KLK OLEO

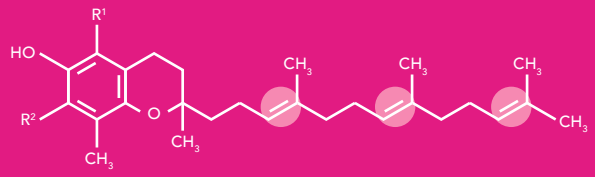
DavosLife E3
Tocotrienols

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.

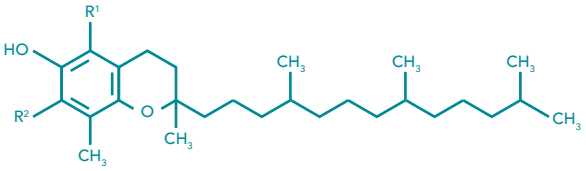
Tocotrienols have up to
60X more antioxidative potency
compared to α-Tocopherol, and have
unique anti-inflammatory properties
not seen in α-Tocopherol (Serbinova *et al.*, 1991).



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.

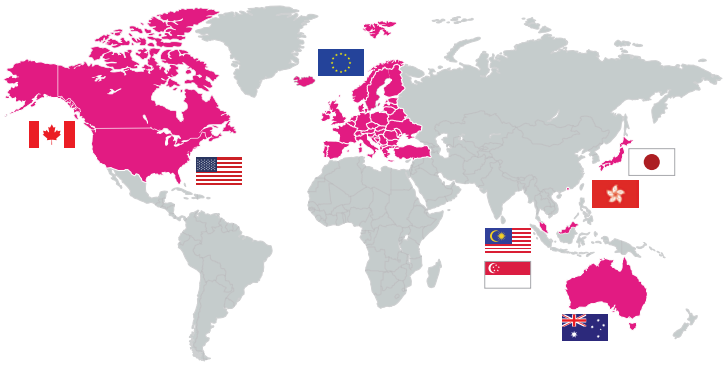
α : R′ = CH_3, R″ = CH_3
β : R′ = CH_3, R″ = H
γ : R′ = H, R″ = CH_3
δ : R′ = H, R″ = H

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



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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.

High Cholesterol

20% ↓ Total Cholesterol

25% ↓ LDL

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

High Triglycerides

28% ↓ Serum Triglycerides

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

High Blood Pressure

19% ↓ Systolic Pressure

30% ↓ Diastolic Pressure

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

Diabetes

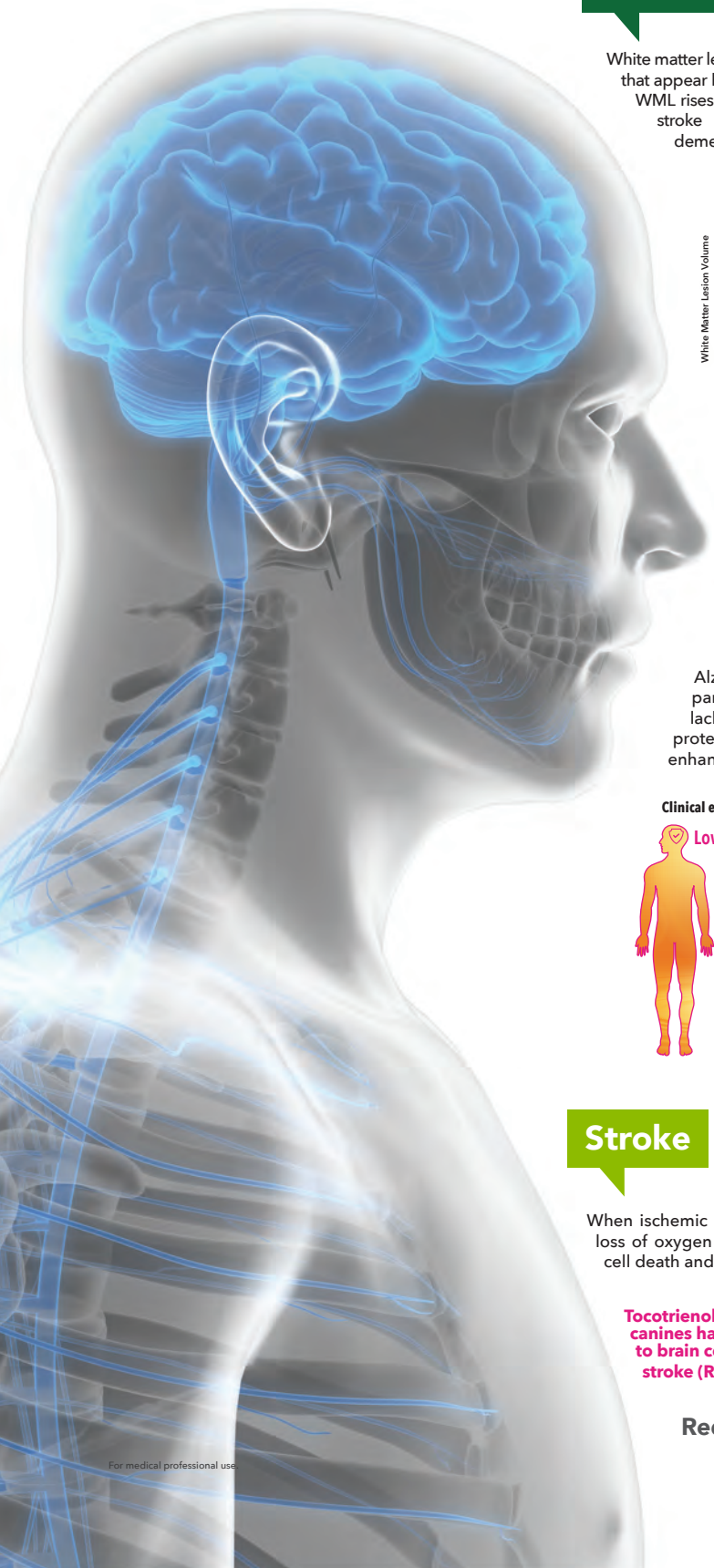
25% ↑ Glucose Tolerance

50% ↑ Insulin Tolerance

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.

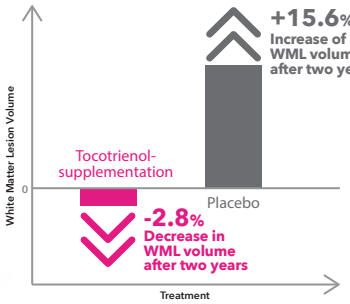
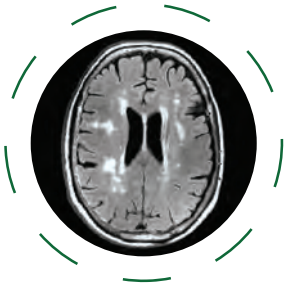


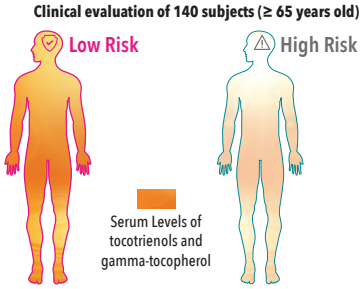
Figure 3: Changes in White Matter Lesion volume after two years of tocotrienol or placebo supplementation

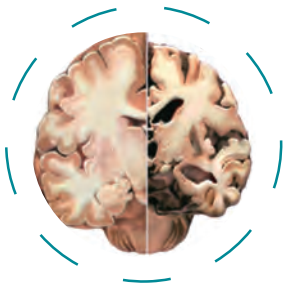


Clinical studies have shown that supplementation with tocotrienols could reduce the progression of white matter lesions (Gopalan *et al.*, 2014).

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 (Aβ), accompanied by enhanced neuroinflammation.





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

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).

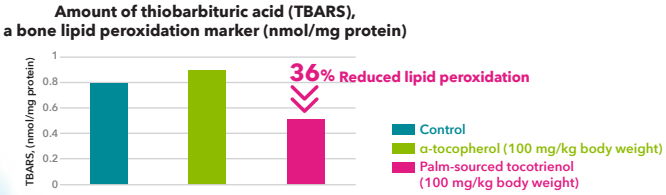


Figure 1: Impact of palm tocotrienol supplementation on lipid peroxidation in the femur of adult rats (Maniam *et al.*, 2008)

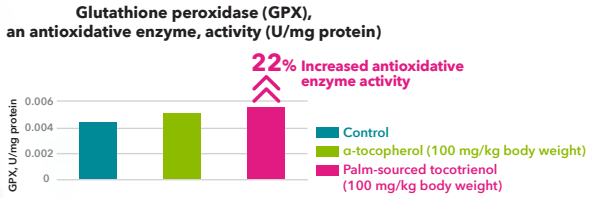


Figure 2: Impact of palm tocotrienol supplementation on antioxidative enzyme activity in the femur of adult rats (Maniam *et al.*, 2008)

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).

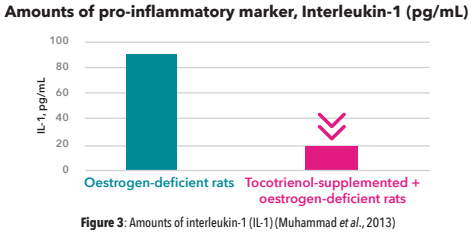


Figure 3: Amounts of interleukin-1 (IL-1) (Muhammad *et al.*, 2013)

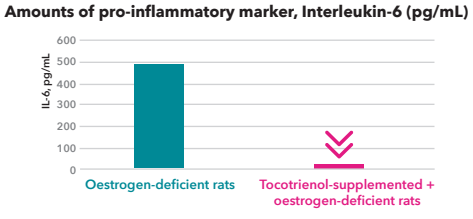
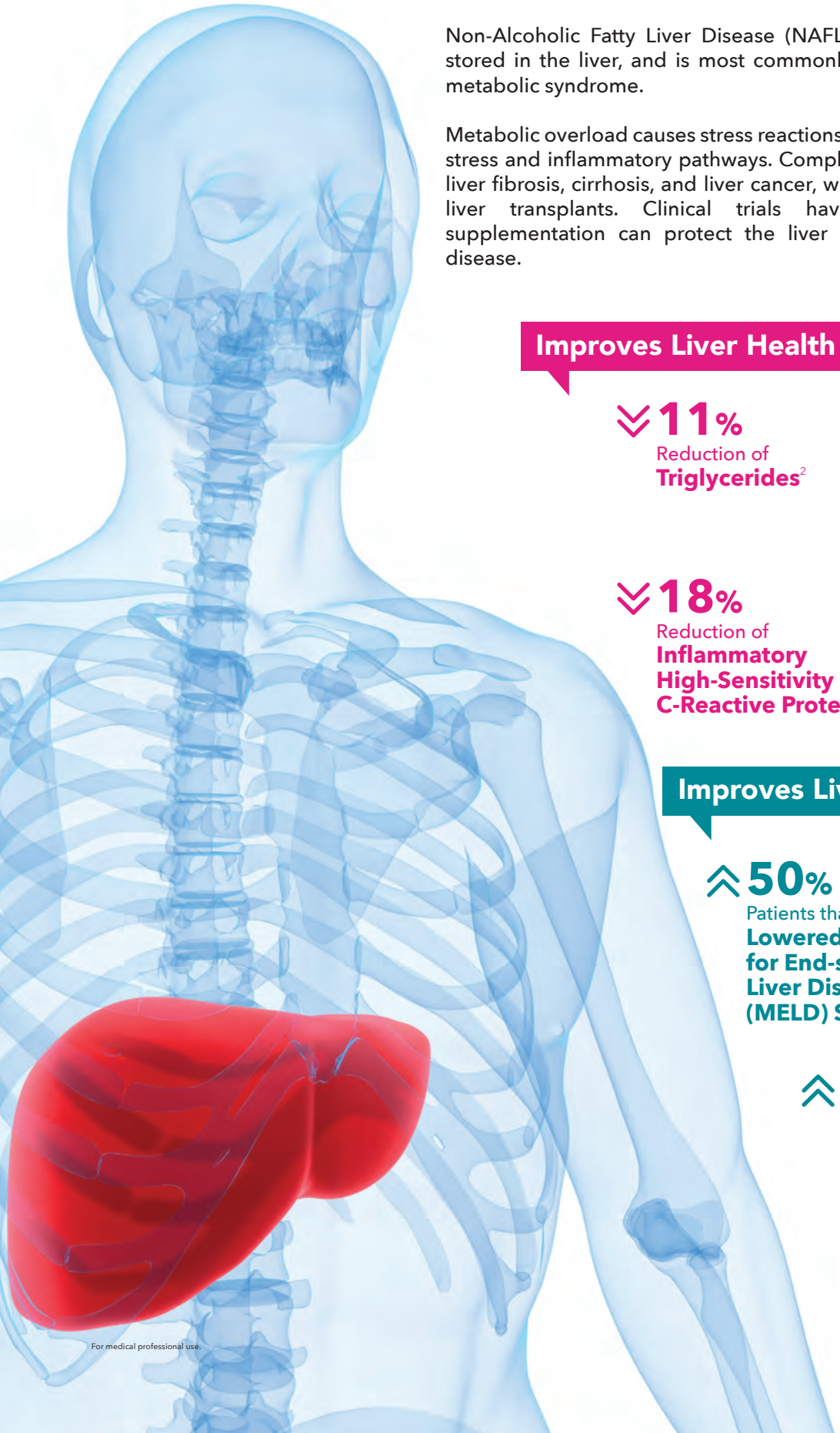


Figure 4: Amounts of interleukin-6 (IL-6) (Muhammad *et al.*, 2013)

Tocotrienols and Liver Health



Non-Alcoholic Fatty Liver Disease (NAFLD) occurs when excess fat is stored in the liver, and is most commonly associated with obesity and metabolic syndrome.

Metabolic overload causes stress reactions in the liver, including oxidative stress and inflammatory pathways. Complications of the disease include liver fibrosis, cirrhosis, and liver cancer, with progressive cases requiring liver transplants. Clinical trials have proven that tocotrienol supplementation can protect the liver from non-alcoholic fatty liver disease.

Improves Liver Health Biomarkers

11% Reduction of **Triglycerides**[2]

14% Reduction of **Oxidative Stress Marker Malondialdehyde**[2]

18% Reduction of **Inflammatory High-Sensitivity C-Reactive Protein**[2]

16% Reduction of **Serum Aminotransferases**[2]

Improves Liver Pathophysiology

50% Patients that had **Lowered Model for End-stage Liver Disease (MELD) Score**[3]

57% Reduction of **Liver Stiffness**[4]

69% Patients with **Improved Liver Imaging Test Results after Supplementation**[5]

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Sun Exposure Damages The Skin via Increased Oxidative Stress and Inflammation

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).

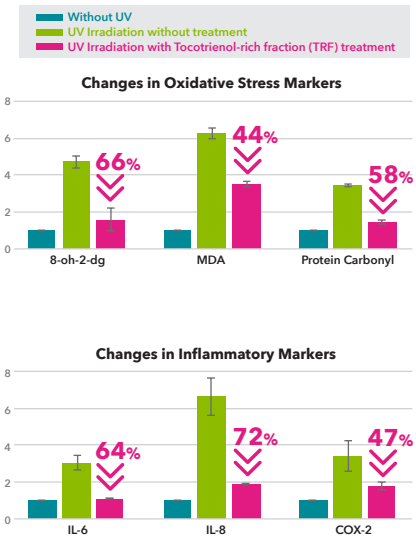

Figure 1: Changes in oxidative stress and inflammatory markers in human keratinocyte cells treated with TRF (Yap WN, 2017).

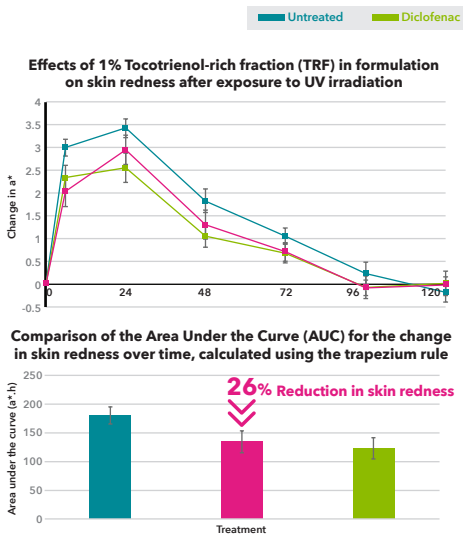

Figure 2: Change in skin redness.

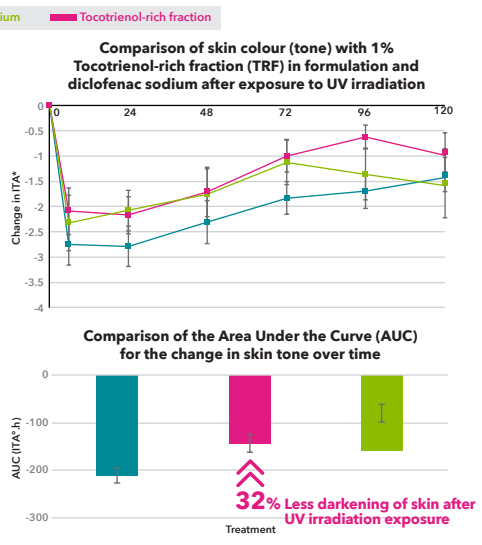

Figure 3: Changes in skin tone.

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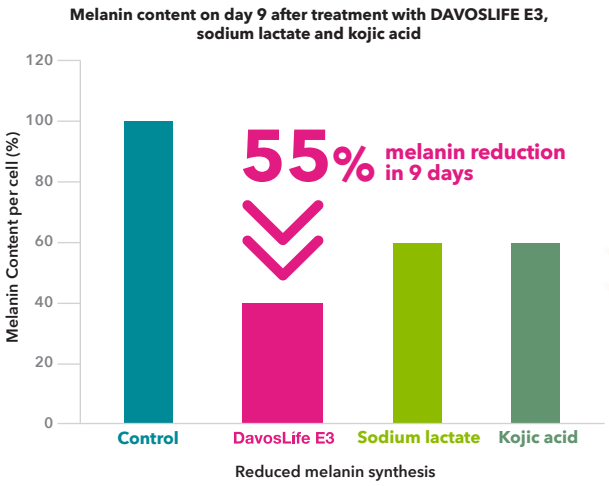
How Do Tocotrienols Reduce Hyperpigmentation?

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).



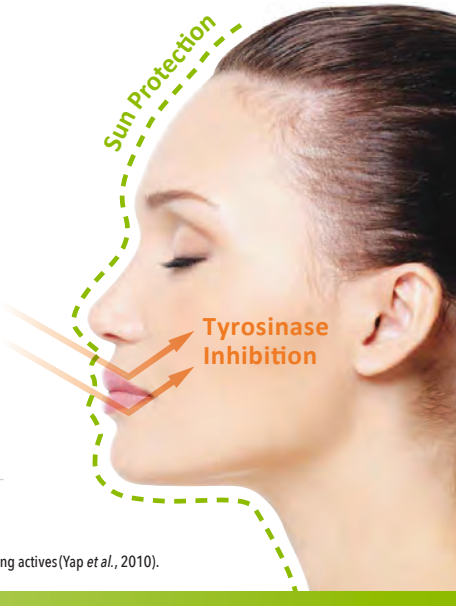


Figure 4: Reduction in melanin content in B16-F1 cells after treatment with different skin lightening actives (Yap *et al.*, 2010).

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 sensitisers (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

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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

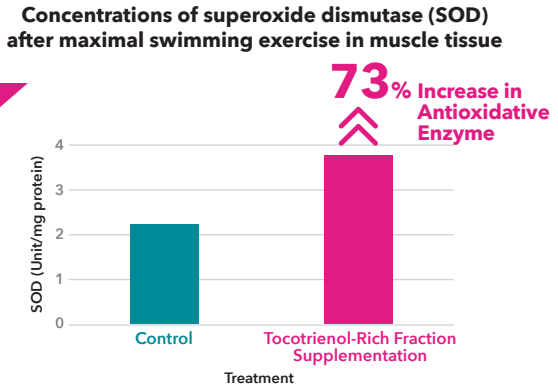

Figure 1: Concentrations of SOD in muscle tissue (Lee *et al.*, 2009).

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

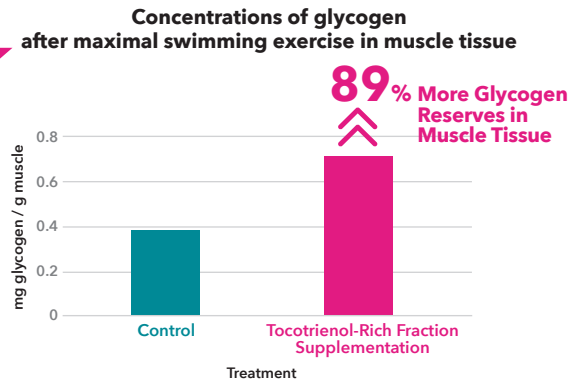

Figure 2: Concentrations of glycogen in muscle tissue (Lee *et al.*, 2009).

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

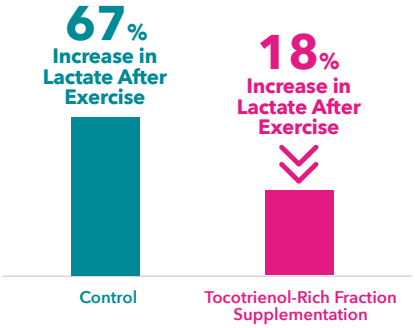

Figure 3: Concentrations of blood lactate in all groups after swimming exercise (Lee *et al.*, 2009).

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& marketers with
ways to differentiate
their finish product for a
competitive advantage

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