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Beta-Carotene May Not Convert to Vitamin A as Easily as Once Thought

The antioxidant beta-carotene has long been thought of as “provitamin A” because the body can convert it to the biologically active vitamin. But a new study raises new doubts about how efficiently people make vitamin A from beta-carotene.

Beta-carotene is found widely in vegetables, particularly carrots, pumpkins, and butternut squash. Most multivitamin supplements contain beta-carotene instead of pure vitamin A, based on the assumption that the conversion occurs consistently.

George Lietz, PhD, of Newcastle University, United Kingdom, and his colleagues analyzed a specific gene known as BCMO1, which regulates the conversion of beta-carotene to vitamin A, also known as “preformed vitamin A.” In their study of 62 women, they found that 29 – almost half – possessed a genetic variation that prevented them from efficiently making vitamin A from beta-carotene.

“This genetic variability should be taken into account in future recommendations for vitamin A supplementation...[people with the genetic variation] may benefit from supplementation with preformed vitamin A rather than increased intake of plant provitamin A sources to combat vitamin A deficiency,” Lietz and his colleagues wrote.

The researchers hope to conduct a similar study of the gene and its variation in men.

In addition to the regulatory role of the BCMO1 gene, intestinal bacteria are also required to convert beta-carotene to vitamin A. The bacteria cleave, or cut off, part of the beta-carotene molecule to make vitamin A. Unbalanced intestinal bacteria, along with some diseases, can also interfere with the conversion of beta-carotene to vitamin A.

Vitamin A is an essential nutrient that, like vitamin D, is a precursor to a specific hormone that enhances immunity and reduces inflammation related to chest infections. An article in a 1928 issue of the *British Medical Journal* described it as the “anti-infective” vitamin.

Vitamin A is also needed to make and replenish rhodopsin, a key eye pigment that enables sight. Night blindness – difficulty seeing in the dark or being blinded by bright lights – is a classic sign of vitamin A deficiency.

In 1995, a study found that pregnant women taking more than 5,000 IU of vitamin A daily around the time of conception had a greater risk of delivering infants with birth defects. Since that time, companies have used either beta-carotene or smaller amounts in vitamin A in vitamin supplements.

Reference: Leung WC, Hessel S, Meplan C, et al. Two common single nucleotide polymorphisms in the gene encoding b-carotene 15,15'-monooxygenase after b-carotene metabolism in female volunteers. *FASEB Journal*, 2009;23:1041-1053. □

Perspectives

Up and Down Media Reports

The media roller coaster continued with recent news reports on the good and bad of nutritional supplements – all without providing any real context.

In one study, published in the *New England Journal of Medicine*, researchers combined either niacin (a form of vitamin B3) and a statin drug or the drug Zetia with a statin (a combination known as Vytorin). The niacin combination worked far better in terms reducing the thickening of the carotid artery, a major blood vessel.

As good as niacin is, the finding was neither new nor surprising. Abram Hoffer, MD, PhD, discovered that niacin lowers cholesterol back in 1955 – and it has been approved by the FDA for that purpose for more than 50 years.

Meanwhile, the *Journal of the American Medical Association* published a study claiming that supplements of the B-vitamin folic acid increased the risk of cancer. The study was a statistical shell game. Folic acid allegedly increased the risk of cancer by 38 percent, but the results were not statistically significant.

More research summaries on next page

If you read the actual study, not just the panicky newspaper and web news, you would have learned that 70 percent of the subjects were current or former smokers, all of the subjects had a high risk of cancer, and nearly all of the cases were lung cancers. Omitting this information was nothing less than sloppy journalism. So, if you smoke, should you stop taking your vitamins or stop smoking? –*JC*

Being Overweight Increases Requirements for Vitamin D

If you're overweight or obese, you're more likely to be vitamin D deficient – and will need larger amounts to restore normal blood levels of the vitamin.

Previous research has found that vitamin D, a fat-soluble nutrient, is sequestered by fat cells, keeping it out of blood circulation and away from other tissues.

Paul Lee, MBBS, of St. Vincent's Hospital, Sydney, Australia, and his colleagues measured the vitamin D levels and weight of 95 outpatients at a medical clinic. The patients' vitamin D levels were inversely related to their weight – that is, heavier people had lower vitamin D levels.

Lee and his colleagues also gave 10,000 IU of vitamin D3 daily for one week to 17 hospital patients who had a severe deficiency of the vitamin. While vitamin D levels increased in the patients, the amount of increase was related to their weight. Again, heavier patients had small increases in their blood levels of vitamin D.

“The current ‘epidemic’ of overweight and obesity is likely to increase the frequency and severity of vitamin D insufficiency encountered in clinical practice,” wrote Lee and his colleagues.

Reference: Lee P, Greenfield JR, Seibel MJ, et al. Adequacy of vitamin D replacement in severe deficiency is dependent on body mass index. *American Journal of Medicine*, 2009;122: 1056-1060. □

Vitamin C Supplements Appear to Reduce Risk of Fractures

A long-term study of elderly men and women has found that taking vitamin C supplements significantly lowers the risk of fractures, but dietary vitamin C alone does not confer this benefit.

Katherine L. Tucker, PhD, of Tufts University, Boston, and her colleagues analyzed dietary and health data from the Framingham Osteoporosis Study, which tracked 365 men and 592 women who averaged 75 years of age when the study began in the late 1980s. The subjects completed a dietary

questionnaire at that time and then were tracked for 15 to 17 years.

Overall, men and women who had the highest intakes of vitamin C – more than 300 mg daily – had the lowest risk of hip and nonvertebral (nonback) fractures, compared with people with the lowest intake of vitamin C.

However, the benefits were related to supplements, not dietary intake of vitamin C. Men and women who took an average of 260 mg of vitamin C or more daily were about 69 percent less likely to experience a hip fracture and 42 percent less likely to suffer a nonvertebral fracture.

Vitamin C is required in biochemical reactions leading to the production of bone, cartilage, and connective tissue.

“More than 1.5 million Americans experience osteoporotic fractures each year with an annual cost of nearly \$14 billion to the U.S. healthcare system,” the researchers wrote.

Reference: Sahni S, Hannan MT, Gagnon D, et al. Protective effect of total and supplemental vitamin C intake on the risk of hip fracture – a 17-year follow-up from the Framingham Osteoporosis Study. *Osteoporosis International*, 2009;20: 1853-1861. □

Case Report: Silymarin Benefit or Spontaneous Cancer Regression?

Silymarin, an extract of the herb milk thistle (*Silybum marianum*), has a long history as a folk remedy for liver disease. Medically, it has been used to improve type 2 diabetes and, in combination with other nutrients, to treat hepatitis C.

It may have potential benefits in the treatment of liver cancer, according to a recent case history published in *Cases Journal*.

Yaw-Sen Chen, MD, and his colleagues at E-Da Hospital, Taiwan, described the case of a 66-year-old man with a large liver cancer. The tumor measured 11 cm (4.3 inches) and appeared related to a history of liver cirrhosis and hepatitis. When examined in March 2006, the patient refused a biopsy and any type of conventional treatment. Instead, he began taking 450 mg of silymarin daily.

Chen and his colleagues conducted regular follow-up exams and ultrasound imaging. By December of that year, the tumor shrank to 4.6 cm (1.8 inches). The tumor did not shrink any further, and the patient agreed to surgery in May 2007.

“The postoperative course of this patient was smooth...Twenty months after the surgery, the patient is doing well and has no signs of tumor recurrence,” wrote Chen and his colleagues.

The researchers noted that spontaneous regressions of cancer are extremely rare, although they cited a 1995 report of liver cancer regression following silymarin supplementation. In general, liver cancer has a poor prognosis and is rapidly fatal.

Reference: Hsu CY, Sun PL, Chang HC, et al. Spontaneous regression of advanced hepatocellular carcinoma: a case report. *Cases Journal*, 2009;2:6251. A free copy of the journal article is available at: www.ncbi.nlm.nih.gov/pmc/articles/PMC2769275/?tool=pubmed □

N-Acetylcysteine, an Antioxidant, Helpful in Treating PCOS

Polycystic ovary syndrome (PCOS) affects an estimated 10 percent of women of reproductive age. The condition is often diagnosed when doctors investigate a cause for infertility and infrequent ovulation. It is also characterized by high levels of testosterone and insulin, insulin resistance (prediabetes), and overweight. PCOS is often treated with anti-diabetic drugs, such as metformin.

A recent study has found supplements of N-acetylcysteine (NAC) led to a variety of improvements, including more frequent ovulation.

Saghar Salehpour, MD, of Shahid Beheshti Medical University, Tehran, Iran, and her colleagues treated 46 women with either NAC or placebos for six weeks. Those getting NAC supplements took 1,800 mg daily. All of the women had been diagnosed with PCOS.

Salehpour reported that NAC led to more frequent monthly ovulations. The supplements also prompted significant decreases in weight, body-mass index, and waist-to-hip ratio. In addition, fasting blood sugar, insulin, total cholesterol, LDL cholesterol, and HOMA-IR (a marker of insulin resistance) decreased. Meanwhile, HDL cholesterol improved, but no changes occurred in female hormone levels.

“Hyperandrogenism [high levels of male hormones] interferes with follicular maturity in women. It seems that to further ovulation induction, NAC preserves more follicles in the ovary...” wrote Salehpour.

She added that “longer treatment with NAC may result in more desirable outcomes, such as more effective control of clinical hyperandrogenism.”

NAC is used medically to treat Tylenol overdose and mucus in the lungs. It is a potent over-the-counter antioxidant that has also been shown to significantly reduce influenza symptoms.

Reference: Salehpour S, Tohidi M, Akhound MR, et al. N acetyl cysteine, a novel remedy for poly cystic ovarian syndrome. *International Journal of Fertility and Sterility*, 2009;3:66-73. □

Green Tea Extract May Reverse Growth of Precancerous Lesions

Very large amounts of green tea extracts can reverse the growth of precancerous lesions in the mouth, according to a study by researchers at the M.D. Anderson Cancer Center in Houston, Texas.

Vassiliki Papadimitrakopoulou, MD, and her colleagues used a standardized, stable green tea extract or placebos to treat 41 patients over 12 weeks. Because of their lesions, all of the patients were at a high risk for developing oral cancers.

Patients received one of three doses of the green tea extract, and they were instructed to take that dose three times daily. Each dose consisted of approximately 1,200 mg, 1,800 mg, or 2,300 mg of the extract for a 150-pound person.

The two higher doses of green tea extract led to a positive clinical response in almost 60 percent of the patients. Only 18 percent of the patients improved in response to the placebos.

After follow up for a little over two years, 15 of the patients developed oral cancer. Although the same percentage of patients taking green tea extract or placebos developed cancer, the green tea did delay the cancer-free time until diagnosis.

The amount of green tea was roughly equal to drinking 10 cups of tea daily.

Reference: Tsao AE, Liu D, Martin J, et al. Phase II randomized, placebo-controlled trial of green tea extract in patients with high-risk oral premalignant lesions. *Cancer Prevention Research*, 2009;2:932-941. □

Royal Jelly Enhances Glucose Tolerance in Healthy Men

Bee products have a strong, even cultish following, but studies have shown that they do have many health benefits. For example, propolis, which bees derive from the resin of trees, is rich in polyphenolic antioxidants.

The latest research along these lines focused on royal jelly, a particular substance bees feed to larvae to turn them into queen bees. It likely contains nutrients to encourage growth and fertility in queen bees.

Karsten Münstedt, MD, PhD, of the Justus-Liebig University Hospital, Giessen, Germany, and his colleagues began their study by administering a 75-gram oral glucose-tolerance test to 20 men between 21 and 27 years of age.

A week later, after one of the subjects was excluded because of abnormal glucose tolerance, the remaining 19 men were asked to take 20 grams of

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Quick Reviews of Recent Research

• Meal timing can affect weight gain

Researchers have known that night-shift workers have a greater than average propensity for gaining weight. In addition, a high-fat diet can affect circadian rhythms and circadian patterns of gene activity. In a study, researchers at Northwestern University, Evanston, Illinois, altered the circadian light/dark cycle of laboratory mice for six weeks. Mice eating a high-fat diet at the “wrong” times were less active physically and more likely to gain significant amounts of weight. The researchers concluded that better timing of meals could slow the increasing incidence of obesity and related diseases.

Arble DM. *Obesity*, 2009;17:2100-2102.

• Supplements may reduce eye strain

Japanese and Singapore researchers asked 22 subjects to take a supplement containing black currant fruit extract (200 mg), lutein (5 mg), and zeaxanthin (1 mg) or a placebo daily for two weeks, after which time the supplements were reversed. When the subjects were asked to proofread for two hours, people who had been taking the supplements showed fewer symptoms of visual fatigue. Lutein and zeaxanthin form the macular pigment, the part of the eye responsible for fine vision.

Yagi A. *Applied Ergonomics*, 2009;40:1047-1054.

• Fruits and veggies reduce lymphoma risk

Researchers from the University of Minnesota and the Mayo Clinic analyzed dietary habits and the risk of non-Hodgkin lymphoma (NHL) among 35,159 women who were in their 50s and 60s when the study began. After 20 years of follow up, high intake of vegetables and fruits was associated with a significant reduction in the risk of developing NHL. Women who ate about seven servings of vegetables or fruits daily were 31 percent less likely to develop NHL. Those who consumed more than 14 servings of

yellow/orange vegetables each month had a 28 percent lower risk of NHL.

Thompson CA. *International Journal of Cancer*, 2009: epub ahead of print.

• Young Canadian adults low in vitamin C

Researchers at the University of Toronto measured blood levels of vitamin C among 979 nonsmoking men and women in their 20s. Fourteen percent of the subjects had outright deficiencies of vitamin C, and 33 percent had higher but still suboptimal levels of the vitamin. Only about half had adequate levels of vitamin C.

Cahill L. *American Journal of Epidemiology*, 2009;170:doi 10.1093/aje/kwp156

• Omega-3 fish oils found of benefit in PCOS

Polycystic ovary syndrome (PCOS) is typically characterized by an excess of male hormones, infertility, prediabetes and overweight. As is often the case in prediabetes and overweight, excess fat accumulates in the liver. Australian researchers asked 25 women with PCOS to take either 4 grams of omega-3 fish oils or placebos daily for eight weeks. Women taking the fish oils benefited from reductions in liver fat, triglycerides, and blood pressure, compared with those taking placebos.

Cussons AJ. *Journal of Clinical Endocrinology and Metabolism*, 2009;94:3842-3848.

• Fish oil derivative potent anti-inflammatory

Some omega-3 fish oil is converted to resolvin D2, a potent anti-inflammatory compound. In animal experiments, researchers from Great Britain and the United States determined that resolvin D2 reduced bacterial counts and controlled sepsis. Resolvin D2 protected laboratory mice from an over-active inflammatory response, reduced unnecessary white blood cell activity, and help clear bacteria from the blood.

Spite M. *Nature*, 2009;461:1287-1292.

Blood Sugar and Royal Jelly...

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royal jelly immediately before undergoing a second glucose-tolerance test.

The royal jelly reduced the glucose response one hour after the test and significantly so two hours after the test. In other words, royal jelly reduced the steep increase in blood sugar after the men consumed 75 grams of sugar. Insulin responses also decreased, but the researchers did not consider that change to be statistically significant.

Reference: Münstedt K, Bargello M, Hauenschild A. Royal jelly reduces the serum glucose levels in healthy subjects. *Journal of Medicinal Food*, 2009;12:1170-1172. □

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