

UTILIZING PLANT-BASED TREATMENT FOR ACCELERATED HEALING OF CHRONIC & SURGICAL WOUNDS IN THE OUTPATIENT CLINIC

While genetic research may offer promise for the future, there are other innovative clinical approaches to care that can be effective today. This article discusses a new adjuvant modality.

Brian Scott Peskin, BSc

A recurring topic of discussion among those tasked with treating chronic wound care patients is **the need for new, effective treatments**. As with many treatment options, when only the symptoms are treated as opposed to the underlying causes, results will be limited or lasting only in the short term. Because chronic wounds are so difficult to heal, there are no ingestible drugs specifically approved for either general or specific wounds such as diabetic foot ulcers (DFUs). Modalities such as moist wound care, bioengineered skin, negative pressure therapy, growth factor enhancers, and hyperbaric oxygen therapy (HBOT) accomplish varying degrees of results but are often limited to specific patient populations. Maximizing the patient's ability to heal more quickly will be rewarded in the changing insurance compensation landscape. Performance-based programs such as the Pioneer Accountable Care Organization and the Medicare Shared Savings Program are the future. The 2015 Medicare Access and CHIP Reauthorization Act established a new framework for practitioner payment that officials with the Centers for Medicare & Medicaid Services hope will reward those who provide "better" care rather than just "more care." An ingestible, plant-based adjuvant that can help expedite healing of chronic and surgical wounds, regardless of a patient's underlying etiologies, may provide a pathway to that end and is one modality for clinicians in the outpatient clinic to consider. **Discovered after more than a decade of interdisciplinary translational medical research, this adjuvant treatment provides key nutrients that are critical to cell repair and function.**

The adjuvant also has the potential to increase the effectiveness of HBOT in patients previously unresponsive to treatment. Because of its positive effects on the vascular system, this ingestible lipid adjuvant is effective in treating venous (stasis) ulcers, the most common type of lower extremity ulcer, and is effective in treating the ever-growing population of patients living with diabetes. The prevalence of DFUs will only increase as the number of patients in the United States living with diabetes increases. **Because this adjuvant improves functionality in multiple metabolic pathways simultaneously, it's also effective in patients living with various comorbidities, such as arterial insufficiency.**

LACK OF WOUND CLOSURE & HEALTHY NUTRITIONAL STATUS

Nearly one-third of patients being treated in wound care hospital-based outpatient departments (HOPDs) may not reach complete epithelial closure, even though they are cared for routinely over a long period of time.¹ There is room for improvement. Because of the additional comorbidities caused by a compromised cardiovascular system, painful arterial ulcers are often more difficult to heal than other chronic wounds.

Patients living with an arterial ulcer also have a higher rate of recurrence and nearly twice as many amputations.² Diabetes also presents additional impediments to healing. Despite best efforts, at least 25% of DFUs never fully heal.³ If we intend to see improvements in long-term outcomes, a new treatment modal-

ity is needed.

Cellular physiology may hold the key to a new treatment modality. Trillions of cells interacting with each other are connected in network fashion. It's no surprise that systemic improvement can be achieved by providing nutrients that are both critical and essential to cellular functionality and restoration. Many wound care patients are likely (and unknowingly) living with nutritional deficiencies that impedes treatment protocols from ensuring successful healing. This ubiquitous impairment occurs because of food manufacturers' need to extend product shelf life. Although nutritional deficiency extends to most patient populations, it's most apparent in patients living with chronic wounds. Once remedied, this improvement will directly accelerate healing in all patient populations. For wound care providers in the HOPD, the solution can be a calibrated ratio of parent essential oils (PEOs).

IMPORTANCE OF PEOs

Modulation of parent essential fatty acids that comprise all cellular membranes is an underutilized tool that **will benefit all wound patients, including those needing expedited healing of related surgical/reconstructive procedures**. Parent omega-6 (linoleic acid [LA]), and parent omega-3 (alpha-linolenic acid [ALA]) are the only true "essential" fatty acids (EFAs). Unfortunately, to obtain a longer supermarket shelf life and extended cooking oil lifespan, a significant amount of LA is functionally impaired — it isn't biologically functional.⁴⁻⁷

Wound patients are undoubtedly

consuming significant amounts of processed foods and are unknowingly impeding the wound clinic's otherwise effective treatment. Because omega-3 oils are not used for cooking, patients will require a small amount to be administered in addition to daily LA. Fortunately, it's possible to rectify this damage with an ingestible lipids-based formulation.^{8,9}

However, because of the confusion between the two true EFAs and their long-chain metabolites, such as eicosapentaenoic acid, docosahexaenoic acid, Gamma-linolenic acid (GLA), and arachidonic acid (AA), this author prefers, for clarity and technical correctness, the term Essential "EFA." Plant-based seeds such as sunflower, pump-kin, evening primrose, flax, as well as nuts, are ideal sources of Essential EFAs. Based on actual human physiology and bio-chemistry, a calibrated quantity and ratio is required for optimal healing of wounds (See Figure 1 at right). Essential EFAs are the only EFAs the human body cannot manufacture. They are critical lipids — they must come from food. All tissue membranes are comprised of significant quantities of them.

The body's production of long-chain metabolites from Essential EFAs produce a naturally limited amount of important eicosanoids (local cellular hormones) — also very important in expeditious healing of all wounds. Because of the insult to epithelial and underlying tissue, often coupled with comorbidities, chronic wound patients require an abundance of fully functional/metabolically active PEOs. Patients living with diabetes often present an added burden to expedited healing. It's common knowledge that DFUs can cause higher mortality rates than many cancers, including prostate and breast cancer, Hodgkin's lymphoma, and colon cancer.^{10,11} Even with adequate arterial blood flow, DFUs have a dismal 31% closure rate at 20 weeks.¹² However, literature and case studies show treatments utilizing ingestible plant-based lipids have produced improvement in healing, starting in just 30 days.¹³

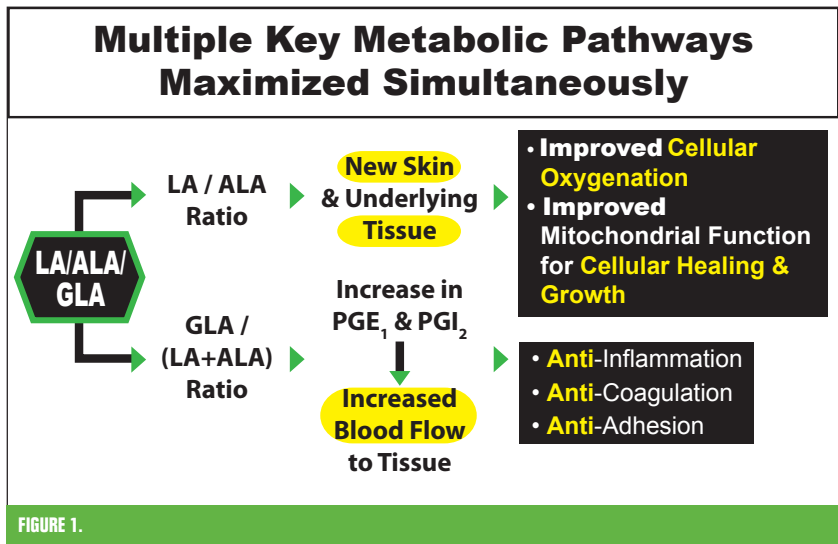


FIGURE 1.

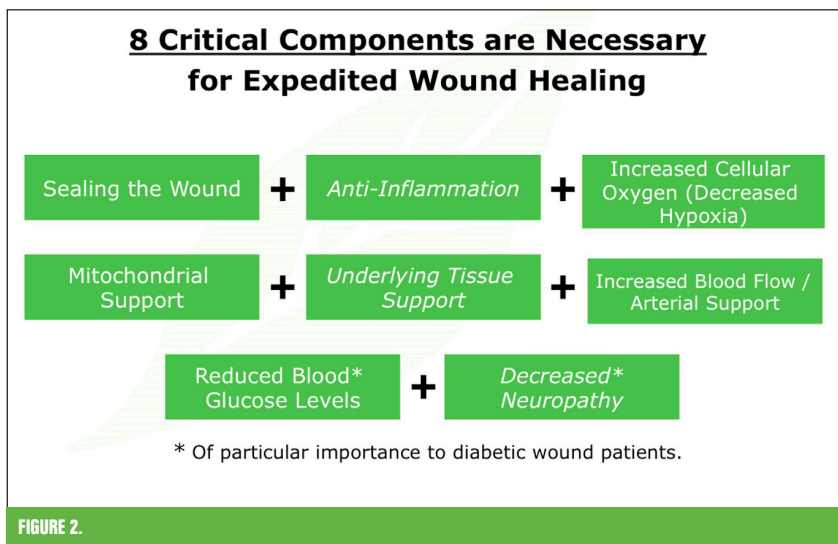


FIGURE 2.

INCREASED HEALING POTENTIAL WITH PLANT-BASED LIPIDS

Directly comprising the patient's 100 trillion bilipid cellular membranes, LA and ALA are the prime lipids directly utilized in significant quantities.¹⁴ They are also metabolized (elongated) to important eicosanoids (local hormones that have specific effects on target cells close to their site of formation). Seed oils present an excellent source of metabolically active Essential EFAs. Essential EFAs and their metabolites have been proven effective in treating complications associated with diabetes and, specifically, in expediting wound healing.¹³ Wound care clinicians can now exploit these findings to better heal their patients. **Surgical wounds and those requiring de-**

bridement procedures will heal more expeditiously because of the adjuvant's profound effects in supporting epithelial tissue. Significantly improved surgical patient outcomes were verified in all patients, resulting in less inflammation, scar tissue and pain among patients participating in a case series study conducted by Dr. Andrea Roncarati, a plastic/reconstructive surgeon based in Ferrara, Italy.¹⁵

REQUIREMENTS FOR EXPEDITED WOUND HEALING

First and foremost is the "sealing of the wound." (See Figure 2 above.) Otherwise, risk of infection significantly increases. Skin (epithelial tissue) is comprised of high amounts of LA. Because of human

skin's high LA content, maximum skin/epithelial tissue healing occurs with ingestible treatment containing significant amounts of the skin's substrate, metabolically active LA.¹³ After the initial inflammatory signaling caused by the wound, this inflammatory stage must be short-lived. Otherwise, neither the surface skin nor its underlying tissue will expeditiously heal. Inflammation pathways promote thrombosis (clogging of arteries and veins), which impedes blood flow and further impedes healing.¹⁶ GLA, the first long-chain metabolite of LA, directly supports maximization of Prostaglandin Series 1 (PGE₁), the most potent of the prostaglandins, a group of physiologically active lipid compounds having diverse hormone-like effects. Their production may be modified by diet.^{8,9}

Because prostaglandins have been found in almost every tissue in humans, we can modulate them to expedite wound healing. PGE₁ is the body's most powerful natural anti-inflammatory, and its production can be easily modulated/maximized in wound patients. We have been told the perils of AA. However, increasing PGE₁ inhibits the AA into its free form, thereby "cooling down" proinflammatory metabolites. AA should not be considered "inflammatory." It is only because of ingested processed/adulterated LA that inflammation occurs. A calibrated formulation of LA, ALA, and GLA ensures optimal regulation of AA and inflammatory response. Patient consumption of GLA-containing lipids has the advantage of bypassing the delta-6 desaturase pathway. This pathway is often impaired in wound patients — particularly in patients living with diabetes. With daily GLA ingestion, protective PGE₁ production is increased, not impeded as with corticosteroids. Corticosteroids, while reducing pain, impede healing because they disrupt production of the eicosanoids required to heal wounds. If a wound care patient must take them, it's even more important he/she consumes the adjuvant.

Increased cellular oxygen accelerates wound healing and protects wounds from infection. Unfortunately, because of the wound's increased oxygen requirements, the environment of early

wounds is always hypoxic (oxygen deficient).¹⁷ Always accompanied by hypoxia, chronic wounds can have as little as 10% of the oxygen content of normal tissue.¹⁷ Parent omega-6 (LA) increases cellular oxygenation.¹⁸ Increasing cellular oxygenation is also a significant feature of HBOT. Therefore, this ingestible medication is an ideal adjuvant to HBOT.

Via critical cardiolipin support in the mitochondria, wound tissue can now obtain the required extra energy for repair, significantly accelerating healing.¹⁹⁻²⁵ By optimizing cellular functionality with a calibrated ratio of LA/ALA, all underlying tissue related to the wound/ulcer heals better because its cellular tissue membranes contain 25-33% LA/ALA.¹⁴

LOWERED BLOOD GLUCOSE, INCREASED BLOOD FLOW

In part because of prolonged elevated blood glucose levels, damage to nerve function (neuropathy) occurs in more than 90% of patients living with diabetes, often exacerbating wound healing. A calibrated LA/ALA formulation maximizes insulin-binding sensitivity, lowering elevated blood glucose levels. Patients ingesting LA lowered their blood sugars by an average of 15 points.²⁶ In 2013, LA's effect in reducing diabetic blood glucose levels was reconfirmed.²⁷ A combination of LA and its metabolite GLA works synergistically in the cell membrane to reduce blood glucose and fortify the cellular fatty acids removed by elevated lipo-protein-associated phospholipase A₂, an inflammatory enzyme, often elevated in patients living with diabetes.²⁸ Although maximum blood flow is required for optimal outcomes, many patients suffer impairment. There is now help for these patients. The plant-based lipids — LA/ALA/GLA — work synergistically to reverse existing cardiovascular disease (CVD, in particular occlusions) in both diabetic and nondiabetic patients.²⁹ For maximum effectiveness, a calibrated ratio of GLA/LA is also required. A calibrated formulation of plant-based lipids also supports "natural blood thinning" via increased production of prostacyclin (PGI₂), a prostaglandin member of the eicosanoid family of lipid molecules that inhibits platelet activation

and is an effective vasodilator, contributing to maximized arterial blood flow.³⁰ A further CVD-related benefit is optimization of multiple protective cardiovascular pathways simultaneously.⁷ Because of its powerful anti-inflammatory properties, it's known that metabolically active plant-based LA is effective in reversing heart disease³¹ and that ALA is associated with less risk of heart attack.³²

FORMULATION REQUIREMENTS

For maximum wound healing results, the following must be adhered to:

- 1) Calibrated blend of Parent omega-6/omega-3 — 1:1-2.5:1 ratio.
- 2) For maximum bioavailability/functionality, the oils must be minimally processed. Organically grown and processed oils are best. Cold pressing alone is insufficient.
- 3) GLA should be utilized for maximum anti-inflammatory PGE1 production.
- 4) High oleic acid oils are not to be used.
- 5) In addition to acceptable peroxide value, the following must be ensured for maximum wound healing: thiobarbituric acid is <0.06, free fatty acids are <1%, and p-Anisidine <4%. Ideally, dosage is approximately 7.5 g/day for a 200-lb patient. After 3-4 months, or when the wound is 75% healed, dosage may be decreased. ■

References

1. Fife CE, Carter MJ, Walker D, Thomson B. Wound care outcomes and associated cost among patients treated in US outpatient wound centers: data from the US wound registry. *Wounds*. 2012;24(1).
2. Armstrong DG, Kanda VA, Lavery LA, Marston W, Mills JL, Boulton AJM. Mind the gap: disparity between research funding and costs of care for diabetic foot ulcers. *Diabetes Care*. 2013;36(7):1815-17.
3. Bijan I, Khorvash F, Ebneshahidi A, Askari G. Prevention of the diabetic foot ulcer. *Int J Prev Med*. 2013;4(3):373-76.
4. Anton SD, Heekin K, Simkins C, Acosta A. Differential effects of adulterated versus unadulterated forms of linoleic acid on cardiovascular health. *J Integr Med*. 2013;11(1):2-10.
5. Staprāns I, Pan XM, Rapp JH, Feingold KR. Oxidized cholesterol in the diet is a source of oxidized lipoproteins in human serum. *J Lipid Res*. 2003;44:705-15.
6. Spittler G. Peroxyl radicals: inductors of neurodegenerative and other inflammatory diseases. Their origin and how they transform cholesterol, phospholipids, plasmalogens, polyunsaturated fatty acids, sugars, and proteins into deleterious products. *Free Radic Biol Med*. 2006;41:362.
7. Felton CV, Crook D, Davies MJ, Oliver MF. Relation of plaque lipid composition and morphology to the stability of human aortic plaques. *Arterioscler Thromb and Vasc Biol*. 1997;17(7):1337-45.
8. Wainwright PE, Huang YS, Bulman-Fleming B, Dalby D, Mills DE, Redden P, McCutcheon D. The effects of dietary n-3/n-6 ratio on brain development in the mouse: a dose response study with long-chain n-3 fatty acids. *Lipids*. 1992;27(2):98-103.
9. Lands W, Morris A, Libelt B. Quantitative effects of dietary polyunsaturated fats on the composition of fatty acids in rat tissues. *Lipids*. 1990;25(9):505-16.
10. Robbins JM. Mortality rates and diabetic foot ulcers: is it time to communicate mortality risk to patients with diabetic foot ulceration? *J Am Podiatr Med Assoc*. 2008;98(6):489-93.
11. Armstrong DG. Guest editorial: are diabetes-related wounds and amputations worse than cancer? *Int Wound J*. 2007;4(4):286-7.
12. Fife CE. Is HBOT cost-effective for diabetic foot ulcers? *Podiatry Today*. 2009; 22(6):18-24.
13. Albina JE. Detrimental effect of an omega-3 fatty acid-enriched diet on wound healing. *JPEN J Parenter Enteral Nutr*. 1993. 17(6):519-21.
14. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. *Molecular Biology of the Cell*. 3rd ed. New York, NY. Garland Science; 1994.
15. Peskin B, Habib A, Matheson J. Chronic wound/diabetic ulcer healing/surgical healing: a new plant-based treatment clinically effective in just 30 days. *Townsend Letter*. 2016;393:73-5.
16. Libby P. Inflammation in atherosclerosis. *Nature*. 2002;420(6917):868-74.
17. Guo S, DiPietro LA. Factors affecting wound healing. *J Dent Res*. 2010;89(3):219-29.
18. Campbell IM, Crozier DN, Caton RB. Abnormal fatty acid composition and impaired oxygen supply in cystic fibrosis patients. *Pediatrics*. 1976;57(4):480-6.
19. Peskin BS. Cancer and mitochondrial defects: new 21st century research. *Townsend Letter*. August 2009;313/314:87-90.
20. Kiebish MA, Han X, Cheng H, Chuang J, Seyfried TN. Cardiolipin and electron transport chain abnormalities in mouse brain tumor mitochondria: lipidomic evidence supporting the Warburg theory of cancer. *J Lipid Res*. 2008;49:2545-56.
21. Krebs JJ, Hauser H, Carafoli E. Asymmetric distribution of phospholipids in the inner membrane of beef heart mitochondria. *J Biol Chem*. 1979;254(12):5308-16. Libby P. Inflammation in atherosclerosis. *Nature*. 2002;420(6917):868-74.
22. Christie W. Cardiolipin (Diphosphatidylglycerol). Structure, Occurrence, Biology and Analysis. The AOCS Lipid Library. Accessed online: <http://aocs.files.cms-plus.com/AnnualMeeting/images/lipidimporthtml/lipidlibrary/Lipids/dpg/index.htm>
23. Rybanski B, Franco-Barraza J, Cukierman E. The wound healing, chronic fibrosis, and cancer progression triad. *Physiol Genomics*. 2014;46(7):223-44.
24. Murray RK. *Harper's Illustrated Biochemistry*. 26th ed. New York, NY. McGraw-Hill; 2003.
25. Guyton AC, Hall JE. *Textbook of Medical Physiology*. 9th ed. St. Louis, MO. W.B. Saunders Co.; 1996.
26. Asp ML, Collene AL, Norris LE, Cole RM, Stout MB, Tang SY, Hsu JC, Belury MA. Time-dependent effects of safflower oil to improve glycemia, inflammation and blood lipids in obese, post-menopausal women with type 2 diabetes: a randomized, double-masked, crossover study. *Clin Nutr*. 2011;30(4):443-9.
27. Kahleova H. Vegetarian diet-induced increase in linoleic acid in serum phospholipids is associated with improved insulin sensitivity in subjects with type 2 diabetes. *Nutr Diabetes*. 2013;3(6)e75.
28. Dutta-Roy A. Effect of evening primrose oil feeding on erythrocyte membrane properties in diabetes mellitus. *Omega-6 Essential Fatty Acids: Pathophysiology and Roles in Clinical Medicine*. New York, NY. Wiley; 1990 (out of print).
29. Weiss C, Regele S, Velich T, Bärtsch P, Weiss T. Hemostasis and fibrinolysis in patients with intermittent claudication: effects of prostaglandin E1. *Prostaglandins Leukot Essent Fatty Acids*. 2000;63(5):271-7.
30. Terano T, Hirai A, Hamazaki T, Kobayashi S, Fujita T, Tamura Y, Kumagai A. Effect of oral administration of highly purified eicosapentaenoic acid on platelet function, blood viscosity and red cell deformability in healthy human subjects. *Atherosclerosis*. 1983;46(3):321-31.
31. Farvid MS, Ding M, Pan A, et al. Dietary linoleic acid and risk of coronary heart disease: a systematic review and meta-analysis of prospective cohort studies. *Circulation*. 2014;130(18):1568-78.
32. Campos H, Baylin A, Willett WC. Alpha-linolenic acid and risk of nonfatal acute myocardial infarction. *Circulation*. 2008;118(4):339-45.