









All Deaths worldwide, or 17.9 Million annually<sup>1</sup>



Heart Attacks and Strokes<sup>1</sup>



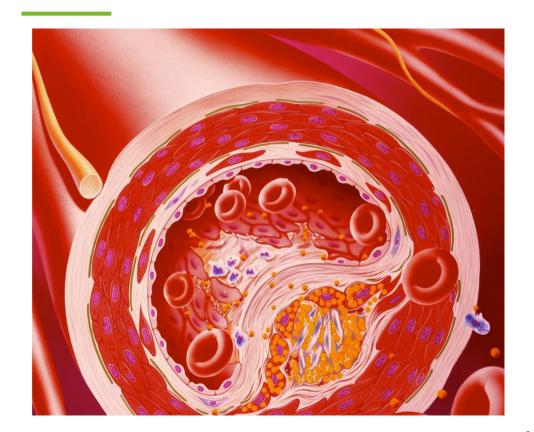
High Cholesterol<sup>1</sup>



# Cardiovascular Disease Cholesterol Regulation is Key



- Important to promote heart and blood vessel health via the reduction of cholesterol and triglycerides.
- HMG-CoA reductase is a key enzyme that mediates cholesterol production in the liver<sup>1</sup>.
- Statins are the most commonly prescribed medication for the treatment of cardiovascular disease (CVD)<sup>1</sup>.





However, statins have potential side effects.







Muscle Soreness<sup>1</sup>



Increased Risk of Diabetes<sup>2,3,4</sup>

<sup>..</sup> Ramanathan et al. (2018) Nutrition & Metabolism; 15 – 6

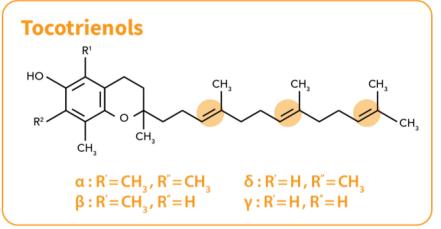
Lee et al. (2016) Therapeutics and Clinical Risk Management; (12): 1533 –1543

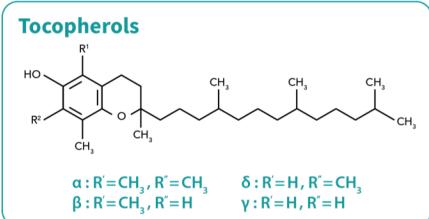
<sup>3.</sup> Jones et al. (2017) Drugs Aging; 34(3): 203-209

Casula et al. (2017) Nutr Metab Cardiovasc Dis.; 27(5): 396-406



## A Better Form of Vitamin E





Tocotrienols have unsaturated isoprenoid side chains (farnesyl isoprenoid tails) with **3** double bonds<sup>1</sup>.

A unique property that makes Tocotrienols efficient at **neutralising free radicals** and **reducing chronic inflammation.** 

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#### HMG-CoA Reductase Inhibition



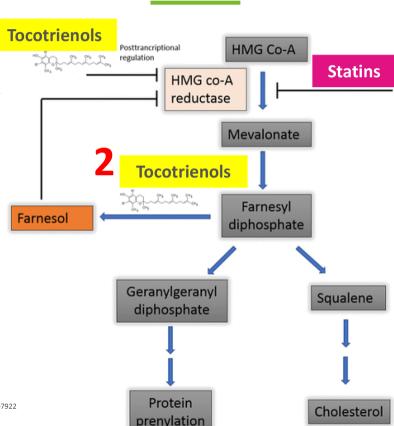
## Tocotrienols work via a Different Pathway

#### **Mechanism 1:**

Tocotrienols inhibit HMG-CoA reductase directly, post-transcriptionally, by blocking the translation of the mRNA<sup>1</sup>.

#### **Mechanism 2:**

Tocotrienols suppress the production of HMG-CoA reductase<sup>2</sup>.



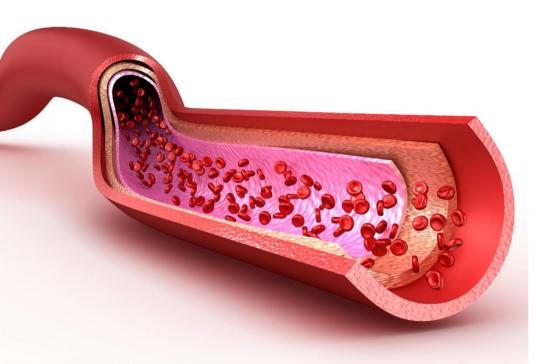
Statins mimic the structure of HMG-CoA and are competitive inhibitors for HMG-CoA Reductase<sup>3</sup>.

- 1. Meigs et al. (1996) The Journal of Biological Chemistry; 271(14): 7916–7922
- 2. Pearce et al. (1992). J Med Chem; 35: 3595 3606.
- 3. Oesterle et al. (2017). Circ Res.; 120: 229-43.
- . Image adapted from Ramanathan et al. (2018) Nutrition & Metabolism; 15 6

#### Side Effects



## Tocotrienols are safe even at high dosages



- Clinical trials on Tocotrienols have not reported any serious adverse events (50 – 400 mg/day for periods of 2 weeks to 18 months)<sup>1</sup>.
- Tocotrienols have a short half-life in the body<sup>1</sup>.
- Self-affirmed to be Generally Recognised as Safe (GRAS)<sup>2</sup>.
- Tocotrienols do not increase risk of developing diabetes mellitus<sup>3</sup>.

Schauss et al (2012). Vitamin E Beyond Tocopherols, Second Ed. Chapter .

FDA, U.S.; GRN307

<sup>3.</sup> Ramanathan et al. (2018) Nutrition & Metabolism; 15 – 6

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1

Clinical studies show that Tocotrienols supplementation in hypercholesterolemic patients is able to reduce lipid profile imbalance, making Tocotrienols a potential safe and natural alternative to statins.

2

Tocotrienols exert cardioprotective benefits via other mechanisms of action, i.e. antioxidative effects (carotid stenosis)



To cotrien ols are able to balance dyslipidemia, but not  $\alpha$ To copherol

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