



Excellence in Oleochemicals

DavosLife E3 Tocotrienols

FOR EVIDENCE-BASED HEALTH BENEFITS
BEYOND ANTIOXIDATION AND
ANTI-INFLAMMATION

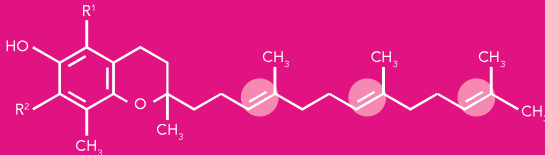


Tocotrienol, A Super Form of Vitamin E

Vitamin E is not just a single molecule, but a family of eight fat-soluble substances that are sub-divided into two classes of structurally-similar molecules. These two classes are tocopherol and tocotrienol, each of which have four structurally and chemically diverse molecules termed as alpha (α), beta (β), delta (δ), and gamma (γ) respectively.



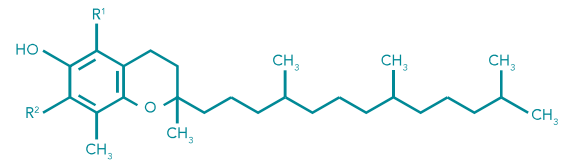
Tocotrienols have up to **60X more antioxidative potency** compared to α -Tocopherol, and have **unique anti-inflammatory properties** not seen in α -Tocopherol (Serbinova *et al.*, 1991).



TOCOTRIENOLS

Tocotrienols have unsaturated isoprenoid side chains with three double bonds. This unique property gives it better flexibility with a higher efficiency of penetrating into the cell membrane. Tocotrienols are potent **ANTIOXIDANTS*** with unique **ANTI-INFLAMMATORY** properties.

α : $R' = CH_3, R'' = CH_3$
 β : $R' = CH_3, R'' = H$
 γ : $R' = H, R'' = CH_3$
 δ : $R' = H, R'' = H$



TOCOPHEROLS

Tocopherols, in contrast, have saturated side chains. They also function as antioxidants, but this chemical structure gives them a lower antioxidative capacity as compared to tocotrienols.

α : $R' = CH_3, R'' = CH_3$
 β : $R' = CH_3, R'' = H$
 γ : $R' = H, R'' = CH_3$
 δ : $R' = H, R'' = H$

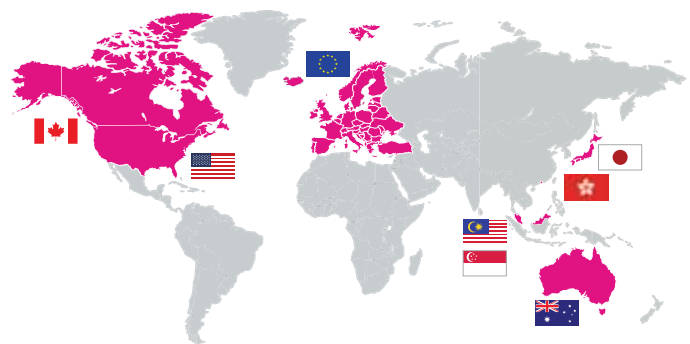
Tocotrienols have Unique Properties that Positively Impact Different Areas of the Body

Tocotrienols are naturally sourced from plant species like oil palm, rice and Annatto seed.

Each analogue of tocotrienol are functionally unique, with α -, β -, δ -, and γ -tocotrienol each exerting different beneficial effects on health and disease that are separate from the biological functions of α -tocopherol.



Countries that Recognise Tocotrienols as a Form of Vitamin E

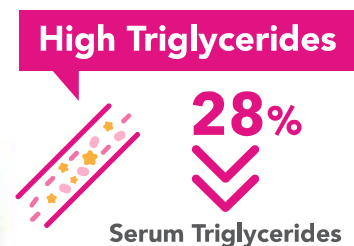


Get to the Heart of the Matter: The Impact of Tocotrienol Supplementation on Cardiovascular Health

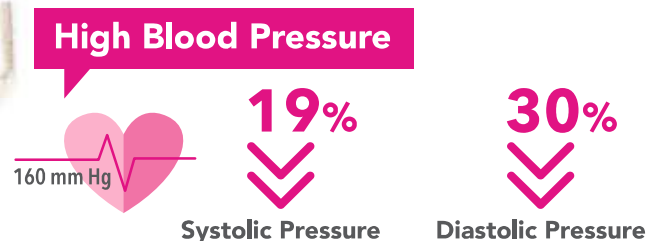
Having high cholesterol, high blood pressure, high triglycerides and diabetes lead to increased risk of cardiovascular disease. Clinical and pre-clinical studies have shown that tocotrienol supplementation is able to reduce the risk factors involved in cardiovascular disease.



Supplementation with tocotrienol-rich fraction reduces total cholesterol and low-density lipoprotein (LDL) in humans (Qureshi *et al.*, 2002).



Tocotrienol supplementation reduces serum triglycerides in humans (Zaiden *et al.*, 2010).



Tocotrienol supplementation gradually lowers systolic and diastolic blood pressure (Cheng *et al.*, 2017).

Diabetes



Tocotrienol supplementation improves glucose and insulin tolerance (Wong *et al.*, 2015).

Food for Thought: Tocotrienols and Brain Health

Cognitive decline can happen gradually, as is the case when a person ages or it can happen suddenly as is the case with ischemic stroke where there is a sudden loss of oxygen to the brain.

White Matter Lesions

White matter lesions (WML) are areas in white brain matter that appear hyperintense in MRI scans. The incidence of WML rises with age and they are linked to increased stroke risk and increased risk of developing dementia.

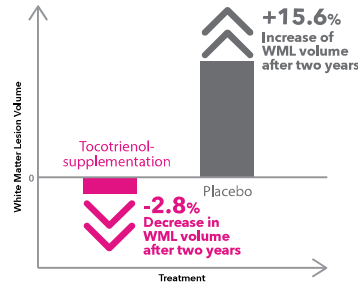


Figure 3: Changes in White Matter Lesion volume after two years of tocotrienol or placebo supplementation

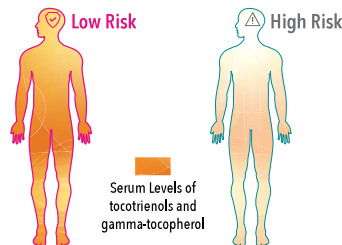


Clinical studies have shown that supplementation with tocotrienols could reduce the progression of white matter lesions (Gopalan *et al.*, 2014).

Alzheimer's Disease and Mild Cognitive Impairment

Alzheimer's Disease is caused in part by the overproduction and lack of clearance of amyloid β protein ($A\beta$), accompanied by enhanced neuroinflammation.

Clinical evaluation of 140 subjects (≥ 65 years old)



Clinical trials have shown that high serum levels of tocotrienols and γ -tocopherol are correlated with a lower risk of getting Alzheimer's Disease and mild cognitive impairment (Mangialasche *et al.*, 2013).

Stroke

When ischemic stroke happens, the sudden loss of oxygen to the brain results in brain cell death and inflammation.

Tocotrienol-supplemented canines had less damage to brain cells caused by stroke (Rink *et al.*, 2011).

40%
Reduced Stroke Damage

Reduced Stroke Damage



Tocotrienol supplementation could stimulate the remodeling of existing blood vessels to immediately expand to supply oxygen to regions of the brain that need it when stroke happens (Rink *et al.*, 2011).

Stand Tall: The Impact of Tocotrienols on Bone Health

Bone tissue is dynamic and constantly being remodeled in a balanced cycle of bone loss and bone formation. Bone diseases arise when this cycle goes out of flux and tips in favour of bone loss and inflammation.

How do Tocotrienols Maintain Bone Health?

In bone disease like osteoporosis, oxidative stress and inflammation lead to increased activity of osteoclast cells that promote bone tissue degradation. Pre-clinical studies have shown that tocotrienol supplementation reduces the amounts of oxidative stress in bone tissue, as evidenced by a reduced amount of bone lipid peroxidation marker (Figure 1) and increased amounts of antioxidative enzyme activity (Figure 2).

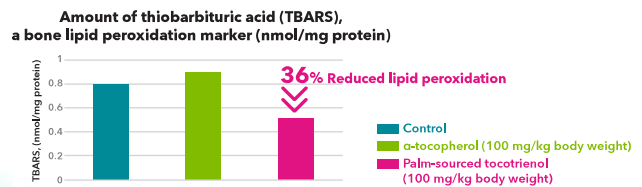


Figure 1: Impact of palm tocotrienol supplementation on lipid peroxidation in the femur of adult rats (Maniam *et al.*, 2008)

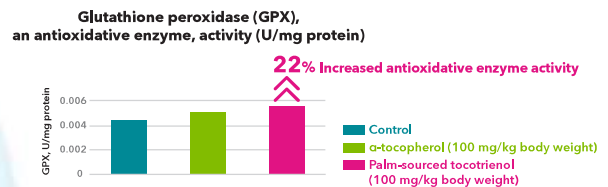


Figure 2: Impact of palm tocotrienol supplementation on antioxidative enzyme activity in the femur of adult rats (Maniam *et al.*, 2008)

In menopause, oestrogen levels drop which leads to an increase in the amounts of pro-inflammatory cytokines like interleukin-1 (IL-1) and interleukin-6 (IL-6) in the body. This leads to low-grade chronic inflammation that further drives osteoclast cell-mediated bone tissue degradation. Pre-clinical studies have found that tocotrienol supplementation is able to prevent this rise in cytokines (Figures 3 and 4).

Amounts of pro-inflammatory marker, Interleukin-1 (pg/mL)

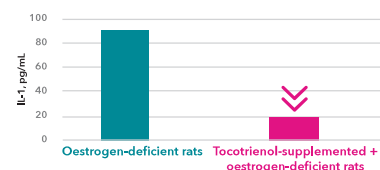


Figure 3: Amounts of interleukin-1 (IL-1) (Muhammad *et al.*, 2013)

Amounts of pro-inflammatory marker, Interleukin-6 (pg/mL)

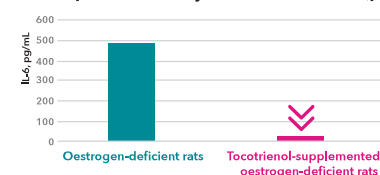


Figure 4: Amounts of interleukin-6 (IL-6) (Muhammad *et al.*, 2013)

Sun Exposure Damages The Skin via Increased Oxidative Stress and Inflammation



Premature Ageing

Hyperpigmentation

How Do Tocotrienols Reduce the Impact of Sun Exposure?

Tocotrienols do not block UV radiation the way more common sunscreens do. Instead, tocotrienols help to soothe the skin by reducing inflammation and by scavenging oxidative species. Clinical trials have confirmed tocotrienols' efficiency in reducing skin redness and pigmentation following UV irradiation (Yap WN, 2017).

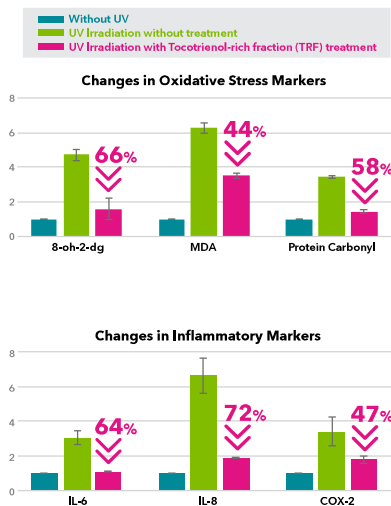


Figure 1: Changes in oxidative stress and inflammatory markers in human keratinocyte cells treated with TRF (Yap WN, 2017).

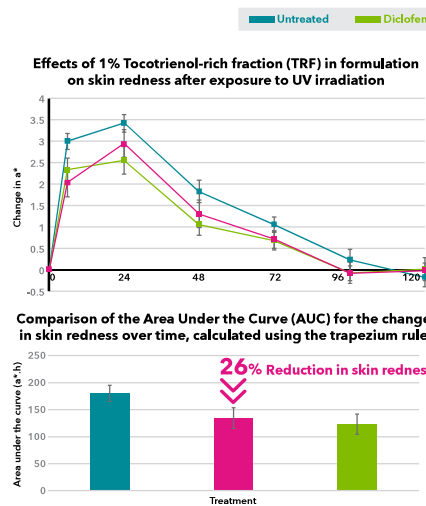


Figure 2: Change in skin redness.

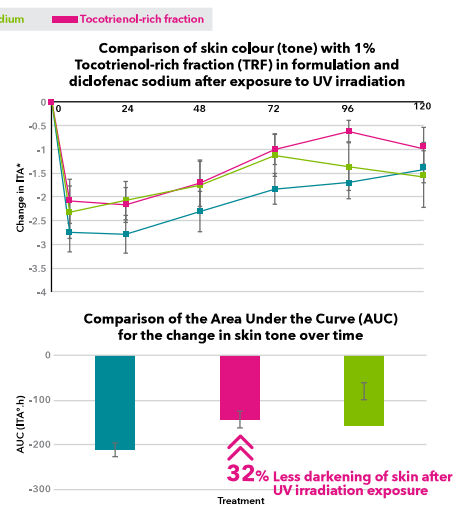


Figure 3: Changes in skin tone.

How Do Tocotrienols Reduce Hyperpigmentation?

Tocotrienols reduce hyperpigmentation by two actions.

First, it inhibits production of the enzyme tyrosinase, thereby reducing the amount of melanin produced (Choi *et al.*, 2013).

Second, it promotes the breakdown of melanin (Makpol *et al.*, 2009).

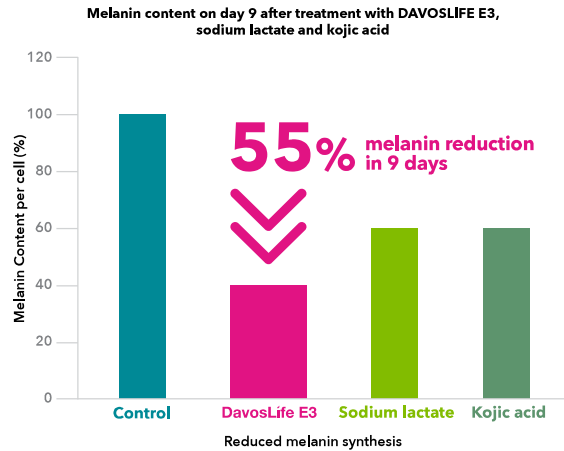


Figure 4: Reduction in melanin content in B16-F1 cells after treatment with different skin lightening actives (Yap *et al.*, 2010).



TOCOTRIENOLS: A Safe Active Cosmetic Ingredient

1. Non Skin Irritant

- ☑ Patch tests and human repeated insult patch tests (HRIPT) concluded that Tocotrienols are not irritants and not sensitizers (Davos Life Science, Data on File).
- ☑ *in vitro* dermal irritation assay (OECD 439) classified Tocotrienols as non-irritants (Hasan *et al.*, 2018).

2. Non Eye Irritant

- ☑ *in vitro* ocular irritation assay (OECD 492) classified Tocotrienols as non-irritating to the eyes (Hasan *et al.*, 2018).

3. Cosmetic Ingredient Review (CIR) Affirmed (Fiume *et al.*, 2018).

4. COSMOS attestation of conformity on DavosLife E3 DVL



Maintain Peak Performance: How Tocotrienols Impact Exercise Endurance

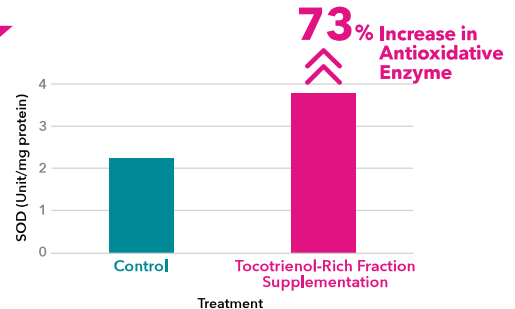
During exercise, muscles contract to create movement and oxidative stress in muscle tissues increases. To counter the harmful effects of oxidative stress, the body produces antioxidative enzymes like superoxide dismutase.



Tocotrienols Enhance the Antioxidant Capacity of Muscle Tissues

Figure 1: Concentrations of SOD in muscle tissue (Lee et al., 2009).

Concentrations of superoxide dismutase (SOD) after maximal swimming exercise in muscle tissue

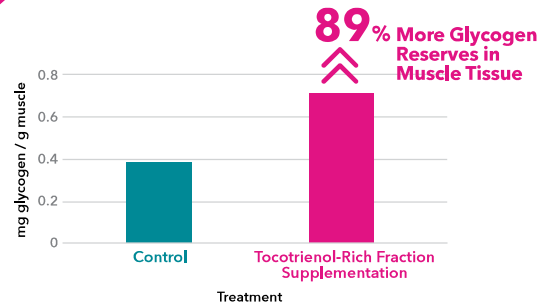


Glycogen reserves reduce during exercise, causing insufficient energy supply or oxygen to the muscles. This induces muscle fatigue.

Tocotrienols Maintain Glycogen Levels in Muscle Tissue

Figure 2: Concentrations of glycogen in muscle tissue (Lee et al., 2009).

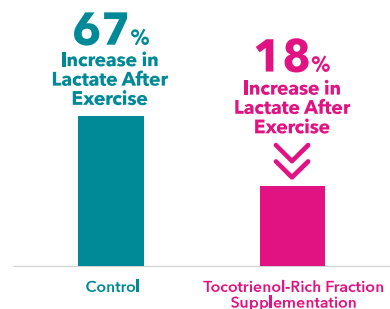
Concentrations of glycogen after maximal swimming exercise in muscle tissue



Exercise also induces an increase in lactate in muscle tissues as a by-product of anaerobic respiration. High lactate levels increase the acidity of muscle tissue and slows its capacity for more work.

Tocotrienols Reduce The Amount of Lactate Produced After Exercise

Figure 3: Concentrations of blood lactate in all groups after swimming exercise (Lee et al., 2009).





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References:

1. Cheng, H.S., Ton, S.H., Tan, J.B.L. and Abdul Kadir, K. (2017). The ameliorative effects of a tocotrienol-rich fraction on the AGE-RAGE Axis and Hypertension in High-Fat-Diet-Fed rats with metabolic syndrome. *Nutrients*, 9: 984.
2. Choi et al. (2013). Tocotrienols enhance melanosome degradation through endosome docking/fusion proteins in B16F10 melanoma cells. *Food and Function*, 4(10): 1481 - 1488.
3. Davos Life Science In-House Data on File.
4. Fiume et al. (2018). Safety Assessment of Tocopherols and Tocotrienols as Used in Cosmetics. *International Journal of Toxicology*, 37(2): 615-945.
5. Gopalan, Y., Shuaib, I.L., Magosso, E., Ansari, M.A., Abu Bakar, M.R., Wong, J.W., Khan, N.A.K., Liong, W.C., Sundram, K., Ng, B.H., Karuthan, C., and Yuen, K.H., (2014). Clinical Investigation of the Protective Effects of Palm Vitamin E Tocotrienols on Brain White Matter. *Stroke*, 45:1422-1428.
6. Hasan et al. (2018). *Journal of Oil Palm Research*, 30(1): 150 - 162.
7. Lee, S.P., Mar, G.Y., and Ng, L.T. (2009). Effects of tocotrienol-rich fraction on exercise endurance capacity and oxidative stress in forced swimming rats. *Eur J Appl Physiol*, 107: 587 - 595.
8. Mangialasche, F., Solomon, A., Kareholt, I., Hooshmand, B., Cecchetti, R., Fratiglioni, L., Soininen, H., Laatikainen, T., Mecocci, P., and Kivipelto, M. (2013). Serum levels of Vitamin E forms and risk of cognitive impairment in a Finnish cohort of older adults. *Experimental Gerontology*, 48: 1428 - 1435.
9. Maniam S, Mohamed N, Shuid AN, Soelaiman IN. (2008). Palm tocotrienol exerted better antioxidant activities in bone than alpha-tocopherol. *Basic Clin Pharmacol Toxicol*, 103(1):55-60.
10. Muhammad N, Luke DA, Shuid AN, Mohamed N, Soelaiman IN. (2013). Tocotrienol supplementation in postmenopausal osteoporosis: evidence from a laboratory study. *Clinics*, 68(10):1338-1343.
11. Malsip et al. (2009). *Afr. J. Biochem. Res.*, 3, 385-392.
12. Qureshi AA, Sami SA, Saeed WA, Khan FA. (2002). Dose-dependent suppression of serum cholesterol by tocotrienol-rich fraction (TRF25) of rice bran in hypercholesterolemic humans. *Atherosclerosis*, 161:199-207.
13. Rink C, Christoforidis G, Khanna S, Peterson L, Patel Y, Khanna S, Abdullatif A, Ifranoglu O, Machiraju, R., Bergdall, V. K., & Sen, C. K. (2011). Tocotrienol Vitamin E Protects against Preclinical Canine Ischemic Stroke by Inducing Arteriogenesis. *Journal of Cerebral Blood Flow and Metabolism*, 31(11), 2218-2230.
14. Serbinova, E., Kagan, V., Han, D., and Pecker, L. (1991). Free radical recycling and intramembrane mobility in the antioxidant properties of alpha-tocopherol and alpha-tocotrienol. *Free Radical Biology and Medicine*, 10: 263 - 275.
15. Wong, W.Y., Ward, L.C., Fong, C.W., Yap, W.N. and Brown, L. (2017). Anti-inflammatory γ - and δ -tocotrienols improve cardiovascular, liver and metabolic function in diet-induced obese rats. *Eur J Nutr.*, 56 (1): 133 - 150.
16. Yap, W.N. (2017). *J. Cosmet. Dermatol.* : 1-11.
17. Yap et al. (2010). *Pigment Cell Melanoma Res.*, 23(5): 688-692.
18. Zaiden, N., Yap, W.N., Ong, S., Xu, C.H., Teo, V.H., Chang, C.P., Zhang, X.W., Nesaratnam, K., Shiba, S. and Yap, Y.L. (2010). Gamma Delta tocotrienols reduce hepatic triglyceride synthesis and VLDL secretion. *Journal of Atherosclerosis and Thrombosis*, 17(10): 1019 - 1032.

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