% for SLP-lutein complex (*DiSilvestro RA et al. Nutr J* 14:104, 2015). The new formulation is currently in the final stages of commercialization and is scheduled to launch in the first quarter of the upcoming year. SLP-lutein complex may prove beneficial to overall eye health and healthy ocular aging in conjunction with administering a lower dose.

[www.nutraingredients-usa.com](http://www.nutraingredients-usa.com) (12/8/2016)

## **NEWS AND VIEWS**

### **Cyp27c1 enzyme red-shifts the spectral sensitivity of photoreceptors by converting vitamin A<sub>1</sub> into A<sub>2</sub>**

Some vertebrate species (freshwater fish and amphibians) have evolved means of extending their visual sensitivity beyond the range of human vision. One mechanism of enhancing sensitivity to long-wavelength (near-infrared) light is to replace the 11-

*cis* retinal chromophore in photopigments with 11-*cis* 3,4-didehydroretinal. Despite over a century of research on this topic, the enzymatic basis of this perceptual switch remains unknown. Here, we show that a cytochrome P450 family member, Cyp27c1, mediates this switch by converting vitamin A<sub>1</sub> (the precursor of 11-*cis* retinal) into vitamin A<sub>2</sub> (the precursor of 11-*cis* 3,4-didehydroretinal). Knockout of *cyp27c1* in zebrafish abrogates production of vitamin A<sub>2</sub>, eliminating the animal's ability to red-shift its photoreceptor spectral sensitivity and reducing its ability to see and respond to near-infrared light. Thus, the expression of a single enzyme mediates dynamic spectral tuning of the entire visual system by controlling the balance of vitamin A<sub>1</sub> and A<sub>2</sub> in the eye.

Enright, J M et al. *Curr Biol*, 25:3048–57, 2015

### **'Blood rain' falls on Spanish villages**

The rainwater that fell in some of the villages of Zamora (Spain) last autumn brought along a strange traveler: a green microalgae that turns a reddish color when in a state of stress. Once this microalgae was deposited into fountains and tanks, the water turned red. Researchers from the University of Salamanca are shining light on this 'blood rain' phenomenon, but they have not yet been able to identify the mysterious origin of these little algae which are also used in the pharmaceutical and food industries. The reddish staining was caused by *Haematococcus pluvialis*, a freshwater microalgae that is capable of synthesizing a red carotenoid pigment astaxanthin. In order to find out where this species is originating from, the researchers analyzed meteorological data, especially wind patterns, corresponding to the days of 'blood rain'. The results of this analysis reveal a connection to prevailing westerly winds that would have affected the north-western area of the Iberian Peninsula during the autumn of 2014. However, the study was not able to identify the exact source of these microorganisms, suggesting that they may have even come from North America. Other species of microalgae, albeit of the saltwater variety, are responsible for the red tides that sometimes occur in estuaries and coastal areas all over the world, from Galicia to California and Australia. 'Blood rain', however, is not as common as these red tides. The most famous 'blood rain' phenomenon was that of Kerala, India, in the summer of 2001, since then happening once again in the southern part of the country and in Sri Lanka. Scientific studies have confirmed that the algae *Trentepohlia* was responsible for this event, while ruling out alien extraterrestrial sources.

[www.laboratoryequipment.com](http://www.laboratoryequipment.com) (11/12/2015)

### **No increase in risk of hip fracture at high serum retinol concentrations**

Norway has the highest hip fracture rates worldwide and a relatively high vitamin A intake. Increased fracture risk at high intakes and serum concentrations of retinol have been observed in epidemiologic studies. We aimed to study the association between serum retinol and hip fracture and whether high serum retinol may counteract a preventive effect of vitamin D. We conducted the largest prospective analysis of serum retinol and hip fracture to date in 21,774 men and women (65–79 y old, mean age 72 y), who attended 4 community-based health studies during 1994–2001. Incident hip fractures occurring up to 10.7 y after baseline were retrieved from electronic hospital discharge registers. Retinol determined by HPLC with UV detection in stored serum was available in 1154 incident hip fracture cases with valid body mass index (BMI) data and in a subcohort defined as a sex-stratified random sample ( $n = 1418$ ). Cox proportional hazards regression weighted according to the stratified case-cohort design was performed. There was a modest increased risk of hip fracture in the lowest compared with the middle quintile of serum retinol (HR: 1.41; 95% CI: 1.09, 1.82) adjusted for sex and study center. The association was attenuated after adjustment for BMI and serum concentrations of  $\alpha$ -tocopherol (HR: 1.16; 95% CI: 0.88, 1.51). We found no increased risk in the upper compared with the middle quintile. No significant interaction between serum concentrations of 25-hydroxyvitamin D and serum retinol on hip fracture was observed ( $P = 0.68$ ). We found no evidence of an adverse effect of high serum retinol on hip fracture or any interaction between retinol and 25-hydroxyvitamin D. If anything, there tended to be an increased risk at low retinol concentrations, which was attenuated after control for confounders. We propose that cod liver oil, a commonly used food supplement in Norway, should not be discouraged as a natural source of vitamin D for fracture prevention.

Holvik K, *Am J Clin Nutr* 102:1289-96, 2015

### **Carotenoids, retinol, tocopherols, and prostate cancer risk: pooled analysis of 15 studies**

Individual studies have suggested that circulating carotenoids, retinol, or tocopherols may be associated with prostate cancer risk, but the studies have not been large enough to provide precise estimates of associations, particularly by stage and grade of disease. The objective of this study was to conduct a pooled analysis of the associations of the

concentrations of seven carotenoids, retinol,  $\alpha$ -tocopherol, and  $\gamma$ -tocopherol with risk of prostate cancer and to describe whether any associations differ by stage or grade of the disease or other factors. Principal investigators of prospective studies provided individual participant data for prostate cancer cases and controls. Risk by study-specific fifths of each biomarker was estimated by using multivariable-adjusted conditional logistic regression in matched case-control sets. Data were available for up to 11,239 cases (including 1654 advanced stage and 1741 aggressive) and 18,541 controls from 15 studies. Lycopene was not associated with overall risk of prostate cancer, but there was statistically significant heterogeneity by stage of disease, and the OR for aggressive disease for the highest compared with the lowest fifth of lycopene was 0.65 (95% CI: 0.46, 0.91;  $P$ -trend = 0.032). No other carotenoid was significantly associated with overall risk of prostate cancer or with risk of advanced-stage or aggressive disease. For retinol, the OR for the highest compared with the lowest fifth was 1.13 (95% CI: 1.04, 1.22;  $P$ -trend = 0.015). For  $\alpha$ -tocopherol, the OR for the highest compared with the lowest fifth was 0.86 (95% CI: 0.78, 0.94;  $P$ -trend < 0.001), with significant heterogeneity by stage of disease; the OR for aggressive prostate cancer was 0.74 (95% CI: 0.59, 0.92;  $P$ -trend = 0.001).

$\gamma$ -Tocopherol was not associated with risk. Overall prostate cancer risk was positively associated with retinol and inversely associated with  $\alpha$ -tocopherol, and risk of aggressive prostate cancer was inversely associated with lycopene and  $\alpha$ -tocopherol. Whether these associations reflect causal relations is unclear.

*Key TJ et al. Am J Clin Nutr 102:1142-57, 2015*

### **High intake of carotenoids associated with reduced risk of advanced AMD**

Despite strong biological plausibility, evidence from epidemiologic studies and clinical trials on the relations between intakes of lutein and zeaxanthin and age-related macular degeneration (AMD) has been inconsistent. The roles of other carotenoids are less thoroughly investigated. Our objective was to investigate the associations between intakes of carotenoids and AMD using a prospective cohort study, with cohorts from the Nurses' Health Study and the Health Professionals Follow-up Study in the United States. A total of 63 443 women and 38 603 men were followed, from 1984 until May 31, 2010, in the Nurses' Health Study and from 1986 until January 31, 2010, in the Health Professionals Follow-up Study. All participants were aged 50 years or older and were free of diagnosed AMD, diabetes mellitus, cardiovascular disease, and cancer at baseline. Predicted plasma carotenoid scores were

computed directly from food intake, assessed by repeated food frequency questionnaires at baseline and follow-up, using validated regression models to account for bioavailability and reporting validity of different foods, and associations between predicted plasma carotenoid scores and AMD were determined. We confirmed 1361 incident intermediate and 1118 advanced AMD cases (primarily neovascular AMD) with a visual acuity of 20/30 or worse by medical record review. Comparing extreme quintiles of predicted plasma lutein/zeaxanthin score, we found a risk reduction for advanced AMD of about 40% in both women and men (pooled relative risk comparing extreme quintiles = 0.59; 95% CI, 0.48-0.73;  $P$ -trend < 0.001). Predicted plasma carotenoid scores for other carotenoids, including  $\beta$ -cryptoxanthin,  $\alpha$ -carotene, and  $\beta$ -carotene, were associated with a 25% to 35% lower risk of advanced AMD when comparing extreme quintiles. The relative risk comparing extreme quintiles for the predicted plasma total carotenoid index was 0.65 (95% CI, 0.53-0.80;  $P$ -trend < 0.001). We did not identify any associations of carotenoids, either as predicted plasma score or calculated intake, with intermediate AMD. Higher intake of bioavailable lutein/zeaxanthin is associated with a long-term reduced risk of advanced AMD. Given that some other carotenoids are also associated with a lower risk, a public health strategy aimed at increasing dietary consumption of a wide variety of fruits and vegetables rich in carotenoids may reduce the incidence of advanced AMD.

*Wu J et al. JAMA Ophthalmol 133:1415-24, 2015*

### **The effects of lutein on cardiometabolic health across the life course: a systematic review and meta-analysis**

The antioxidant lutein is suggested as being beneficial to cardiometabolic health because of its protective effect against oxidative stress. We aimed to evaluate the effects of lutein (intake or concentrations) on cardiometabolic outcomes in different life stages. This is a systematic review with meta-analysis of literature published in MEDLINE, Embase, Cochrane Central, Web of Science, PubMed, and Google Scholar up to August 2014. Included were trials and cohort, case-control and cross-sectional studies, in which the association between lutein concentrations, dietary intake, or supplements and cardiometabolic outcomes was reported. Two independent investigators reviewed the articles. Seventy-one relevant articles were identified that included a total of 387,569 participants. Only one article investigated the effects of lutein during pregnancy, and 3 studied lutein in children. Furthermore, 31 longitudinal, 33 cross-

sectional, and 3 intervention studies were conducted in adults. Meta-analysis showed a lower risk of coronary heart disease (pooled RR: 0.88; 95% CI: 0.80, 0.98) and stroke (pooled RR: 0.82; 95% CI: 0.72, 0.93) for the highest compared with the lowest tertile of lutein blood concentration or intake. There was no significant association with type 2 diabetes mellitus (pooled RR: 0.97; 95% CI: 0.77, 1.22), but higher lutein was associated with a lower risk of metabolic syndrome (pooled RR: 0.75; 95% CI: 0.60, 0.92) for the highest compared with the lowest tertile. The literature on risk factors for cardiometabolic diseases showed that lutein might be beneficial for atherosclerosis and inflammatory markers, but there were inconsistent associations with blood pressure, adiposity, insulin resistance, and blood lipids. Our findings suggest that higher dietary intake and higher blood concentrations of lutein are generally associated with better cardiometabolic health. However, evidence mainly comes from observational studies in adults, whereas large-scale intervention studies and studies of lutein during pregnancy and childhood are scarce.

*Leermakers ETM, et al.  
Am J Clin Nutr 103:481-94, 2016*

#### **Higher levels of serum lycopene are associated with reduced mortality in individuals with metabolic syndrome**

Metabolic syndrome increases the risk of mortality. Increased oxidative stress and inflammation may play an important role in the high mortality of individuals with metabolic syndrome. Previous studies have suggested that lycopene intake might be related to the reduced oxidative stress and decreased inflammation. Using data from the National Health and Nutrition Examination Survey (NHANES), we examined the hypothesis that lycopene is associated with mortality among individuals with metabolic syndrome. A total of 2,499 participants with metabolic syndrome, 20 years and older, were divided into three groups based on their serum concentration of lycopene using the tertile rank method. NHANES from 2001-2006 were linked to the mortality file for mortality follow-up data through December 31, 2011 to determine the mortality rate and hazard ratios (HR) for the three serum lycopene concentration groups. The mean survival time was significantly higher in the group with the highest serum lycopene concentration (120.6 months, 95% CI: 118.8 - 122.3) and the medium group (116.3 months, 95% CI: 115.2 - 117.4); compared to the group with lowest serum lycopene concentration (107.4 months, 95% CI: 106.5 - 108.3). After adjusting for possible confounding factors, participants in the highest (HR =

0.61,  $p = 0.0113$ ) and in the second highest (HR = 0.67,  $p = 0.0497$ ) serum lycopene concentration groups showed significantly lower hazard ratios of mortality when compared to participants in the lower serum lycopene concentration. The data suggest that higher serum lycopene concentration has a significant association with the reduced risk of mortality among individuals with metabolic syndrome.

*Han G-M, et al. Nutr Res 2016 (in press)*

DOI: [10.1016/j.nutres.2016.01.003](https://doi.org/10.1016/j.nutres.2016.01.003)

#### **Plasma carotenoids, vitamin C, tocopherols, and retinol and the risk of breast cancer**

Carotenoids and vitamin C are thought to be associated with reduced cancer risk because of their antioxidative capacity. This study evaluated the associations of plasma carotenoid, retinol, tocopherol, and vitamin C concentrations and risk of breast cancer. In a nested case-control study within the European Prospective Investigation into Cancer and Nutrition cohort, 1502 female incident breast cancer cases were included, with an oversampling of premenopausal ( $n = 582$ ) and estrogen receptor-negative (ER-) cases ( $n = 462$ ). Controls ( $n = 1502$ ) were individually matched to cases by using incidence density sampling. Prediagnostic samples were analyzed for  $\alpha$ -carotene,  $\beta$ -carotene, lycopene, lutein, zeaxanthin,  $\beta$ -cryptoxanthin, retinol,  $\alpha$ -tocopherol,  $\gamma$ -tocopherol, and vitamin C. Breast cancer risk was computed according to hormone receptor status and age at diagnosis (proxy for menopausal status) by using conditional logistic regression and was further stratified by smoking status, alcohol consumption, and body mass index (BMI). All statistical tests were 2-sided. In quintile 5 compared with quintile 1,  $\alpha$ -carotene (OR: 0.61; 95% CI: 0.39, 0.98) and  $\beta$ -carotene (OR: 0.41; 95% CI: 0.26, 0.65) were inversely associated with risk of ER- breast tumors. The other analytes were not statistically associated with ER- breast cancer. For estrogen receptor-positive (ER+) tumors, no statistically significant associations were found. The test for heterogeneity between ER- and ER+ tumors was statistically significant only for  $\beta$ -carotene ( $P$ -heterogeneity = 0.03). A higher risk of breast cancer was found for retinol in relation to ER-/progesterone receptor-negative tumors (OR: 2.37; 95% CI: 1.20, 4.67;  $P$ -heterogeneity with ER+/progesterone receptor positive = 0.06). We observed no statistically significant interaction between smoking, alcohol, or BMI and all investigated plasma analytes (based on tertile distribution). Our results indicate that higher concentrations of plasma  $\beta$ -carotene and  $\alpha$ -carotene are associated with lower breast cancer risk of ER- tumors.

Bakker MF, et al. *Am J Clin Nutr* 103:454-64, 2016  
**Modeling of  $^{13}\text{C}$ -lycopene absorption,  
isomerization and distribution kinetics in healthy  
adults**

Lycopene, a red carotenoid in tomatoes, has been hypothesized to mediate disease-preventive effects associated with tomato consumption. Lycopene is consumed primarily as the all-*trans* geometric isomer in foods, whereas human plasma and tissues show greater proportions of *cis* isomers. With the use of compartmental modeling and stable isotope technology, we determined whether endogenous all-*trans*-to-*cis*-lycopene isomerization or isomeric-bioavailability differences underlie the greater proportion of lycopene *cis* isomers in human tissues than in tomato foods. Healthy men ( $n = 4$ ) and women ( $n = 4$ ) consumed  $^{13}\text{C}$ -lycopene (10.2 mg; 82% all-*trans* and 18% *cis*), and plasma was collected over 28 days. Unlabeled and  $^{13}\text{C}$ -labeled total lycopene and lycopene-isomer plasma concentrations, which were measured with the use of HPLC-MS, were fit to a 7-compartment model. Subjects absorbed a mean  $\pm$  SEM of  $23\% \pm 6\%$  of the lycopene. The proportion of plasma *cis*- $^{13}\text{C}$ -lycopene isomers increased over time, and all-*trans* had a shorter half-life than that of *cis* isomers ( $5.3 \pm 0.3$  and  $8.8 \pm 0.6$  d, respectively;  $P < 0.001$ ) and an earlier time to reach maximal plasma concentration than that of *cis* isomers ( $28 \pm 7$  and  $48 \pm 9$  h, respectively). A compartmental model that allowed for interindividual differences in *cis*- and all-*trans*-lycopene bioavailability and endogenous *trans*-to-*cis*-lycopene isomerization, was predictive of plasma  $^{13}\text{C}$  and unlabeled *cis*- and all-*trans*-lycopene concentrations. Although the bioavailability of *cis* ( $24.5\% \pm 6\%$ ) and all-*trans* ( $23.2\% \pm 8\%$ ) isomers did not differ, endogenous isomerization ( $0.97 \pm 0.25$   $\mu\text{mol/d}$  in the fast-turnover tissue lycopene pool) drove tissue and plasma isomeric profiles.  $^{13}\text{C}$ -Lycopene combined with physiologic compartmental modeling provides a strategy for following complex *in vivo* metabolic processes in humans and reveals that postabsorptive *trans*-to-*cis*-lycopene isomerization, and not the differential bioavailability of isomers, drives tissue and plasma enrichment of *cis*-lycopene.

Moran NE, *Am J Clin Nutr* 102:1436-49, 2015

**Absorption and Distribution Kinetics of the  $^{13}\text{C}$ -  
Labeled Phytoene in Healthy Adults**

Phytoene is a tomato carotenoid that may contribute to the apparent health benefits of tomato consumption. Although phytoene is a less prominent tomato carotenoid than lycopene, it is a major carotenoid in various human tissues. Phytoene distribution to plasma lipoproteins and tissues differs

from lycopene, suggesting different kinetics of phytoene and lycopene. The objective of this study was to characterize the kinetic parameters of phytoene absorption, distribution, and excretion in adults, to better understand why biodistribution of phytoene differs from lycopene. Four adults (2 males, 2 females) maintained a controlled low phytoene diet (1–5 mg/d) for 42 d. On day 14, each consumed 3.2 mg  $^{13}\text{C}$ -phytoene, produced using tomato cell suspension culture technology. Blood samples were collected at 0, 1–15, 17, 21, 24 h, and 2, 3, 4, 7, 10, 14, 17, 21, 28 days after  $^{13}\text{C}$ -phytoene consumption. Plasma-unlabeled and plasma-labeled phytoene concentrations were determined using ultra-HPLC–quadrupole time-of-flight-MS, and data were fit to a 7-compartment carotenoid kinetic model using WinSAAM 3.0.7 software. Subjects were compliant with a controlled phytoene diet, consuming a mean  $\pm$  SE of  $2.5 \pm 0.6$  mg/d, resulting in a plasma unlabeled phytoene concentration of  $71 \pm 14$  nM/L. A maximal plasma  $^{13}\text{C}$ -phytoene concentration of  $55.6 \pm 5.9$  nM/L was achieved  $19.8 \pm 9.2$  h after consumption, and the plasma half-life was  $2.3 \pm 0.2$  d. Compared with previous results for lycopene, phytoene bioavailability was nearly double at  $58\% \pm 19\%$ , the clearance rate from chylomicrons was slower, and the rates of deposition into and utilization by the slow turnover tissue compartment were nearly 3 times greater. Although differing from lycopene only by the absence of 4 double bonds, phytoene exhibits markedly different kinetic characteristics in human plasma, providing insight into metabolic processes contributing to phytoene enrichment in plasma and tissues compared with lycopene.

Moran N et al. *J Nutr* 146:368-76, 2016

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