



30 plant extracts



GLA Safflower Oil

The Woman's Essential Fatty Acid

Essential fatty acids (EFAs), which have become basic staples in today's nutritional marketplace, are used in a variety of applications based on a spectrum of structure and function claims. But what about an omega fatty acid, oriented to the needs of women, providing a cornerstone for vibrant health? One that contributes to the maintenance of normal hormonal balance, offers nutritional support for menstrual and menopausal discomfort, sustains healthy skin, supports joint health, aids in mastalgia (breast pain) and delivers dietary defence against osteoporosis and cardiovascular health? That omega fatty acid, which can undoubtedly be called the "Woman's EFA," is gamma-linolenic acid (GLA), and can be found, most commonly, in evening primrose, borage seed oils... and, now, in High GLA Safflower Oil.

Erratic availability and unstable supplies of GLA have limited its acceptance and growth, particularly when compared with omega-3 oils. Growing GLA demand, and increasing interest in more concentrated and economical sources, encouraged Arcadia Biosciences (Davis, California, USA) to develop a new, consistent and dependable GLA source. A product of modern biotechnology, Arcadia's High GLA Safflower Oil contains 40% GLA and is the first GMO developed, specifically, as a human nutritional product.

Arcadia's High GLA Safflower Oil will be produced exclusively in the US and will be in full commercial production by early 2009.

Anatomy of the Omega-6 Family

Each of the omega families originates from a "parent" fatty acid. For the omega-3s, it is α -linolenic acid (ALA) which is commonly found in walnuts, soybean oils and flaxseed. The omega-6 parent is linoleic acid (LA), and is present in most common seed and vegetable-based cooking oils.



The first downstream metabolite of linoleic acid is gamma-linolenic acid, formed via the activity of the delta-6 desaturase (D6D) enzyme. Because the D6D enzyme is often impaired in humans, many of us are GLA deficient. However, when GLA is present, it is quickly elongated, forming the intermediate dihomono- γ -linolenic acid (DGLA). DGLA is the building block to a number of important anti-inflammatory agents. A limited amount of DGLA can be converted to arachidonic acid (ARA) by the delta-5 desaturase (D5D) enzyme. Like D6D, D5D activity is very limited. In fact, most of the ARA in our bodies comes from dietary animal sources rather than via this pathway.

GLA: Its Origins and Pathways

For well over 500 years, before Columbus reached the Americas, the Algonquin Indians were chewing the seeds of the evening primrose plant and rubbing the seed oil onto flesh wounds.¹ In the 16th Century, when the Europeans became aware of the medicinal value of this plant, it quickly became one of the first wild edibles transplanted to that continent. As a result of its curative properties, the seed oil from this plant was referred to as the "King's Cure All." As we now understand, the properties of evening primrose oil are attributable to its gamma-linolenic acid content. GLA is also prevalent in the seed oil of the borage plant, which was first introduced to Spain by the Persians during the Middle Ages. Likewise, GLA is found in the seeds of the berries of the black currant shrub, native to central and northern Europe.

GLA's systemic influence lies in the conversion of its intermediate DGLA into anti-inflammatory, signalling molecules called eicosanoids. These include two major classes, prostaglandins and leukotrienes. Depending upon the type of cell, DGLA is either principally converted into prostaglandins or both prostaglandins and leukotrienes. The cyclooxygenase (COX) enzyme converts DGLA into 1-series prostaglandins

(PGE1) that possess powerful anti-inflammatory properties. Additionally, PGE1 inhibits platelet aggregation, produces vasodilation, suppresses cholesterol biosynthesis, regulates immune responses and reduces blood pressure.²⁻³ DGLA can also be converted to 15-OH-DGLA (or 15-HETrE) by the activity of the 15-lipoxygenase (LOX) enzyme. 15-OH-DGLA impedes the activity of the 5- and 12-lipoxygenases, preventing the formation of pro-inflammatory 4-series leukotrienes from ARA. Studies have shown that the long-term intake of GLA by rheumatoid arthritis patients reduced their need for non-steroidal anti-inflammatory drug (NSAID) analgesics, such as aspirin, acetaminophen and Celebrex, by competing for the COX and LOX enzymes that convert ARA to pro-inflammatory, 2-series prostaglandins (PGE2).

However, as previously mentioned, the body's ability to produce GLA is quite limited. The delta-6 desaturase enzyme is not plentiful in humans and is significantly inhibited by age, lifestyle factors and dietary consequences. Stress, ageing, alcohol, sugar, nicotine, caffeine, illness and saturated fats all impede D6D.⁴ Dietary deficiencies of zinc, magnesium and vitamins C, B3, and B6 also hinder the activity of this enzyme. To compound the problem, ALA, the omega-3 parent, also competes for the attention of this enzyme, further abbreviating de novo synthesis of GLA.

GLA's Core Metabolic Activities

Part of GLA's core function centres around the many biochemical pathways influenced by its prostaglandin and leukotriene metabolites. GLA is so effective as an anti-inflammatory that it is currently used to modulate inflammation by inclusion in medical foods that are administered daily to thousands of critically ill people in hospitals around the world. Furthermore, a recent clinical study of intensive care patients, using a combination of GLA plus omega-3 EPA, resulted in a reduction of confinement from 17.5 to 12.8 days.⁵ More than 40 years of clinical research has been done →



on GLA and its inflammatory control, with countless human clinical trials consistently demonstrating pronounced efficacy. Not coincidentally, for the last 10 years, the Danish Olympic Team has used a supplement containing GLA plus EPA/DHA for the treatment of inflammatory over-use injuries.⁷

The Woman's Essential Fatty Acid

The anti-inflammatory properties of GLA make it ideal for the support of PMS/PMT and mastalgia. Mastalgia is clinically manifested as pain associated with the abnormal sensitivity of breast tissues to normal hormone levels. Those afflicted typically have blood levels that are low in GLA and high in saturated fats. Elevated saturated fat levels will prolong and increase the effects of hormones, specifically prolactin, on breast tissues. Dietary GLA balances fatty acid ratios and mitigates this sensitivity.⁸ In fact, a British health care company once had an EPO-based product approved as a registered pharmaceutical for the treatment of cyclical mastalgia. Menopausal and menstrual support are some of the more widely used applications of GLA. With symptoms ranging from water retention to fatigue and breast pain, nutritional support is essential. Hormonal imbalance and associated breast pain can be ameliorated by controlling fatty acid imbalances with dietary GLA. Inflammatory control also helps with the swelling and bloating caused by fluid retention. In a clinical trial, GLA was administered to 68 women reporting severe PMS symptoms. Subjects were given GLA three days before the expected onset of symptoms and continued until the start of menstruation. At the conclusion, 61% experienced complete relief whereas 21% had partial relief.⁹

GLA also has a clinical foundation in the support of healthy hearts. It offers support for hypertension (high blood pressure), atherosclerosis and, similarly, aids in cholesterol control^{10,11}, all of which are increasingly important, as women have become more aware that cardiovascular disease (CVD) is more prevalent in females than their male counterparts. Through years of clinical research, the role of blood lipids in the progression of CVD is well understood. However, to further clarify the role of EFAs, a recent clinical study of 32 women was designed to vary levels of omega-3 and omega-6 EFAs. During a 28-day period, certain groups displayed dramatic and statistically significant serum lipid reductions. Subjects receiving 4g/day of EPA/DHA and GLA presented a 14.7% reduction in total cholesterol to HDL while mean LDL:HDL ratios decreased by 19.9%. It was concluded that the group had a 43% reduction in the 10 year risk of myocardial infarction.¹²

Common skin conditions, such as eczema, (affecting almost 25% of the US population), and psoriasis,

benefit from the use of dietary GLA. Improvement of the saturated to unsaturated fat ratio provides for cellular lubricity, which benefits skin tone and reduces transepidermal water loss to prevent dryness.^{13,14} GLA is also well indicated for the control of epithelial swelling and general inflammation, as our skin contains no GLA. Most people only absorb about 50% of their calcium intake and the typical female diet contains far less calcium than men's diets. Therefore, it is vital to take steps to enhance its absorption and utilization. While most women understand the need for adjuncts, such as vitamin D and magnesium, the inclusion of GLA plus EPA lends a new level of support. This combination has been demonstrated to significantly enhance calcium absorption while minimizing its excretion. An 18 month study of 65 female subjects using a GLA/EPA combination, revealed a 4.7% increase in femoral bone density.¹⁵

The female populace should also be vitally aware of the vast benefits of dietary GLA for the symptomatic control of rheumatoid arthritis (RA). While the cause remains unknown, no part of the world or ethnicity is free of the disease, which affects about 1% of the population of western countries. While declining, RA is significantly more prevalent amongst women, comprising almost 70% of those afflicted. And, commonly used NSAIDs may actually exacerbate the difficulties. Inhibition of the cyclo-oxygenase enzyme is not selective and there will be decreased production of the positive, anti-inflammatory, 1-series prostaglandins (PGs) as well as the 2-series, pro-inflammatory, ARA metabolites. Moreover, this model allows for unabated production of 4-series leukotrienes (LTs), a potent inflammatory mediator. Many of the side-effects of NSAIDs, such as gastric bleeding, headaches, high blood pressure and excessive platelet aggregation, are a result of the broadly directed inhibition of prostaglandins. Dietary GLA acts as a competitive inhibitor of the 2-series PGs and 4-series LTs and, thus, suppresses inflammation.¹⁶ Numerous clinical studies have shown that GLA reduces all symptoms, including morning stiffness and the number of joints affected.^{17,18} A Meta Analysis in April 2000 clearly indicated that symptomatic joint stiffness was reduced by 60-65%. And treatment with GLA presented fewer side-effects than the commonly applied pharmaceutical therapies.¹⁹

Diabetic Neuropathy

Although demonstrating no gender specificity, diabetic neuropathy remains a painful and debilitating neurological complication of long-term diabetes. Effective treatment is now much more important as the incidence of this affliction continues to rapidly increase, now nearing epidemic proportions in the US. This disease has a foundation in fatty acid abnormalities, with particularly low DGLA and high ARA levels in nerve membranes and red blood cell membranes. Low DGLA levels result in reduced levels of PGE1 and prostacyclin, impairing circulation. Low PGE1 also increases phospholipase A2 activity, resulting in the release of ARA from membranes and increasing membrane stiffness. Free ARA forms vasoconstrictors, restricting circulation and, with time, a deterioration of motor, sensory and autonomic nerve response. GLA supplementation has repeatedly been shown to improve nerve conduction velocity, resulting in significant clinical improvements.^{20,21}

Emerging New Science

The science of GLA continues to grow dramatically. Since 2001, there have been some 1,300 new patents on applications of GLA and hundreds of new clinical publications. The US National Institutes of Health and the *American Journal of Clinical Nutrition* each has hundreds of citations involving GLA. Among these are a considerable number of studies in combination with the omega-3 EPA/DHA oils. The pronounced synergy of such combinations suggests a complementary interaction, as both →



GLA and EPA are, subsequently, converted into anti-inflammatory prostaglandins of the 1- and 3-series, respectively. On the forefront of GLA science is its application in cancer treatment therapy, where in vitro studies have established GLA's selective cytotoxic effects on more than 30 different types of cancer cells.²² Further studies have shown evidence of the suppression of breast cancer genes, tumour growth and metastasis.²³ Very promising results have also been demonstrated with GLA's use as an adjunct in combination with current anti-cancer drugs, specifically Tamoxifen and also Taxol, a natural pharmaceutical that can be extracted from the bark of the Pacific Yew.²⁴

Weight management is another new prospective application area for GLA. In June 2007, a human clinical study was published documenting the mitigation of weight regain after significant weight loss in patients with chronic obesity. After one year of daily supplementation with 890 mg of GLA, there was a 6 kg reduction in weight regain versus the control group, suggesting a role for essential fatty acids in fuel partitioning for obesity prone humans.²⁵

Advantages in Advanced Biotechnology

Arcadia's High GLA Safflower Oil, with 40% GLA, offers considerable economic advantages and immense consumer convenience. As those who are familiar with EPO and borage oil already know, these oils are considerably lower in GLA concentration, about 10% and 20%, respectively. Numerous researchers suggest that daily supplements containing between 500 and 2,000 mg of GLA may provide pharmacological benefits. To realize the upper threshold, twenty 1,000mg EPO capsules would be required. The same GLA level could be achieved with only five High GLA Safflower capsules. Additionally, the high concentration allows for formulation flexibility and delivery of therapeutic amounts with far fewer calories. Those 20 EPO capsules also provide 15 g or 135 calories of unnecessary fat. In addition to the obvious concentration advantages, the safflower is considered to be the ideal oilseed background for GLA. With several defined growing regions in North America where safflower is already successfully contract produced, identity preservation and segregation from other safflower fields will be readily accomplished. Given its powerful concentration and potential for a more dependable supply, Arcadia's High GLA Safflower Oil should make GLA as popular as omega-3s. 🌻



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