

EZTREK™

Novel DFU Treatment

- The Problem
- **EZTREK™** Explained
- How **EZTREK™** Works

The Problem: DFU

Patient Statistics

>1.75 Million patients in US are annually diagnosed with a DFU (6% of all diabetics)^{1,2}

Lifetime: 12% - 25% of diabetics will develop DFU³

25% of DFUs never completely heal^{2,3,4}

40% Recurrence within 1 year after ulcer healing⁴

50% Recurrence after 3 years⁵

- **Closure: 24% at 12 weeks³ / 30% at 20 weeks³**
- **Unhealed: 70% unhealed after 20 weeks⁶**

46% of DFU Patients - Microvascular Complications⁷

65% of DFU Patients - Macrovascular Complications⁷

56% Become Infected⁸

28% 3-Year mortality⁹ / 42% 5-year mortality⁹

1. Rice, JB, et al., "Burden of diabetic foot ulcers for Medicare and private insurers," *Diabetes Care*, Vol. 37, 2014, pages 651-658.
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3. Game, FL, et al., "A systematic review of interventions to enhance the healing of chronic ulcers of the foot in diabetes," *Diabetes/ Metabolism Research and Reviews*, 2012; 28 (Suppl 1): 119-141.
4. Armstrong D, et al., "Diabetic foot ulcers and their recurrence," *New England Journal of Medicine*, 376:24, June 15, 2017.
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EZTREK™ Explained

Expedited DFU Healing — The New Patented Medical Food

It is well documented that diabetic patients have *impaired delta-6 desaturase (D6D) metabolic pathways* from impaired insulin production.^{1,2,3} In particular, this metabolic defect causes a poor anti-inflammatory response in Type I patients. Even with insulin therapy, the pathway is still deficient.⁴ Type II patients also have significant impairment of D6D activity.⁵ Diabetic foot ulcer (DFU) wound healing is impaired.

This deficiency directly decreases PGE₁ output. Both a powerful anti-inflammatory and vasodilator, PGE₁ is critical to expedited DFU healing. Diabetic patients may possess *only 42% of PGE₁'s binding functionality* — a 58% decrease compared with normal, non-diabetic patients.⁶ Steroids (glucocorticoids) further impair the Δ -6 desaturase pathway.^{1,7} During hypoglycemic episodes, the hormone glucagon is produced, further impeding the Δ -6 desaturase pathway (by means of cAMP).^{1,8}

Compensating for impaired Δ -6 desaturase deficiency, the new medicament EZTREK™ —uniquely addresses underlying etiology — and simultaneously optimizes multiple metabolic pathways:

1. The Δ -6 desaturase metabolic pathway favors the omega-3 series. Alpha-linolenic acid is important for tissue structure and support. However, PGE₁ is produced exclusively from the omega-6 series. EZTREK™ solves this issue by specific calibration of both omega-6 / -3 series and with specific modulation of their long-chain metabolites.^{1,2,9,10}

2. EZTREK™ further enhances patients' production of PGE₁ by calibration of gamma-linolenic acid with docosahexaenoic acid.^{7,11}

3. Diabetic patients frequently consume (processed) foods that decrease the most fundamental substrate precursor of PGE₁ — functional linoleic acid.^{1,2,12} Furthermore, the important cellular unfolded protein response (UPR) in secretory cells, such as the pancreas, is activated not only by unfolded proteins, but also by aberrant lipid composition (induced by the diet) of the ER membrane referred to as lipid bilayer stress. This response can trigger long-term stress (chronic inflammation) in cells.¹³ EZTREK™ calibrated EFA / eicosanoid modulating ratios are formulated to compensate for this and other obstacles that may impede the Δ -6 desaturase pathway.

4. Fibroblasts in the dermis — important in allowing skin to regenerate connective tissue to recover from injury and maintain the extracellular matrix — are not maximized with Δ -6 desaturase deficiency.¹⁴

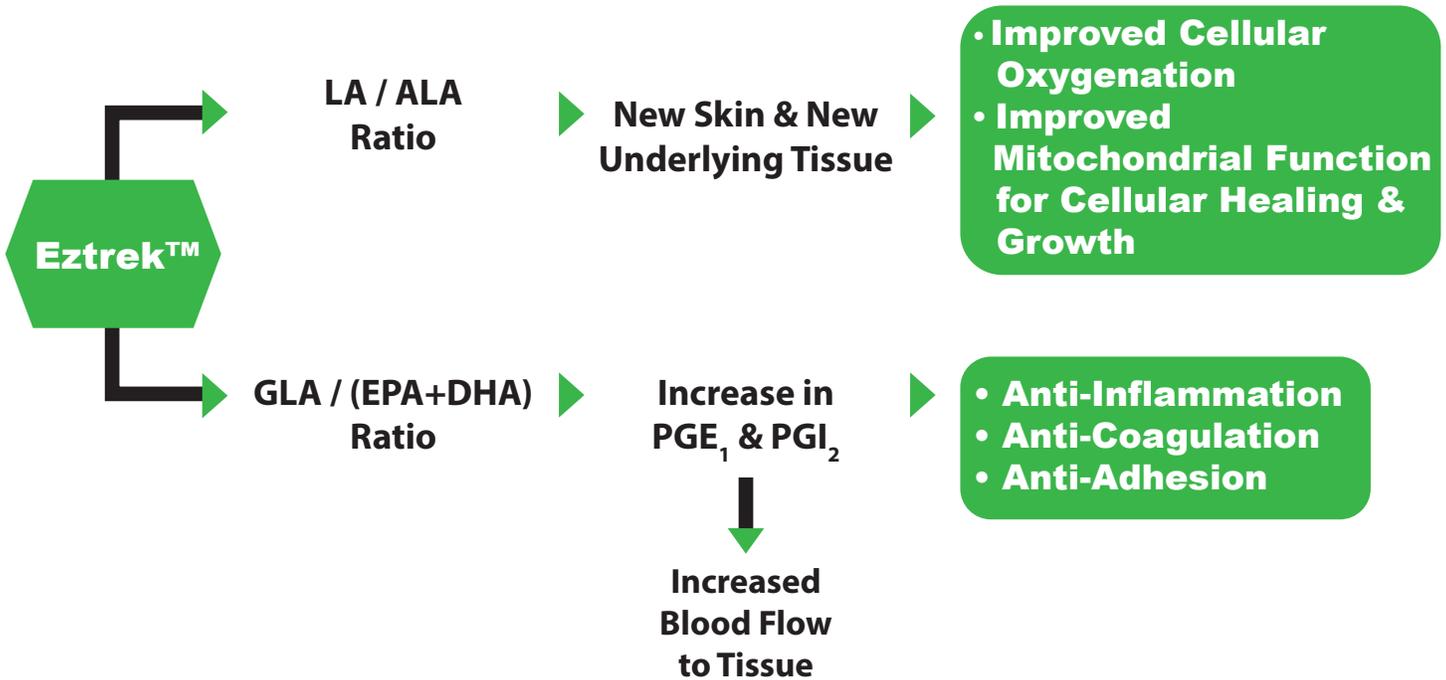
With continued EZTREK™ use, both acute and chronic DFUs heal faster.

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 2. Das, UN, "Essential fatty acids: biochemistry, physiology and pathology," Biotechn., 2006, 1, 420-439.
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 6. Dutta-Roy, Asim, "Effect of Evening Primrose Oil Feeding on Erythrocyte Membrane Properties in Diabetes Mellitus," Omega-6 Essential Fatty Acids: Pathophysiology and Roles in Clinical Medicine, Wiley-Liss, NY, 1990, pages 505-511.
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 14. Willard, DE, et al., "Identification of a fatty acid Δ -6 desaturase deficiency in human skin fibroblasts," J. Lipids Res., 42, 2001, pages 501-508.

How EZTREK™ Works

Uniquely Treating DFU

Utilizing Novel Mechanisms of Action



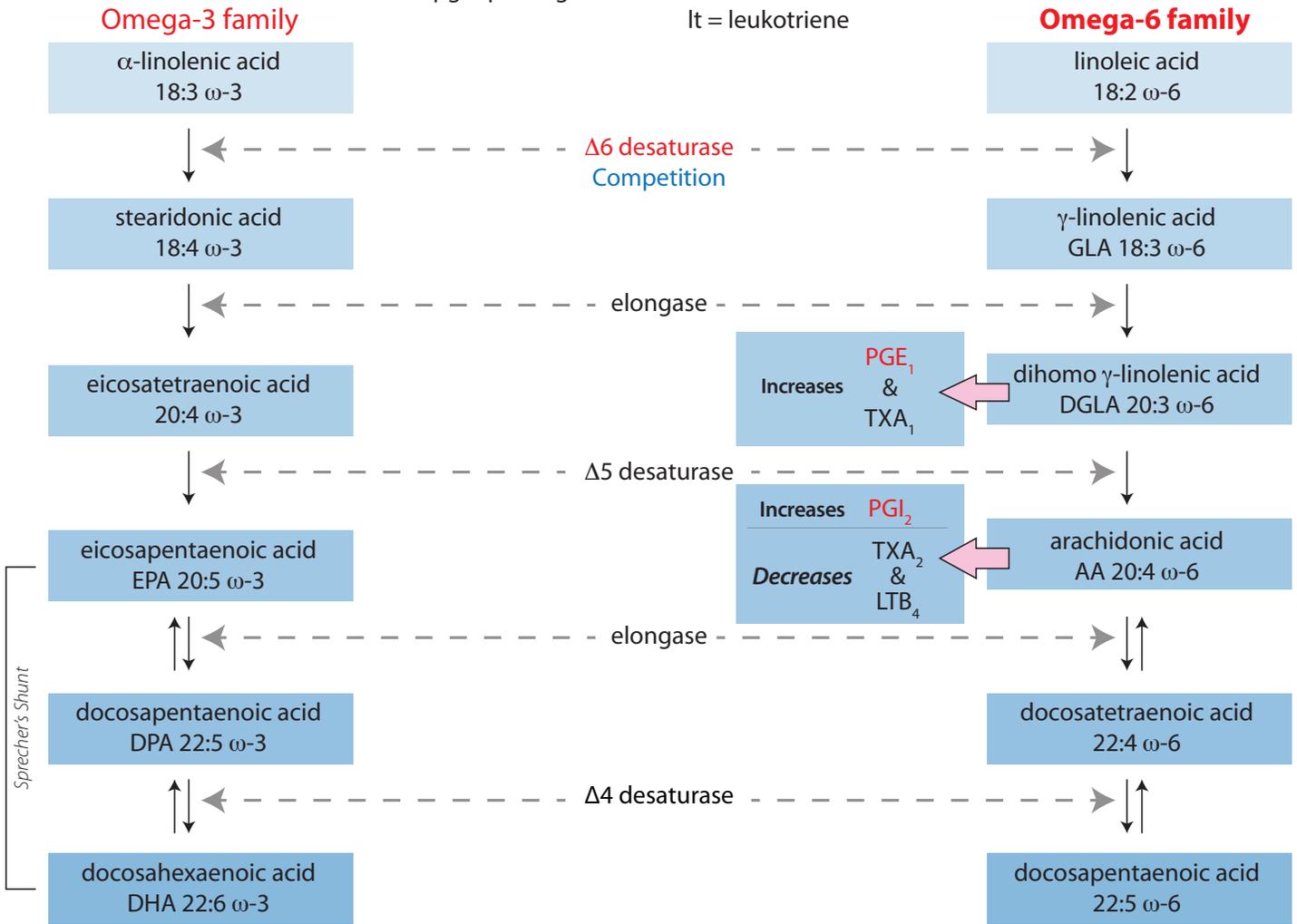
Lipids are the #1 (Modifiable) Variable in Tissue Composition with Potential to Impact Healing.^{1,2}

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Eicosanoid Optimization

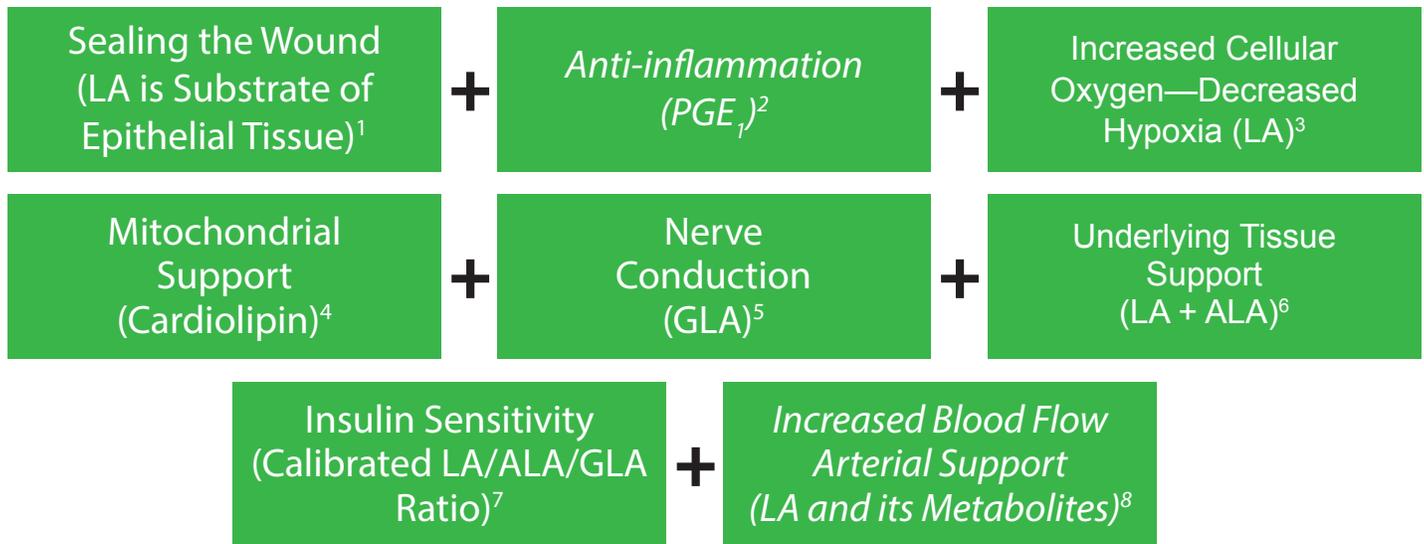
pg = prostaglandin tx = thromboxane
lt = leukotriene



EZTREK™, the new patented Medical Food — specifically and uniquely formulated for the DFU population. Positively impacts multiple metabolic pathways simultaneously. EZTREK™ distinctively compensates for impaired Δ -6 desaturase functionality — increasing PGE₁ output to expedite DFU wound healing.

With continued use, faster healing of both acute and chronic DFUs will occur.

Metabolic Pathways Required For Optimal Wound Healing



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