

Exploring the Role of Palm Tocotrienol for Bone and Joint Health

| Page number | Table of Content |
|-------------|--|
| 1 | Bone Health |
| 2 | Supplements: Part of the Wholesome Bone Health Plan |
| 3 | Tocotrienol for Bone Health, What Does the Science Say? |
| 5 | Palm Tocotrienols for Bone Health and Support |
| 5 | Studies using Palm Tocotrienol on Bone |
| 6 | Additional Benefits in Joint Health |
| 7 | EVNol SupraBio™ : Bioavailable Bone Health Solution? |
| 8 | The Bottom Line |
| 8 | References |
| 9-10 | 6 Reasons to Trust Excelvite On Your Product Development Journey |

Bone Health

Since the onset of the COVID-19 pandemic, there has been rising health awareness where many people are beginning to take preventive measures against present health issues by living a healthy lifestyle. In the same way, bone and joint health should also be seen as a health priority at all stages of life.

Bone health is no longer a concern for the elderly only, these days, people aged 20 or even younger have started to take note. The period of childhood, adolescence, and early adulthood are the golden times for people to build bone density and increase peak bone mass (the point where the bone reaches its maximum density and

strength). Peak bone mass will be reached when people enter into their late 20s. Those who have more "deposited" bone mass during their youth will more likely be better protected against osteoporosis and other bone-related problems later in life.

With aging, women tend to lose bone mass at a faster rate compared to men, especially in the first few years after menopause. Osteoporosis is not a normal part of aging although it is common in old age. For women older than 50 years of age, the rate of getting

osteoporosis and osteopenia is increased four and two times respectively [2]. Although men usually experience fractures 10 years later compared with women, the fatality rate after hip fracture is higher than women [3]. Hence, taking good care of our bones since young is no longer inconsequential. Given the knowledge that both genders can be affected by bone ailments at different ages and rates, it makes sense for every one of us to invest in bone health that can make a difference in the quality of our lives, eventually.

According to the International Osteoporosis
Foundation, 1 out of 3 women over the age of 50 and 1 in 5 men have experienced osteoporotic fractures in their lifetime.

This global epidemic has led scientists and industries to relentlessly seek an effective osteoporosis-preventive agent. As this article would show, new findings have demonstrated that Vitamin E - specifically palm tocotrienol could be a promising alternative nutrient beyond calcium and Vitamin D for bone health optimization. With the growing body of science, ExcelVite's EVNol™ series of tocotrienol complex have the potential to benefit bone and joint health.

Supplements: Part of The Wholesome Bone Health Plan



healthy Having bones considerably important for overall good health. However, there is no single "magic" solution to keeping your bone healthy. Consistent lifestyle habits that can be adopted to maintain bone health are - staying physically active. maintaining healthy weight, consuming well-balanced diets, and avoiding smoking and drinking. By practicing these, a person's bone density can be maintained or boosted slowly but surely over time. Having said that, diet and specific nutrient intake also contribute a major role in this big-picture or life-long plan for maintaining bone health.

Sufficient levels of calcium and Vitamin D are crucial for building and maintaining bone health. However, some people may find it difficult to attain recommended levels for the nutrients solely through diet.

For instance, people who are lactose intolerant, vegan and those who avoid dairy products may have a harder time meeting the daily requirements of calcium for optimum bone health.

Likewise, getting adequate Vitamin D from food alone is also difficult, more so if a person stays indoors most of the time and not getting enough sunlight to trigger the skin to synthesize vitamin D. For these reasons, supplements are often recommended in one's bone health plan for a more effective approach especially as we age.

Today, many innovative and safe ingredients are increasingly recognized as significant contributors in optimizing bone and joint health besides calcium. These include magnesium, glucosamine, omega-3 fatty acids, collagen, Vitamin K, B, C, and E. According to Nutrition Insight.com, the top 5 ingredients with bone health claims that have been seen in recent supplements and sports nutrition product launches are Vitamin D3, C magnesium, Vitamin B6, and Vitamin E (Figure 1).

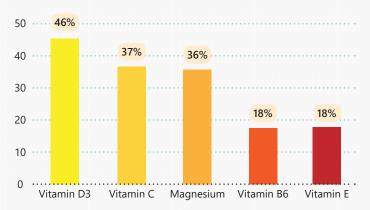


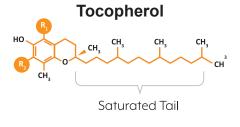
Figure 1: Top 5 Ingredients as a percentage (%) of Supplements & Sports Nutrition Launches Tracked with a Bone Health Claim (Global, 2021)

Tocotrienols For Bone Health, What Does the Science Say?

Tocotrienol and tocopherol belong to the Vitamin E family. The chemical structures of tocotrienol and tocopherol may look similar but they are differentiated by tocotrienol having three double bonds in the "tail" of its structure whereas tocopherol has no double bond, meaning that it has a fully saturated tail. These two groups of compounds can be subdivided into 4 isoforms: alpha, beta, gamma, and delta. In the past several decades, tocopherol was the focus of research due to it being found more abundantly in human and various kinds of fruits, plants, and seed oils. Yet, with the growing body of science, it now appears that tocotrienol is the more potent form of Vitamin E in terms of biological functions [4].

The way tocotrienol benefits bone health with respect to improving bone mineral density (BMD) and bone microstructure can be attributed primarily to its role as a powerful antioxidant and its anti-inflammatory properties.

Tocotrienol HO CH, CH, CH, CH, CH, CH, CH,







Research has shown that tocotrienol confers bone protection through the following mechanisms of action:

A normal bone remodelling process involves the balance between bone formation (performed by osteoblast) and resorption (performed by osteoclast). On the contrary, the imbalance between bone formation and resorption can lead to metabolic bone diseases such as osteoporosis. Oxidative stress has been implicated as a factor in osteoporosis as it can cause the imbalance between osteoclast and osteoblast activity during the bone remodelling process ^[5].

In fact, osteoblast which is the cell involved in bone formation is sensitive to oxidative stress. The stimulation of oxidative stress can eventually cause osteoblast death. In this regard, tocotrienol, being a potent antioxidant, is able to fight against free radicals and thus protect osteoblast from oxidative stress ^[6].

Antioxidant Action by Tocotrienol

Effect of Tocotrienol on the Mevalanote Pathway

Another way tocotrienol preserves bone is through the mevalonate pathway. In the current treatment for preserving bone health, statins and bisphosphonates are the commonly prescribed drugs ^[9, 10]. Similar to statins and bisphosphonates, tocotrienol may offer bone protective effects by its action on the same mevalonate pathway.

This pathway is not only related to cholesterol synthesis but is also relevant for bone metabolism. Early research evidence showed that tocotrienol may protect against bone loss via its HMG-CoA reductase inhibition mechanism in the mevalonate pathway [11].



Concurrently, oxidative stress is tightly linked with inflammation, where chronic inflammation could also be an etiology of osteoporosis. Excessive free radicals in the body will increase proinflammatory cytokines, called Interleukin-1 and Interleukin-6. Both of these cytokines are important regulators in bone resorption ^[7]. A previous study has shown that tocotrienol is able to suppress these pro-inflammatory cytokines which can cause bone resorption and thus prevent bone loss ^[8].

Anti-inflammatory Action by Tocotrienol

Gene Modulation by Tocotrienol

Our genes play a crucial role in governing the activity of both osteoblast and osteoclast in bone metabolism. In nicotine-induced osteoporosis, gene expression is significantly downregulated. It was found that palm tocotrienol has the ability to reverse the effect in a way that it enhances the gene expression that involves in osteoblast differentiation [12]. In layman's terms, tocotrienol is effective in restoring bone metabolism that was impaired by nicotine [13].

Palm Vitamin E Tocotrienol for Bone Health and Support

Palm oil (Elaeis guineensis) is one of the most concentrated sources of Vitamin E, which 78% naturally contains tocotrienol (predominantly gamma-tocotrienol) along with 22% of alpha-tocopherol. Due its powerful antioxidant properties, it was believed that tocotrienol can be helpful in bone ailments like osteoporosis which has been linked to oxidative stress.

Of note, pertaining to bone health, most of the studies reported on the potential effect from **tocotrienol** rather than tocopherol.



Furthermore, there are studies to show that high doses of alpha-tocopherol supplementation might exert detrimental effects on the bone of normal animals [14]. On the other hand, it is suggested that palm tocotrienol could be a better choice than alphatocopherol in bone protection. There are findings that demonstrated palm tocotrienol as more effective in fighting against free radical damage and suppressing lipid peroxidation in bone [15].

Studies using Palm Tocotrienol on Bone

The beneficial effects of palm tocotrienol on bone health are backed by a myriad of scientific evidence.

Amongst these studies, one of them investigated the effect of palm tocotrienol supplementation on osteoporosis and metabolic syndrome concurrently as both medical conditions are interrelated. The administration \circ f EVNol™ (natural full spectrum palm tocotrienol/tocopherol complex) has proven in-vivo to possess the protective effect against bone Upon supplementation of palm tocotrienol, it also showed significant improvement in some of the metabolic syndrome parameters including lipid profile, pressure, and glycemic status [16].



Tocotrienol/Tocopherol Complex

In the study, **EVNol™** was able to alleviate metabolic syndrome and bone loss through its strong anti-inflammatory properties [17]. Interestingly, at a lower dose, palm tocotrienol has been touted to be more effective than annatto tocotrienol (90% delta tocotrienol), due to its mixed composition of tocotrienol and tocopherol. It was suggested to have possible interaction between these two vitamin E compounds, where they work synergistically to alleviate oxidative stress and inflammation

Apart from the preventive effect on bone, tocotrienol was also newly discovered to have the potential in reversing incidences of osteoporosis. Fracture healing is an intricate process, which normally takes 6 to 8 weeks to heal completely. The healing process can even be delayed, notably in the case of osteoporosis. Although the investigation of the "reversing effect" of tocotrienol in bone is still in the preliminary stage, yet the research outcomes seem promising.

Another study performed by the same group of researchers has also cast a new light on the mechanism of action of palm tocotrienol in protecting the bones.

In an in-vivo study, the effect of palm tocotrienol and alphatocopherol supplementation on fracture healing was examined in rat models with postmenopausal osteoporosis.

Two months of palm tocotrienol supplementation have led to an improvement in the biomechanical properties such as strength and quality of the healed fracture [16].

Alpha-tocopherol supplementation, however, did not appear to confer the same effect on the biochemical properties of fractured bone but it only aided in the acceleration of the healing process [19, 20].

In the meantime, the effect of supplementation of palm tocotrienol and calcium were also being compared on estrogen-deficient models. The study revealed that palm tocotrienol significantly increased bone formation evidenced

by several bone markers whereas calcium alone did not seem to make a difference in the bones [21]. In short, in preventing estrogen-deficient bone loss, tocotrienol plays a more crucial role compared to calcium.

Additional Benefits in Joint Health

Vitamin E tocotrienol not only supports bone protection but it has also been shown to support joint health maintenance.

Supplementation of palm tocotrienol show improvement in arthritis mostly in in-vivo studies at this stage. The finding revealed a significant reduction in the seriousness of histopathological changes when the arthritic subject is treated with palm tocotrienol supplementation [22].

It is also reported that the potential role of palm tocotrienol in reducing the symptoms of osteoarthritis is comparable with glucosamine sulphate, which is a common supplement that helps in pain relief for patients with osteoarthritis [23].



Tocotrienol/Tocopherol Complex

Together, the combined treatment of palm tocotrienol (EVNol[™]) and glucosamine sulphate is way more effective than the individual treatment in terms of improving the grip strength and sustaining the body weight in osteoarthritis study subjects ^[24].

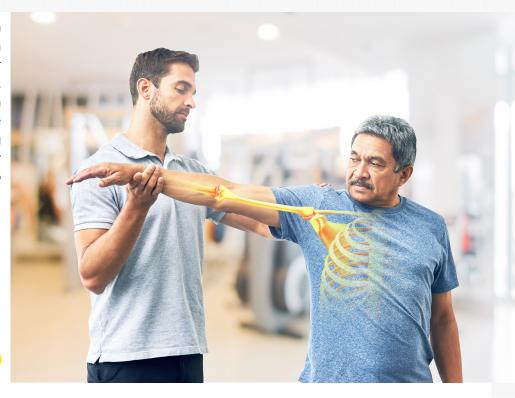
EVNol SupraBio[™]: Bioavailable Bone Health Solution?

From available research, palm tocotrienol has the potential in providing substantive benefits for bone and joint health. However, consuming an entire cup of palm oil could be a tough way to achieve the tocotrienol amount that is being suggested by experts in order to obtain the beneficial effect to improve wellness.

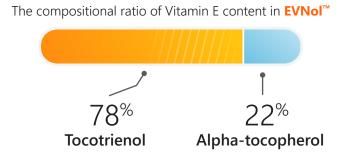
EVNol™ series of tocotrienol products could be a valuable solution for consumers who would like to include palm tocotrienol complex for their bone health.



Full Spectrum Palm Tocotrienol/Tocopherol Complex



EVNol™ is a natural full spectrum tocotrienol/tocopherol complex which is extracted and concentrated from the oil of palm fruits (*Elaeis guineensis*) through ExcelVite's patented technology. The compositional ratio of Vitamin E content in **EVNol™** is approximately 78% of tocotrienol and 22% of alpha-tocopherol. Since it is minimally processed from oil palm fruits, **EVNol™** also contains minute amounts of other naturally occurring phytonutrients such as phytosterols, squalene, and ProVitamin A alpha and beta carotene.



EVNol SupraBio™ - Enhanced Delivery System **That Optimizes Tocotrienol Absorption**

Considering tocotrienol's naturally low and erratic absorption behavior and the scarce level of tocotrienol found in our diets, it is near impossible for consumers to achieve beneficial levels of tocotrienol through food alone. To overcome this hurdle, **EVNol SupraBio**™has been developed as the second generation self-emulsifying tocotrienol system improve the absorption of individual tocotrienol isoform by 2 to 3 times [25]. This unique feature SupraBio™ **EVNol** dietary supplement companies to formulate a tocotrienol product at a lower dosage (compared to a regular tocotrienol oil extract), yet



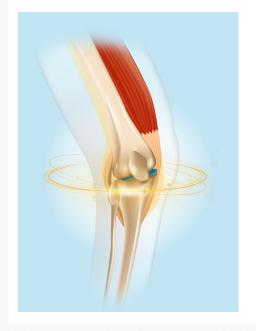
Patented and Bioenhanced Full Spectrum Palm Tocotrienol/Tocopherol Complex



able to achieve beneficial plasma levels. This significantly reduces the cost and thereby allowing companies to formulate effective tocotrienol products at an affordable price for the consumers.

EVNol SupraBio¹

Bioenhanced Tocotrienol Complex is the main form of tocotrienol vitamin E to support efficient tocotrienol delivery in the human body backed by human tissue distribution data [26].



Bottom Line

The notion of using palm Vitamin E tocotrienol as an antioxidant in one's bone and joint health plan is quite novel and it is getting increased attention from sports or active nutrition market. Palm tocotrienol is able to improve bone mineral density, preserve bone mass, as well as support healthy bone turnover as shown by research. The increasing number of research studies supporting the role of tocotrienol in bone health are underscoring the need to incorporate tocotrienol of the bone health solutions. This will inevitably lead to more breakthroughs for the dietary supplement companies developing innovative bone health products. Based on past clinical studies, supplementing Vitamin E tocotrienol at appropriate doses is thought to be safe and may promote beneficial effects on overall wellness.

References

- de Villiers, T. J., & Goldstein, S. R. (2022). Climacteric, 25(1), 1-3. Alswat, K. A. (2017). Journal of clinical medicine research, 9(5), 382.
- Adler, R. A. (2014). Bone research, 2(1), 1-8. Sen, C. K., et al. (2006). Life sciences, 78(18), 2088-2098.
- Domazetovic, V., et al. (2017). Clinical Cases in Mineral and Bone Metabolism, 14(2), 209.
- Nizar, A. M., et al. (2011). *Clinica Terapeutica, 162*(6), 533. McLean, R. R. (2009). *Current osteoporosis reports, 7*(4), 134-139.
- Nazrun, A. S., et al. (2011). Advances in pharmacological sciences, 2012. Garrett, I. R., & Mundy, G. R. (2002). Arthritis research & therapy, 4(4), 1-4

- Lewiecki, E. M. (2010). Therapeutic advances in chronic disease, 1(3), 115-128.

 Deng, L., et al. (2014). Bone, 67, 200–207.

 Abukhadir, S. S. A., et al. (2012). Evidence-Based Complementary and Alternative Medicine, 2012.

 Norazlina, M., et al. (2010). Archives of medical science: AMS, 6(4), 505.
- [14] Chin, K. Y., & Ima-Nirwana, S. (2014). Nutrients, 6(4), 1424-1441.

- [15] Maniam, S., et al. (2008). Basic & clinical pharmacology & toxicology, 103(1), 55-60.
 [16] Wong, S. K., et al. (2018). International journal of environmental research and public health, 15(9),
- Wong, S. K., et al. (2018). Journal of Functional Foods, 44, 246-254.
- [17] World, S. K., et al. (2016). Journal of Functional Foods, 74, 240-254.
 [18] Wong, S. K., et al. (2012). Journal of Functional Foods, 74, 104209.
 [19] Mohamad, S., et al. (2012). Evidence-Based Complementary and Alternative Medicine, 2012.
 [20] Shuid, A. N., et al. (2011). Journal of Orthopaedic Research, 29(11), 1732-1738.
 [21] Soelaiman, I. N., et al. (2012). International journal of endocrinology, 2012.
 [22] Zainal, Z., et al. (2019). Scientific reports, 9(1), 1-11.

- [23] Haflah, N. H., et al. (2009). Saudi Med J, 30(11), 1432-1438.
 [24] Al-Saadi, H. M., et al. (2021). Applied Sciences, 11(18), 8577.
- [25] Ho D, et al. (2003). U.S. Patent No. 6,596,306.
- [26] Patel V, et al. (2012). The Journal of Nutrition, 142(3), 513-9.

6 Reasons To Trust ExcelVite On Your Product Development Journey







GMP & HACCP

All of our ingredients are manufactured according to the PIC/S cGMP standard (GMP standard for pharmaceutical actives). ExcelVite is also HACCP certified and our products are Kosher and Halal-certified.





Sustainability

ExcelVite commits itself to protect the Earth by ensuring that we practice sustainable sourcing for our raw material. We are a member of the RSPO and MSPO and we are certified under the RSPO and MSPO Supply Chain Certifications.



Accreditation

Our laboratory testing is accredited to ISO 17025. We run stability testing for our products in our laboratory.



We invest in research. The academia and research professionals prefer ExcelVite's ingredients (EVNol SupraBio™ Bioenhanced Tocotrienol Complex and EVTene™ Mixed-Carotene Complex) due to their consistent quality and availability. Scientific research is how ExcelVite supports our customers to develop products that work, and be able to differentiate from other products.





Disclaimer: The statements in the above article have not been evaluated by the Food and Drug Administration. They are not intended to diagnose, treat, cure or prevent any disease.

Copyright 2022 ExcelVite Sdn. Bhd.



















