



Carotenoid News

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Errare humanum est.

(Seneca, Roman philosopher, 4 BC – AD 65)

Although it is human to err, we must strive to avoid error in reporting the results of our research. One prevalent source of error is the experimental bias in collecting data when the researcher is aware of the treatment group and intentionally or unintentionally exaggerates the effect to confirm his predictions. The infamous tactics are known as *p*-hacking, data peeking, or selective exclusion of outliers. Such scientific malpractice can be prevented by blind data recording. Double blind studies are the gold standard in life sciences, but only about 20% of reported experiments in medical and health sciences are blind, with the proportion much lower in biological, cognitive, psychological and agricultural sciences (Holman L. *et al.* *PLOS Biology* July 8, 2015, *online*). The Australian scientists used text mining and a literature review, searching about 20,000 papers in the Open Access collection of PubMed. They also compared 83 pairs of publications with similar blind and non-blind experiment. They concluded that a lack of blindness is associated with reported increase in effect size of 27% on average, and also increases the probability of finding a significant effect ($p < 0.05$). All that evidence suggests that blind protocols are very important to research practice. As St Augustine amended Seneca, "to err is human, but to persist in error is diabolical".

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) or Sherry Tanumihardjo (sherry@nutrisci.wisc.edu).

News from CARIG Steering and Advisory Committee

We would like to remind all CARIG members to mark their calendars for several upcoming CARIG sponsored events to be held next spring at Experimental Biology 2016 in San Diego. The CARIG 2016 Conference will be held on April 1, Friday afternoon before the Saturday opening of the ASN program. EB 2016 also will feature a CARIG trainee poster and award session, and business meeting during the annual social following the CARIG Conference.

RIS Officers 2015-2016:

Chair – Sherry Tanumihardjo, University of Wisconsin-Madison

Chair Elect – Lisa Jahns - USDA-ARS, North Dakota

Treasurer – Jessica Campbell, General Mills

Immediate Past Chair – Zeina E. Jouni, Kellogg Company

After serving on the steering committee for a long time, Earl Harrison stepped off the steering committee and Helen Evert, also from Ohio State University, was elected to take his place. The current membership of the Committee includes, in addition to the above mentioned RIS officers:

Helen Evert – Ohio State University

Mario Ferruzzi – Purdue University

Elizabeth Johnson – Tufts University

Klaus Kraemer – Task Force Sight and Life

Georg Lietz - Newcastle University

John Landrum - Florida International University (liaison to the International Carotenoid Society, ICS Secretary)

Lewis Rubin – University of South Florida

Maria Stacewicz-Sapuntzakis (newsletter editor)

Student representative:

Bryan Gannon - University of Wisconsin

Postdoc representatives:

Jessica Copperstone - Ohio State University

Matthew Toomey – Washington University

UPCOMING EVENTS

November 3-5, 2015

11th International Food Data Conference, Hyderabad, India. Food Composition and Public Health Nutrition. Website: www.ifdc2015.com

E-mail: ifdc2015@gmail.com

April 1, 2016

CARIG Annual Conference, San Diego, CA.
Contact: Sherry Tanumihardjo, CARIG RIS Chair, E-mail: sherry@nutrisci.wisc.edu

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, website: 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

FORTHCOMING / RECENT PUBLICATIONS

SIGHT AND LIFE Magazine 29 (1) 2015 . PO Box 2116, 4002 Basel, Switzerland, tel: 41-61-815-8756, e-mail: klaus.kraemer@sightandlife.org, website: www.sightandlife.org. See especially:

Thurnam DI. Inflammation and biomarkers of nutrition, pp 51-59.

Fenech M. Perspectives in nutrigenomics and nutrigenetics, pp 64-70.

Carotenoids in Human Nutrition. Bowen PE, Stacewicz-Sapuntzakis M, Diwadkar-Navsariwala V. Chapter in **Pigments in Fruits and Vegetables**, ed. Chunxian Chen, Springer 2015, pp 31-67.

Lutein and cataract: from bench to bedside. Manai A, Abdollahi M, Raman T, Nabavi SF, Habtemariam S, Daglia M, Nabavi SM, *Crit Rev Biotechnol*. doi:10.30109/07388551.2015.1049510

Lycopene as a carotenoid provides radioprotectant and antioxidant effects by quenching radiation-induced free radical singlet oxygen: an overview. Pirayesh Islamian J, Mehrali H, *Cell J* (2015) 16(4):386-91.

Opening Pandora's box: cause and impact of errors on plant pigment studies. Opinion article. Fernández-Marín B, Artetxe U, Barrutia O, Esteban R, Hernández A, García-Plazaola JI, *Front. Plant Sci* 3/12/2015 doi.org/10.3389/fpls.2015.00148

An evidence based systematic review of lutein by the National Standard Research Collaboration. Ulbricht C. *J Diet Suppl* January 2015, doi:10.3109/19390211.2014.988577

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

MEETING REPORTS

CARIG Conference at EB 2015

This year's conference on March 27, in Boston, focused on "*Carotenoids, Retinoids and Cancer*" and covered a wide spectrum of disciplines, including epidemiology, mechanisms of action, fundamental, foundational and clinical research. The *J. Olson Memorial Lecture* entitled "*Conversion of Dietary Carotenoids and Vitamin A into Bioactive Retinoids: Exploring Trails Blazed by Jim Olson*" was given by Earl Harrison (The Ohio State University). Other featured CARIG presentations were "*Retinoic Acid Biosynthesis Defects in Cancer*" by Maureen Kane (University of Maryland), "*The Antioxidant Conundrum: Just Do It???*" by Harold Seifried (National Cancer Institute – National Institutes of Health), "*Tomato Carotenoids and Fatty Liver Disease*" by Xiang-Dong Wang (Tufts University), and "*Tomato Carotenoids and Risk of Prostate Cancer*" by John W. Erdman, Jr. (University of Illinois, Champaign-Urbana). Sherry Tanumihardjo chaired the meeting.

The winners of the CARIG poster competition this year were:

1) **Emily Mohn**, Elizabeth Johnson. *Distribution of lutein in membranes of rhesus macaque brain*. Tufts University.

2) **Joshua Smith**, Xiaoming Gong and Lewis Rubin. *Selective Carotenoid Growth Inhibition in Breast Cancer: Independence of Hormonal Sensitivity*. University of Texas and Texas Tech.

3) **Michael La Frano**, **Bryan Gannon**, Sherry Tanumihardjo, John W. Newman. *Targeted Metabolomic Profiling of Lipid Mediators and Bile Acids Influenced by Vitamin A Status in a Rodent Model*. University of California, Davis and University of Wisconsin-Madison).

The Macular Carotenoid Conference

The Macular Carotenoid Conference on July 8-7, 2015 brought together scientists from various countries with a mutual interest in the role of xanthophylls in human health. The conference setting at Downing College in Cambridge, UK,

facilitated stimulating presentations and discussions from investigators with varied expertise. Discussions focused on lutein and zeaxanthin in visual and cognitive health throughout the lifespan, with perspectives on how this field will move forward. The meeting was very productive and a wonderful time for all who attended. George Britton gave a nice introductory talk, as expected. You will find the program, as well as videos of the talks on the conference site www.macularcarotenoids.org. The abstracts of all presentations were published as: **Abstracts from the Macular Carotenoids Conference 2015, Cambridge, UK - July 8-10, 2015.** *Eur J Ophthalmol* 2015; 25(4): e59 - e73.

TECHNICAL NOTES

Water-soluble astaxanthin powder

Algatech, based in Israel, has been a leader in the production of natural astaxanthin from algae, which it cultivates in a closed tube system in the Negev desert in Israel. The system allows for a highly controllable and reliable output, and the company has been acknowledged as producing some of the purest raw material in commerce. Astaxanthin is an insoluble, lipophilic carotenoid, whose popularity has recently soared, especially in sports nutrition. Getting it into the bloodstream, or adding it to food and drink has been the challenge. Virun, based in Walnut, CA, is a biotech development company that specializes in new delivery technologies for pharmaceuticals and dietary supplement ingredients. They found a way to produce a diester form of vitamin E. Mixed with astaxanthin it creates a water soluble powder with neutral taste. Astaxanthin by itself has kind of a fishy flavor. In addition, bicarbonate is also encapsulated with astaxanthin, helping to stabilize it and buffering the taste. At 30 mg of astaxanthin per gram of powder, the beverage is clear and shelf stable. For a higher dosage, the ingredient is also offered at a 60 mg/g dose, which results in a more opaque beverage.

www.nutraingredients-usa.com (5/1/2015)

NEWS AND VIEWS

Control of carotenoid biosynthesis through a heme-based *cis-trans* isomerase

Plants synthesize carotenoids, which are essential for plant development and survival. These metabolites also serve as essential nutrients for human health. The biosynthetic pathway for all plant carotenoids occurs in chloroplasts and other plastids and requires 15-*cis*- ζ -carotene isomerase (Z-ISO). It was not known whether Z-ISO catalyzes isomerization alone or in combination with other

enzymes. We found that Z-ISO is a bona fide enzyme and integral membrane protein. Z-ISO independently catalyzes the *cis-trans* isomerization of the 15-15' carbon-carbon double bond in 9,15,9'-*cis*- ζ -carotene to produce the substrate required by the subsequent biosynthetic-pathway enzyme. We discovered that isomerization depends upon a ferrous heme *b* cofactor that undergoes redox-regulated ligand switching between the heme iron and alternate Z-ISO amino acid residues. Heme *b*-dependent isomerization of a large hydrophobic compound in a membrane was previously undescribed. As an isomerase, Z-ISO represents a new prototype for heme *b* proteins and potentially uses a new chemical mechanism.

Beltrán J, *Nature Chem Biol* 11:598–605, 2015

Plasma and prostate lycopene response to typical servings of tomato soup, sauce or juice

Tomato product consumption and estimated lycopene intake are hypothesized to reduce the risk of prostate cancer. To define the impact of typical servings of commercially available tomato products on resultant plasma and prostate lycopene concentrations, men scheduled to undergo prostatectomy ($n=33$) were randomized either to a lycopene-restricted control group (<5 mg lycopene/day) or to a tomato soup (2.0–2.75 cups prepared/day), tomato sauce (142–198 g/day or 5–7 ounces/day) or vegetable juice (325–488 ml/day or 11–16.5 fl. ounces/day) intervention, providing 25–35 mg lycopene/day. Plasma and prostate carotenoid concentrations were measured by HPLC. Tomato soup, sauce and juice consumption significantly increased plasma lycopene concentration from 0.68 (SEM 0.1) to 1.13 (SEM 0.09) $\mu\text{M/L}$ (66%), 0.48 (SEM 0.09) to 0.82 (SEM 0.12) $\mu\text{M/L}$ (71%) and 0.49 (SEM 0.12) to 0.78 (SEM 0.1) $\mu\text{M/L}$ (59%), respectively, while the controls consuming the lycopene-restricted diet showed a decline in plasma lycopene concentration from 0.55 (SEM 0.60) to 0.42 (SEM 0.07) $\mu\text{M/L}$ (-24%). The end-of-study prostate lycopene concentration was 0.16 (SEM 0.02) nmol/g in the controls, but was 3.5-, 3.6- and 2.2-fold higher in tomato soup ($p=0.001$), sauce ($p=0.001$) and juice ($p=0.165$) consumers, respectively. Prostate lycopene concentration was moderately correlated with post-intervention plasma lycopene concentrations ($r=0.60$, $p=0.001$), indicating that additional factors have an impact on tissue concentrations. While the primary geometric lycopene isomer in tomato products was all-*trans* (80–90%), plasma and prostate isomers were 47% and 80% *cis*, respectively, demonstrating a shift towards *cis* accumulation. Consumption of typical servings of processed tomato products results in differing plasma and prostate lycopene

concentrations. Factors including meal composition and genetics deserve further evaluation to determine their impacts on lycopene absorption and biodistribution.

*Grainger EM et al. Br J Nutr 2015
doi: 10.1017/S0007114515002202*

Long term supplementation with lutein and zeaxanthin improves retinal function in early age-related macular degeneration

A randomized, double-blind, placebo-controlled trial was conducted to investigate functional and macular pigment (MP) changes in patients with early age-related macular degeneration (AMD) after multiple supplementation with lutein and zeaxanthin. Patients ($n=112$) with early AMD were randomly (1:1:1:1) assigned to receive 10 mg lutein, 20 mg lutein, lutein (10 mg) + zeaxanthin (10 mg), or placebo daily for 2 years. MP optical density (MPOD) was recorded at baseline, 48 weeks and 2 years. Retinal sensitivities were measured by multifocal electroretinogram for peak-to-trough amplitude (N1P1) at baseline and at 48 weeks, and in terms of microperimeter-determined mean retinal sensitivity (MRS) at 48 weeks and 2 years. Supplementation with lutein and zeaxanthin augmented MPOD significantly in active treatment groups (all $p<0.05$). N1P1 response densities showed significant increases in ring 1 and ring 2 after 48 weeks of supplementation, while no significant changes were seen in rings 3–6. Significant increases in MRS were detected after supplementation with either 10 or 20 mg lutein, whereas no such increases were seen in the placebo arm. In conclusion, the supplementation with lutein and/or zeaxanthin increases MPOD, and supplemental lutein enhances retinal sensitivity in patients with early AMD.

Huang Y-M et al. Br J Ophthalmol 99:371-75, 2015

Cognitive function and its relationship with macular pigment optical density

Macular pigment (MP) levels correlate with brain concentrations of lutein (L) and zeaxanthin (Z), and have also been shown to correlate with cognitive performance in the young and elderly. The objective of the study was to investigate the relationship between MP, serum concentrations of L and Z, and cognitive function in subjects free of retinal disease with low MP (Group 1, $n=105$) and in subjects with AMD (Group 2, $n=121$). MP was measured using customized heterochromatic flicker photometry and dual-wavelength autofluorescence; cognitive function was assessed using a battery of validated cognition tests; serum L and Z concentrations were

determined by HPLC. Significant correlations were evident between MP and various measures of cognitive function in both groups ($r = -0.273$ to 0.261 , $p \leq 0.05$, for all). Both serum L and Z concentrations correlated significantly ($r=0.187$, $p \leq 0.05$ and $r = 0.197$, $p \leq 0.05$, respectively) with semantic (animal) fluency cognitive scores in Group 2 (the AMD study group), while serum L concentrations also correlated significantly with Verbal Recognition Memory learning slope scores in the AMD study group ($r=0.200$, $p=0.031$). Most of the correlations with MP, but not serum L or Z, remained significant after controlling for age, gender, diet, and education level. In conclusion, MP offers a potential non-invasive clinical biomarker of cognitive health, and appears more successful in this role than serum concentrations of L or Z.

Kelly D et al. J Alzheimer Dis 48:261-77, 2015

Plasma carotenoids are inversely associated with dementia risk in elderly French

Although intake of fruits and vegetables has been associated with a decreased risk of dementia, studies focusing on nutrients underlying this association are lacking. Our objective was to analyze the relation between plasma carotenoids and the risk of dementia and Alzheimer's disease (AD) in French elderly community dwellers. The study population consisted of 1,092 non-demented older participants, from the Three-City-Bordeaux cohort followed for up to 10 years (range: 1.8-10.8 years, median: 9.5 years). Dementia and AD were diagnosed by a committee of neurologists. The concentration of plasma carotenoids (β -carotene, α -carotene, lycopene, lutein, zeaxanthin, and β -cryptoxanthin) was determined at baseline. Longitudinal analyses of the association between each plasma carotenoid, either crude or expressed as a ratio to plasma lipids (total cholesterol + triglycerides), and the risk of dementia or AD were performed by multivariate Cox models. During follow-up, 199 dementia cases, including 132 AD, occurred. After adjustment for sociodemographic data, diet quality, and clinical variables, including baseline cognitive performances, only higher lutein concentration, considered as a function of plasma lipids, was consistently significantly associated with a decreased risk of all-cause dementia and AD (hazard ratio=0.808, 95% CI=0.671–0.973, $p=0.024$ and hazard ratio=0.759, 95% CI=0.600–0.960, $p=0.021$, respectively for +1 SD). This large cohort of older participants suggests that maintaining higher concentrations of lutein in respect to plasma lipids may moderately decrease the risk of dementia and AD.

*Feart C, J Gerontol Series A Biol Sci Med Sci
August 2015 doi: 10.1093/gerona/glv135*



Effects of egg consumption on carotenoid absorption from raw vegetables

Dietary lipids are one of the most effective stimulators of carotenoid absorption. The co-consumption of whole egg with carotenoid-rich foods may increase overall carotenoid absorption via lipid-rich egg yolk. We designed this study to assess the effects of egg consumption on carotenoid absorption from a carotenoid-rich, raw mixed-vegetable salad. Healthy young men ($n=16$) consumed the same salad (all served with 3 g canola oil) with no egg (control), 75 g scrambled whole eggs (1.5 eggs) [low egg (LE)], and 150 g scrambled whole eggs (3 eggs) [high egg (HE)] (a randomized crossover design). Control, LE, and HE meals contained 23 mg, 23.4 mg (0.4 mg from eggs), and 23.8 mg (0.8 mg from eggs) total carotenoids and 3 g, 10.5 g (7.5 g from eggs), and 18 g (15 g from eggs) total lipids, respectively. Blood was collected hourly for 10 h, and the triacylglycerol-rich lipoprotein (TRL) fraction was isolated. Total and individual carotenoid contents, including lutein, zeaxanthin, α -carotene, β -carotene, and lycopene in TRL were analyzed, and composite areas under the curve (AUCs) were calculated. The total mean (\pm SE) carotenoid AUC_{0-10h} in TRL was higher for the HE meal than for LE and control meals [125.7 ± 19.4^a compared with 44.8 ± 9.2^b and 14.9 ± 5.2^b nmol/L·10 h, respectively (values with superscripts without a common letter differ); $p<0.0001$]. The TRL AUC_{0-10h} of lutein and zeaxanthin increased 4–5-fold ($p<0.001$), and the TRL AUC_{0-10h} of carotenoids not present in eggs, including α -carotene, β -carotene, and lycopene, increased 3–8-fold ($p<0.01$) for the HE meal compared with the control meal. These findings indicate that co-consuming cooked eggs is an effective way to enhance carotenoid absorption from other carotenoid-rich foods such as a raw mixed-vegetable salad.

Kim JE, *Am J Clin Nutr*, May 27, 2015
doi:10.3945/ajcn.115.111062



Colorful cauliflowers

The first orange cauliflower was found in the Bradford Marsh in Canada in 1970. It was smaller than its white cauliflower cousin, but the unusual color made it interesting to plant breeders. Through successive generations of traditional crossbreeding with other varieties of cauliflower by Michael Dickson of Cornell University, a variety of larger and more flavorful orange cauliflower was developed. Besides the attractive color, the new variety of cauliflower was found to have important nutrients at levels many times higher than its ordinary white cousin. Over the years, plant breeders used similar, traditional techniques to develop the purple and green cauliflower varieties, each with its own unique nutritional profile, and mild, nutty flavor. Orange cauliflower contains 320 μ g of β -carotene/100 g, approximately 25 times more than white cauliflower. Purple cauliflower gets its beautiful color from purple pigments called anthocyanins, which are antioxidant flavonoids. One cup of raw green cauliflower provides 2% of the recommended daily value of vitamin A compared to 0% from the same serving of white cauliflower. Also, one cup of green cauliflower provides 94% of the recommended daily value of vitamin C compared to 77% from the same serving size of the ordinary white variety.

<http://colorfulharvest.com/Cauliflower.php>

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