Phytonutrient Profile

Vitamin A - Carotenoids

RIGHT IN THE CAROTENOIDS

When I start uttering words like "carotenoids" to people in casual situations who have never heard the term, they typically chuckle and make a joke about what the word reminds them of. Well, guess what? I do, too, because it helps keep this complex and sometimes boring topic light and fun. If you are offended, feel free to kick me right in the carotenoids if you ever see me out (fat chance, I'll be too busy on my next project).

Carotenoids may sound weird, but just think of the familiar word **beta-carotene** . . . carotene=carotenoid. That makes it somewhat clearer, doesn't it? There's also alpha-carotene, but the remainder of the commonly recommended carotenoids do not have the word "carotene" to help you categorize them. That's ok, though, as there's no need to memorize them. Just know that the next 3 phytonutrients in this section of the class (beta-crypoxanthin, Lutien/Zeaxanthin, and Lycopene) are all carotenoids. I just wanted you to know.

What makes a carotenoid a carotenoid anyway? The dictionary of chemistry terms phrases it this way:

ca·rot·e·noid
/kəˈrät(ə)nˌoid/ *noun*
"any of a class of mainly yellow, orange, or red fat-soluble pigments, including carotene, which give color to plant parts such as ripe tomatoes and autumn leaves."

It's that simple . . . Carotenoids give plants yellow, orange, and red colors. Why? To help plants trap light for photosynthesis and protect clorophyll from oxidation. They absorb blue-green-violet light and reflect earthy reds, yellows and oranges. In the Fall, when plants produce less chlorophyll, colors you see are all due to carotenoids.

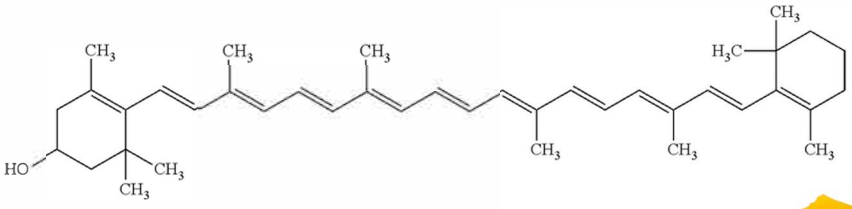
That's nice and all but what do they do for ME?

Without getting too technical, they do similar things for humans. Carotenoids are primarily known to protect us from oxidation (antioxidant), convert to vitamin A, and for keeping our eyes healthy by absorbing (effectively blocking) blue-violet light While that's what the group as-a-whole is known for, each **individual** carotenoid packs some amazing benefits, as well.

As carotenoids are grouped as forms of Vitamin A, you never really know which one you're getting just by looking at a label. All you see is Vitamin A. You could go your entire life meeting the recommended .8 mg (800 mcg) a day of vitamin A and yet still be deficient in one of the carotenoids. Well, maybe before this course you could have, but not by the time you're done with this section. You can thank me later.

Phytonutrient Profile

Beta-Cryptoxanthin - Butternut Squash



YOUR BACKSTAGE PASS

You may not have heard of it until this course, but beta-cryptoxanthin (BCX) is the rockstar of the carotenoids. Nutrition research has been buzzing about it for some time, and I fully expect it to end up a common household term in the coming years. Thanks to this course, you can beat the crowd and get a front row seat to its benefits. One day, you'll be able to say you were hip to it way before it was cool . . . just don't start hating on it once it's famous.

In a pure form, cryptoxanthin is a red crystalline solid with a metallic luster. While it is typically found in orange colored produce, along with red peppers, you have to seek out certain foods in order to get what you need. Obviously butternut squash is the #1 source or I wouldn't use it in so many recipes, but there are also other sources, to a lesser extent, that we will review on the next page.

A CAROTENOID ABOVE THE REST

While all of the carotenoids are important, if not mandatory, for keeping yourself fully functional, beta-cryptoxanthin (BCX) is turning out to be quite the over-achiever. Like its close cousin beta-carotene, beta-cryptoxanthin is used in the body as a source of pro-vitamin A retinol, which is needed for eyesight, maintenance of the skin, and human development. But, from there, BCX stands apart due to the impressive list of common diseases and conditions it protects against.

I like to show you how these phytonutrients actually work in the body, and I try to keep it brief, but BCX has so many functions and benefits that one or two paragraphs would be massively over-generalizing.

I'll make this easy and treat each disease it protects against as its own paragraph summary, with a sentence or two on how BCX actually does what it does for each.

Cool? Ok. Here we go!

< This good pupper, like BCX, is an over-achiever

Phytonutrient Profile

Beta-Cryptoxanthin - Butternut Squash

ADDING YEARS TO YOUR LIFE AND LIFE TO YOUR YEARS

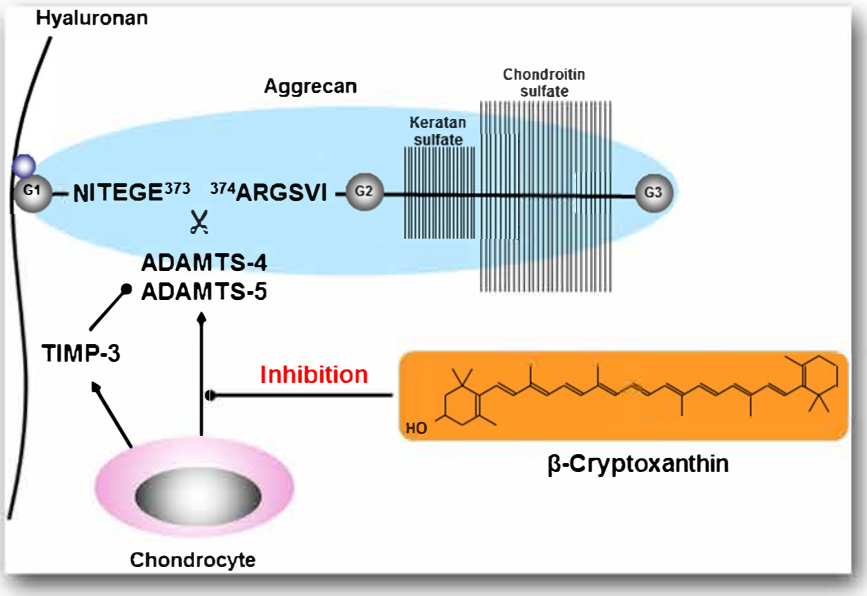
Following the guidelines set forth in this program WILL add years to your life, compared to eating S.A.D. (Standard American Diet). Beta-cryptoxanthin (BCX), however, is one the the phytonutrients that can also add LIFE to your YEARS. Here's how . . .

DO YOU LIKE BEING ABLE TO WALK/RUN?

Because there's no guarantee you'll always be able to, no thanks to osteoarthritis, rheumatoid arthritis, and osteoporosis. Having consulted many elderly clients on nutrition and exercise, I can tell you first hand that one of their biggest regrets is not taking better care of themselves in order to be able to still play and interact with family, go hiking, do simple things like walking the dog or even opening a jar of pickles. Staying active with frequent exercise and adequate calcium/vitamin D intake is obviously part of the battle, but that might not keep arthritis or bone loss from setting in. BCX, on the other hand, can do just that!

Anti-arthritic actions of βCX against the degradation of articular cartilage in vivo (tested in an actual living organism) and in vitro (tested in lab equipment)

This 2016 study showed us that BCX directly affects a crucial aspect of cartilage structure known as Aggrecan. Aggrecan is broken down by the enzyme Aggrecanase (enzymes always end in suffix -ASE). While bones and cartilage are constanly in a balanced state of breaking down and rebuilding, it is possible for the balance to be disrupted in favor of breakdown, leaving cartilage damaged, weak, or non-existent. **BCX shields cartilage from being broken down in 3 ways by:**



-slowing and decreasing aggrecanase activity

-down-regulating the expression of aggrecanase 1 (ADAMTS-4) and aggrecanase 2 (ADAMTS-5) in human chondrocytes (cartilage matrix).

-augmenting the expression of aggrecan core protein in human chondrocytes.

Source: Biochem Biophys Res Commun. 2016 Aug 5;476(4):352-358. doi: 10.1016/j.bbrc.2016.05.126. Epub

Phytonutrient Profile

Beta-Cryptoxanthin - Butternut Squash

...continued

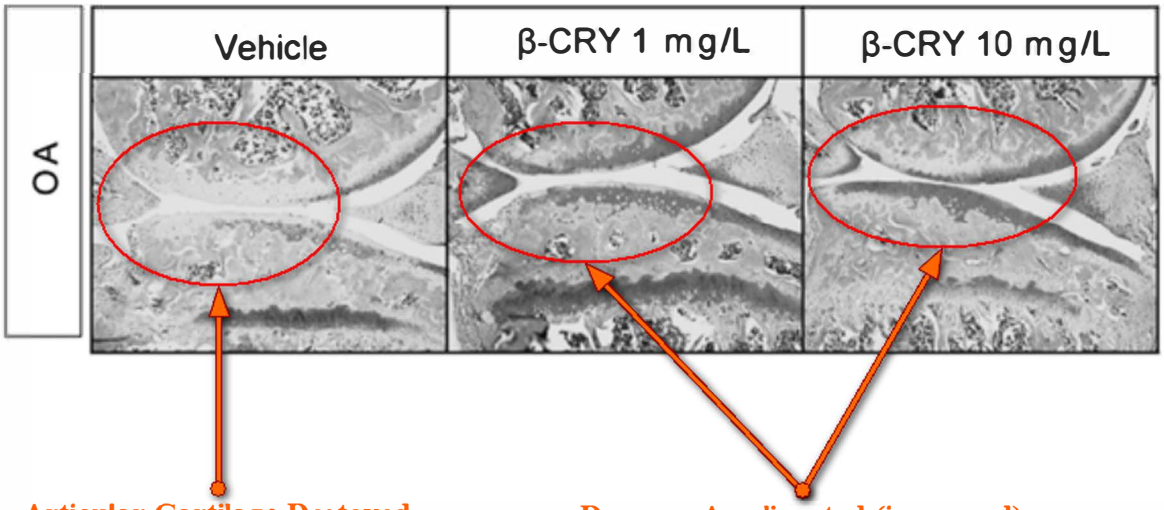
The study came to the conclusion that there is " . . . novel evidence that β-cryptoxanthin exerts anti-arthritic actions and suggest that β-cryptoxanthin may be useful in blocking the progression of **rheumatoid arthritis** and **osteoarthritis (OA)**.

OA, which is characterized by progressive articular cartilage destruction, is caused by various factors, including joint injury, obesity, and aging, and frequently leads to a loss of ability and stiffness in the elderly. Loss of ability = loss of independence and self reliance. Everyone is at risk in their later years, particularly post-menopausal women, but that can be prevented by the food choices made throughout one's lifespan.

To date, no effective medical therapies have been developed that prevent OA cartilage destruction. Supplementation of glucosamine and chondroitin sulfates has been used to relieve pain or slow the degradation of cartilage in joints; however, it has recently been reported that glucosamine and chondroitin sulfates, even in combination, do not have a clinically relevant effect on perceived joint pain or on joint space narrowing. Furthermore, long-term treatment of patients with OA with analgesics and non-steroidal anti-inflammatory drugs (Ibuprofen, Advil, etc) can lead to serious gastrointestinal and cardiovascular adverse events.

BCX might be the remedy. It's safe, has no side effects, is immune to patents and price gouging by pharmaceutical companies (try to patent butternut squash, I dare ya), cheap, and tasty. Look at the articular cartilage of mice with OA in the figure below. The left panel (vehicle) was not treated with BCX, panel 2 was treated with 1mg and 3 with 10mg.

Osteoarthritis in 3 models - No treatment (Vehicle), 1mg BCX, and 10mg BCX



Articular Cartilage Destoyed
Significant Damage to Structure
Boundaries Non-Existant - Grinding

Damage Ameliorated (improved)
Boundaries Re-Established
Healthy Cartilage Restored

Phytonutrient Profile

Beta-Cryptoxanthin - Butternut Squash

...continued

As mentioned earlier, our bones are not like rocks embedded in our bodies, rather, they are constantly breaking down (thanks to osteoclast cells) and rebuilding (osteoblast cells). Even those who avoid osteoarthritis may face significant age-related bone loss. This brand of bone weakening is called osteoporosis (osteo-bone, porosis-porous = porous bone). Does it sound like something you want to deal with? Nope. Would you be willing to prep butternut squash if it could prevent it? Because it probably can.

Aging induces bone loss due to decreased osteoblastic (building) bone formation and increased osteoclastic (breakdown) bone resorption. Osteoporosis with its accompanying decrease in bone mass is widely recognized as a major public health problem. **βCX has stimulatory effects on osteoblastic bone formation and inhibitory effects on osteoclastic bone resorption in vitro, thereby increasing bone mass.** The intake of βCX may have a preventive effect on bone loss in animal models for osteoporosis and in healthy human or postmenopausal women. The researchers concluded that there is a role for **BCX as a " . . . sustainable nutritional approach to improving bone health of human subjects"** (Yamaguchi, 2012). This 2012 study was performed in-vitro (lab equipment), and not in humans, so the results are encouraging but need to be confirmed in humans. Although, looking at all of the other research, I'm confident it will be. (see references below)

STRESS REDUCED - METABOLISM UPREGULATED - PAIN RELIEF AND MORE

A study published just this year showed that **" . . . BCX revealed upregulation of the energy metabolism, response to stress, and protein homeostasis" as its main metabolic targets**, and provides " . . . new in vivo evidence of the potential therapeutic use of BCX in the prevention of diseases related to metabolic syndrome and aging" (Llopis, et al, 2019).

Preliminary data suggested that the ingestion of β-CRX had an anti-stress effect in female participants, so the effect was evaluated in another set of female participants. Salivary α-amylase activity (sAA), a marker of sympathetic nervous system activity, was significantly higher in the evening than in the morning in the placebo-group during pharmacy practice, but not in the β-CRX-group. **This result supports the anti-stress effect of β-CRX.** (Unno, K et al, 2019).

Allodynia is an unusual symptom that can result from several nerve-related conditions. When you're experiencing it, you feel pain from stimuli that don't normally cause pain. For example, lightly touching your skin or brushing your hair might feel painful. Park, et al, found that **BCX ameliorated (made better) tactile allodynia.**

There are additional benefits and studies, too numerous to include here, that are published or underway. I look forward to posting more about it on my blog.

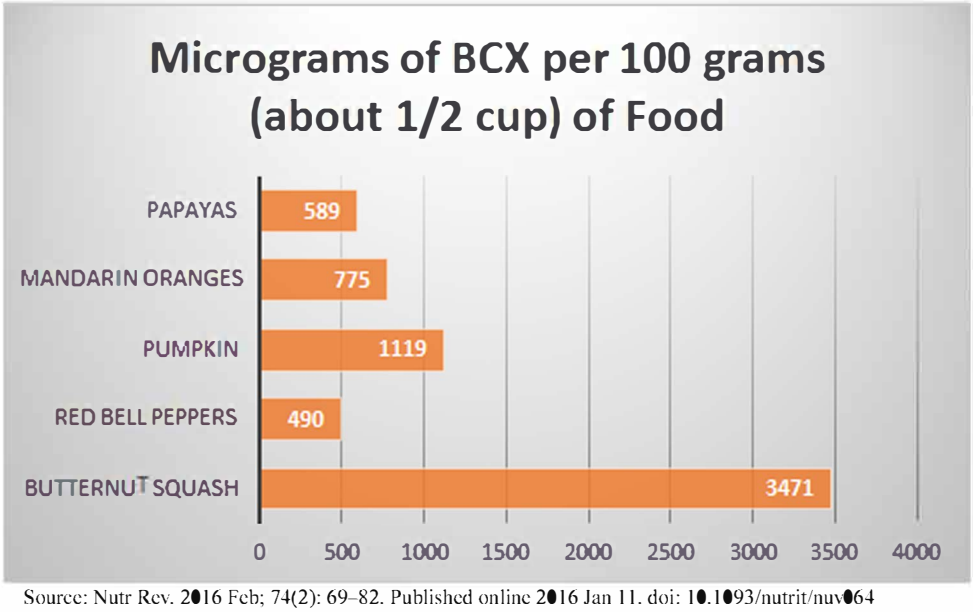
Phytonutrient Profile

Beta-Cryptoxanthin - Butternut Squash

IS IT REALISTIC TO EAT ENOUGH SQUASH TO HAVE AN EFFECT, OR DO I NEED A PILL?

Vitamin A and all of the carotenoids are fat soluble, which means we can store it in our body for small periods of time. Just from that knowledge alone, one could deduce that it is realistic to eat enough butternut squash to get clinically relevant benefits. We don't need to deduce, however, because we've studied it. Park, et al (2017) found that " . . . long-term intake of βCX-rich foods gradually increases blood βCX levels in both humans and animals . . . daily consumption of βCX-rich foods could achieve a pharmacologically relevant dose of βCX similar to that used in this study."

Llopis, et al. was smart to study the effect of BCX in isolation (by itself) as well as BCX along-side lycopene, beta-carotene, and other carotenoids. Things don't exist in isolation in nature or in our bodies, and sometimes things dont work as well for us when they are removed from their natural "packaging", if you will. They concluded that " . . . a comparative analysis with other carotenoids, such as lycopene and β-carotene, showed a stronger effect of BCX" (2019). So there you have your answer. **Yes, you can build up a clinically relevant blood concentration of BCX by eating foods rich in it often, and No, taking a BCX pill probably wouldn't have the same effect as butternut squash.** Amazing, isn't it?



Source: Nutr Rev. 2016 Feb; 74(2): 69–82. Published online 2016 Jan 11. doi: 10.1093/nutrit/nuv064

COME AND GET IT!

Above is a list of foods with the highest concentration of BCX. As you can see, good old butternut squash is #1. Butternut squash also adds a unique flavor and texture to dishes that you will enjoy without a bunch of sugar. I needed you to see this to justify how often I use butternut squash in my recipes and to show you that it truly is worth the hassle. I mean, which is more of a hassle, prepping and eating butternut squash, or a painful decline in joint health until you can barely function? SHOW ME THE CUTTING BOARD!

Beta-Cryptoxanthin - The Research

You can trust me, but don't take my word for it....

As part of my Bachelor Degree Curriculum, we learned how to read those technically accurate, painfully thorough scientific research papers published in journals. Do you need special training, too? I think we all do, but you don't need an entire course in it.

Reading through the references I provide gives you a few benefits:

*You can see any limitations or flaws in the experiment
*You can find information I may have left out that is relevant to YOU
*You can get a clear picture of the researchers assumptions, as well as mine, and decide if YOU agree with us or not.

If you are new to research, please follow this link to Purdue University's "How To Read A Scientific Paper" PDF. It's cartoony and full of pictures, in case you were worried about it being technical. ***Just copy this link and paste it into your browser.***
https://www.lib.purdue.edu/sites/default/files/libraries/engr/Tutorials/Newest%20Scientific%20Paper.pdf

On that note, scan through the titles below and find one that piques your interest. Copy the title in BOLD print and paste it into your search engine. I use google and never have a problem getting the study to pop right up. If you have any trouble pulling up a study, please let me know and I will help you immediately.

References

Burri BJ1, Chang JS, Neidlinger TR. (2011). **ß-Cryptoxanthin- and a-carotene-rich foods have greater apparent bioavailability than ß-carotene-rich foods in Western diets.** Br J Nutr. 2011 Jan;105(2):212-9. doi: 10.1017/S0007114510003260.

Burri, et al (2016). **Absorption, metabolism, and functions of β-cryptoxanthin.** Nutr Rev. 2016 Feb; 74(2): 69–82. Published online 2016 Jan 11. doi: 10.1093/nutrit/nuv064

Johnell O, Kanis JA (2006, 17). **An estimate of the worldwide prevalence and disability associated with osteoporotic fractures.** Osteoporos Int. 1726-1733. 10.1007/s00198-006-0172-4.

Bonjour J-P, Schurch M-A, Rizzori R: **Nutritional aspects of hip fracture.** Bone. 1996, 18: 1395-1445.

Yamaguchi M: **Isoflavone and bone metabolism: its cellular mechanism and preventive role in bone loss.** J Health Sci. 2002, 48: 209-222. 10.1248/jhs.48.209.

Beta-Cryptoxanthin - The Research

Yamaguchi M: **Regulatory mechanism of food factors in bone metabolism and prevention of osteoporosis.** Yakugaku Zasshi. 2006, 126: 1117-1137. 10.1248/yakushi.126.1117.

Yamaguchi M: **Role of nutritional zinc in the prevention of osteoporosis.** Mol Cell Biochem. 2010, 338: 241-254. 10.1007/s11010-009-0358-0.

Yamaguchi M, Hamamoto R, Uchiyama S, lshiyama K: **Effects of flavonoid on calcium content in femoral tissue culture and parathyroid hormone-stimulated osteoclastogenesis in bone marrow culture in vitro.** Mol Cell Biochem. 2008, 303: 83-88.

Yamaguchi M, Hachiya S, Hiratsuka S, Suzuki T: **Effect of marine algae extract on bone calcification in the femoral-metaphyseal tissues of rats: Anabolic effect of Sargassum horneri.** J Health Sci. 2001, 47: 533-538. 10.1248/jhs.47.533.

Williams JA, Kondo N, Okabe T, Takeshita N, Pilchak DM, Koyama E, Ochiai T, Jensen D, Chu M-L, Kane MA, Napoli JL, Enomoto-Iwamoto M, Ghyselinck N, Chambon P, Pacifici M, Iwamoto M: **Retinoic acid receptors are required for skeletal growth, matrix homeostasis and growth plate function in postnatal mouse.** Dev Biol. 2009, 328: 315-327. 10.1016/j.ydbio.2009.01.031.

Park CK, lshimi Y, Ohmura M, Yamaguchi M, lkegami S: **Vitamin A and carotenoids stimulate differentiation of mouse osteoblastic cells.** J Nutr Sci Vitaminol {Tokyo). 1997, 43: 281-296. 10.3177/jnsv.43.281.

Conaway HH, Persson E, Halen M, Granholm S, Svensson 0, Pettersson U, Lie A, Lerner UH: **Retinoids inhibit differentiation of hematopoetic osteoclast progenitors.** FASEB J. 2009, 23: 3526-3538. 10.1096/fj.09-132548.

Caire-Juvera G, Ritenbaugh C, Wactawski-Wende J, Snetselaar LG, Chen Z: **Vitamin A and retinol intakes and the risk of fractures among participants of the Women's Health Initiative Observational Study.** Am J Clin Nutr. 2009, 89: 323-330.

Promislow JHE, Goodman-Gruen D, Slymen DJ, Barret-Connor E: **Retinol intake and bone mineral density in the elderly: the rancho brenardo study.** J Bone Miner Res. 2002, 17: 1349-1358. 10.1359/jbmr.2002.17.8.1349.

Yamaguchi M, Uchiyama S: **Effect of carotenoid on calcium content and alkaline phosphatase activity in rat femoral tissues in vitro: the unique anabolic effect of 13-cryptoxanthin.** Biol Pharm Bull. 2003, 26: 1188-1191. 10.1248/bpb.26.1188.

Yamaguchi M, Uchiyama S: **13-Cryptoxanthin stimulates bone formation and inhibits bone resorption in tissue culture in vitro.** Mol Cell Biochem. 2004, 258: 137-144.

Parfitt AM: **Bone-forming cells in clinical conditions. The Osteoblast and Osteocyte. Bone.** Edited by: Hall BK. 1990, Boca Raton, FL: Telford Press and CRC Press, 1: 351-429.

Raggatt LJ, Partridge C: **Cellular and molecular mechanisms of bone remodeling.** J Biol Chem. 2010, 285: 25103-25108. 10.1074/jbc.R109.041087.

Beta-Cryptoxanthin - The Research

Maggio D, Polidori MC, Barabani M, Tufi A, Ruggiero C, Cecchetti R, Aisa MC, Stahl W, Cherubini A: **Low levels of carotenoids and retinal in involutional osteoporosis.** Bone. 2006, 38: 244-248. 10.1016/j.bone.2005.08.003.

Rao LG, Krishnadev N, Banasikowska K, Rao AV: **Lycopene effects on osteoclasts: lycopene inhibits basal and parathyroid hormone-stimulated osteoclast formation and mineral resorption mediated by reactive oxygen species in rat bone marrow cultures.** J Med Food. 2003, 6: 69-78. 10.1089/109662003322233459.

Rao LG, Mackinnon ES, Josse RG, Murray TM, Strauss A, Rao AV: **Lycopene consumption decreases oxidative stress and bone resorption markers in postmenopausal women.** Osteoporos Int. 2007, 18: 109-115. 10.1007/s00198-006-0205-z.

Mackinnon ES, Rao AV, Josse RG, Rao LG: **Supplementation with the antioxidant lycopene significantly decreases oxidative stress parameters and the bone resorption marker N-telopeptide of type I collagen in postmenopausal women.** Osteoporos Int. 2011, 22: 1091-1101. 10.1007/s00198-010-1308-0.

McEligot AJ, Rock CL, Shanks TG, Flatt SW, Newman V, Farber S, Pierce JP: **Comparison of serum carotenoid responses between women consuming vegetable juice and women consuming raw or cooked vegetable.** Cancer Epideminol Biomarkers Prev. 1999, 8: 227-231.

Uchiyama S, Yamaguchi M: **13-Cryptoxanthin stimulates cell proliferation and transcriptional activity in osteoblastic MC3T3-Elcells.** Int J Mol Med. 2005, 15: 675-681.

Uchiyama S, Yamaguchi M: **13-Cryptoxanthin stimulates cell differentiation and mineralization in osteoblastic MC3T3-El cells.** J Cell Biochem. 2005, 95: 1224-1234. 10.1002/jcb.20496.

Centrella M, McCarthy TL, Canalis E: **Receptors for insulin-like growth factor-I and -II in osteoblast-enriched cultures from fetal rat bone.** Endocrinology. 1990, 126: 39-44. 10.1210/endo-126-1-39.

Yamaguchi M, Weitzmann MN: **The bone anabolic carotenoids p-hydroxycinnamic acid and 13-cryptoxanthin antagonize NF-KB activation in MC3T3 preosteoblasts.** Mol Med Rep. 2009, 2: 641-644.

Yamaguchi M, Weitzmann MN: **The bone anabolic carotenoid 13-cryptoxanthin enhances transforming growth factor-131-induced SMAD activation in MC3T3 preosteoblasts.** Int J Mol Med. 2009, 24: 671-675.

Uchiyama S, Yamaguchi M: **Inhibitory effect of 13-cryptoxanthin on osteoclast-like cell formation in mouse marrow cultures.** Biochem Pharmacol. 2004, 67: 1297-1305. 10.1016/j.bcp.2003.11.011.

Uchiyama S, Yamaguchi M: **13-Cryptoxanthin stimulates apoptotic cell death and suppresses cell function in osteoclastic cells: Change in their related gene expression.** J Cell Biochem. 2006, 98: 1185-1195. 10.1002/jcb.20824.

Uchiyama S, lshiyama K, Hashimoto K, Yamaguchi M: **Synergistic effect of 13-cryptoxanthin and zinc sulfate on the bone component in rat femoral tissues in vitro: the unique anabolic effect with zinc.** Biol Pharm Bull. 2005, 28: 2142-2145. 10.1248/bpb.28.2142.

Beta-Cryptoxanthin - The Research

Yamaguchi **M,** lgarashi A, Morita S, Sumida T, Sugawara K: **Relationship between serum 13-cryptoxanthin and circulating bone metabolic markers in healthy individuals with the intake of juice (Citrus unshiu) containing 13-cryptoxanthin.** J Health Sci. 2005, 51: 738-743. 10.1248/jhs.51.738.

Yamaguchi M, lgarashi A, Uchiyama S, Sugawara K, Sumida T, Morita S, Ogawa H, Nishitani M, Kajimoto Y: **Effect of 13-cryptoxanthin on circulating bone metabolic markers: Intake of juice (Citrus unshiu) supplemented with 13-cryptoxanthin has an effect in menopausal women.** J Health Sci. 2006, 52: 758-768. 10.1248/jhs.52.758.

Wang Y, Hodge AM, Wluka AE, English DR, Giles GG, O'Sullivan R, Forbes A, Cicuttini FM: **Effect of antioxidants on knee cartilage and bone in healthy, middle-aged subjects: a cross-sectional study.** Arthritis Res Ther. 2007, 9: R66-10.1186/ar2225.

Sugiura M, Nakamura M, Ogawa K, lkoma Y, Ando F, Yano M: **Bone mineral density in post-menopausal female subjects is associated with serum antioxidant carotenoids.** Osteoporos Int. 2008, 19: 211-219. 10.1007/s00198-007-0457-2.

Granado-Lorencio F, Olmedilla-Alonso B, Herrero-Barbuda C, Blanco-Navarro I, Perez-Sacristan B: **Seasonal variation of serum alpha- and beta-cryptoxanthin and 25-OH-vitamin D3 in women with osteoporosis.** Osteoporos Int. 2008, 19: 717-720. 10.1007/s00198-007-0470-5.

Sahni S, Hannan MT, Blumberg J, Cupples LA, Kiel DP, Tucker KL: **Protective effect of total carotenoid and lycopene intake on the risk of hip fracture: a 17-year follow-up from the Framingham osteoporosis study.** J Bone Miner Res. 2009, 24: 1086-1094. 10.1359/jbmr.090102.

Yang Z, Zhang Z, Penniston KL, Binkley N, Tanumihardjo SA: **Serum carotenoid concentrations in postmenopausal women from the United States with and without osteoporosis.** Int J Vitm Nutr Res. 2008, 78: 105-110. 10.1024/0300-9831.78.3.105.

S Llopis, M Rodrigo, N Gonzalez, S Genoves, L Zacarias, D Ramon, P Martorell {2019). **13-Cryptoxanthin Reduces Body Fat and Increases Oxidative Stress Response in Caenorhabditis elegans Model.** Cell Bio Lab, Food Biotech Department, Midland, Paterna, 46890 Valencia, Spain

Unno K, et al.Anti-stress **Effect of 13-Cryptoxanthin in Satsuma Mandarin Orange on Females**. Biol Pharm Bull. 2019;42{8):1402-1408. doi: 10.1248/bpb.b19-00325.

Sugiura M, Nakamura M, Ogawa K, lkoma Y, Ando F, Shimokata H, Yano **M: Dietary patterns of antioxidant vitamin and carotenoid intake associated with bone mineral density: findings from post-menopausal Japanese female subjects.** Osteoporos Int. 2010, 36: 2293-2298.

Tsuda **M,** Masuda T, Tozaki-Saitoh H, et al. **Microglial regulation of neuropathic pain.** J Pharmacol Sci. 2013;121:89-94.10.1254/jphs.12R14CP [Crossref], [PubMed], [Web of Science ®]

G Park, T Horie, T lezaki, M Okamoto, K Fukasawa, T Kanayama, **Daily oral intake of 13-cryptoxanthin ameliorates neuropathic pain.** p.1014-1017 .23 Jan 2017