



Planting Wellness

The Ultimate Guide to High Concentrate
Gamma Linolenic Acid (GLA) Safflower
Oil - GLASO™



Moolec's Innovation: The GLASO™ product

Moolec has developed a high-GLA safflower variety that contains approximately three times more GLA than natural sources, making it the most concentrated GLA oil available on the market.

Introduction

In the past decade, the spotlight in nutritional science has predominantly shone on omega-3 fatty acids, particularly those found in fish such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These fatty acids have garnered significant attention due to a robust body of scientific research linking their consumption to a reduced risk of numerous diseases. The most compelling evidence supports a strong association between fish oil intake and a lower incidence of coronary heart disease (CHD). This has led to widespread public and scientific endorsement of omega-3 fatty acids as essential components of a healthful diet.

However, the conversation around dietary fats is not limited to omega-3s. Omega-6 fatty acids have also been discussed extensively, often in a less favorable light. The negative reputation stems from epidemiological studies indicating that an imbalance between omega-3 and omega-6 fatty acids can contribute to various health issues. The typical Western diet, characterized by a high intake of omega-6 fatty acids—primarily linoleic acid (LA) and arachidonic acid (ARA)—and a low intake of omega-3 fatty acids, leads to an omega-3 to omega-6 ratio ranging from 1:8 to 1:15. This imbalance is linked to adverse health outcomes, prompting recommendations from health authorities, such as Japan's Ministry of Health, Labour and Welfare, for a more balanced ratio of 1:4.

A critical but often overlooked member of the omega-6 family is gamma-linolenic acid (GLA). Unlike LA and ARA, GLA is consumed in relatively small amounts, yet it holds significant potential for promoting health, comparable to that of omega-3 fatty acids. GLA is mainly found in certain vegetable oils. GLA is synthesized in the body from LA, the essential fatty acid in the omega-6 pathway, using enzymes that are naturally present.

Today, GLA is utilized in various applications, including food supplements, pet food, skincare products, and medical nutrition.

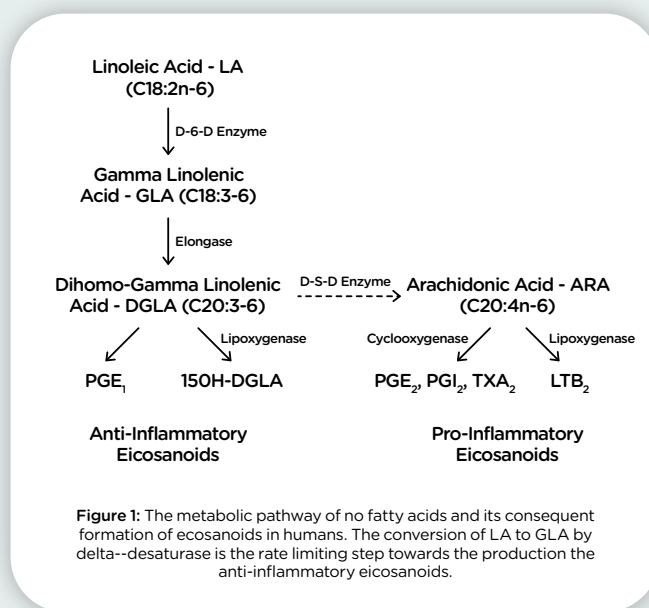
Inflammation, a crucial physiological response for defense and healing, can become detrimental when chronic or uncontrolled, leading to diseases such as arthritis, psoriasis, and numerous other chronic conditions like heart disease, cancer, and diabetes. Modern research has increasingly focused on the role of diet in modulating inflammatory processes and gene expression, highlighting the importance of fats, including GLA, in maintaining health and preventing disease.

GLA and its metabolism

Gamma-linolenic acid (GLA), scientifically known as cis-6, cis-9, cis-12-octadecatrienoic acid, plays a crucial role in the polyunsaturated fatty acid (PUFA) pathway. It is

produced in the body as an intermediate in the metabolism of linoleic acid (LA), an essential omega-6 fatty acid. The conversion of LA to GLA is facilitated by the enzyme delta-6-desaturase, a reaction that is notably slow and further impeded by various factors such as nutritional deficiencies (including vitamins and minerals like zinc and cobalt) and inflammatory conditions such as arthritis and psoriasis. Additionally, diseases like hypertension and diabetes can impair this enzyme's activity, leading to insufficient production of GLA. Lifestyle factors such as stress, smoking, alcohol consumption, and diets high in saturated and trans fats, as well as preformed arachidonic acid (ARA) and eicosapentaenoic acid (EPA), also inhibit the delta-6-desaturase enzyme.

Once synthesized or ingested, GLA is quickly elongated to dihomo-gamma-linolenic acid (DGLA). DGLA is then incorporated into cell membrane phospholipids through acylation, a process catalyzed by acyl transferases. DGLA serves as the active form of GLA, mediating most of its physiological actions. It can also be converted to ARA by the enzyme delta-5-desaturase, although this reaction is slow and heavily influenced by dietary and environmental factors. Substances like preformed ARA from meat and dairy, EPA from fish, and sesamin from sesame seeds inhibit delta-5-desaturase, thereby reducing ARA formation from DGLA.



Membrane-bound DGLA is released by the enzyme phospholipase A₂ (PLA₂). Once released, DGLA competes with ARA for enzymes like cyclooxygenases (COX) and lipoxygenases (LOX) to produce short-lived second messengers that are crucial for cell-to-cell communication and mediation of physiological effects. COX action on DGLA generates prostaglandins of the series 1 (PGE₁) and thromboxane A₁ (TxA₁), which exert anti-inflammatory, vasodilatory, and anti-aggregatory effects. DGLA also produces 15-hydroxyeicosatrienoic acid (15-HETE) via the action of 15-LOX. 15-HETE is a potent inhibitor of 5-lipoxygenase, thereby inhibiting the production of leukotriene B₄ (LTB₄), a pro-inflammatory mediator from inflammatory cells such as neutrophils.

The synthesis and metabolism of GLA are integral to maintaining the balance and function of essential fatty acids in the body. Despite the plentiful availability of linoleic acid in the typical Western diet, the activity of the delta-6-desaturase enzyme is often impaired, necessitating GLA supplementation to support health and alleviate symptoms associated with various diseases.

GLA Uses and Health Benefits

Gamma-linolenic acid (GLA), an omega-6 fatty acid, has gained recognition for its potential health benefits across various conditions. Despite being less studied compared to omega-3 fatty acids, GLA has demonstrated significant efficacy, primarily due to its anti-inflammatory properties.

Anti-inflammatory Properties

GLA's anti-inflammatory activity is primarily mediated through its conversion to DGLA, which produces anti-inflammatory prostaglandins (PGE1) and inhibits pro-inflammatory leukotrienes. This makes GLA beneficial for conditions such as rheumatoid arthritis, psoriasis, and atopic dermatitis. Clinical trials have shown that GLA supplementation reduces inflammation, tender joint scores, and the need for non-steroidal anti-inflammatory drugs (NSAIDs), making it a valuable adjunct therapy for arthritis patients. [1,13,14]

Nutritional Supplements & Pharmaceuticals

GLA nutritional supplements are often marketed for their benefits in alleviating premenstrual syndrome (PMS) symptoms, arthritis pain, and improving skin health. Evening primrose oil was previously licensed as a pharmaceutical in the UK for treating cyclical mastalgia (Efamast™) and atopic eczema (Epogam™) but has since been delisted due to its widespread availability as a supplement. [12]

Coronary Heart Disease

While the benefits of omega-3 fatty acids in preventing coronary heart disease (CHD) are well-established, GLA has also shown potential. Studies indicate that GLA supplementation can reduce VLDL and LDL cholesterol levels, atherosclerotic lesions, and blood pressure, contributing to cardiovascular health. [2-6]

Weight Maintenance

Recent advancements categorize obesity as a chronic metabolic disease, shifting treatment towards sustainable, effective options. Traditional therapies often result in transient benefits and weight regain. GLA, a bioactive nutritional supplement, counters obesity-associated membrane imbalances and aids long-term weight maintenance. Studies show GLA reduces weight regain by 50-75%, making it a promising adjunct to traditional weight loss methods. As a naturally occurring component of human fat metabolism, Initiating GLA consumption during weight loss treatments can enhance outcomes and minimize relapse, offering a novel approach to chronic obesity management. [38-42]

Skin Health

GLA improves skin smoothness and moisture, with significant improvements observed after 12 weeks of supplementation. It is effective in treating eczema and psoriasis, reducing inflammation, itching, and other symptoms. GLA supplementation has shown promising results in improving the quality of life for individuals with these skin conditions.

Cosmetics

GLA oils are valued in cosmetics for their skin-softening and moisturizing properties. As dietary supplements, GLA oils enhance skin health, making them among the first recognized cosmeceuticals. Lower-cost, higher-concentration GLA oils are particularly attractive for use in skincare products, ensuring the application of functional levels of GLA for optimal skin benefits. [12]

Atopic Eczema and Dermatitis

Atopic eczema, or dermatitis, is characterized by itching, rashes, and lesions, often persisting from childhood into adulthood. Patients with atopic eczema typically exhibit elevated levels of linoleic acid and lower levels of GLA, DGLA, and arachidonic acid (ARA). Studies have shown that GLA supplementation, combined with topical steroids and emollients, can improve eczema symptoms, though results may take several months to manifest. While some studies report conflicting outcomes, GLA's potential in this application warrants further research.

Diabetic Neuropathy

Diabetic neuropathy, a painful complication of diabetes, is associated with abnormal blood sugar levels and fatty acid deficiencies, particularly low DGLA and ARA in nerve membranes. Low DGLA levels result in reduced PGE1, impairing circulation and nerve function. Supplementing with GLA, often in the form of evening primrose oil, has been shown to improve nerve conduction velocity and alleviate neuropathy symptoms in diabetic patients. [12,43,44]

Infant Nutrition

GLA is considered a safer alternative to direct ARA supplementation in infant formulas. Given that GLA is a metabolic precursor to ARA, several GLA-containing formulas have been introduced in Europe and the Far East. These formulas aim to support the developmental needs of preterm and term infants by providing essential long-chain polyunsaturated fatty acids. [12,43,44]

Cancer

GLA has demonstrated tumoricidal activity against various cancers, including breast, pancreatic, colon, and brain cancers. It inhibits cancer cell migration, angiogenesis, and promotes apoptotic cell death. GLA also enhances the efficacy of anticancer drugs like tamoxifen, reducing side effects and improving therapeutic outcomes. Clinical studies have shown that GLA can reduce tumor size and improve survival in patients with advanced cancers when used in combination with traditional treatments. [13,16-30]

Insulin Resistance and Diabetes

GLA supplementation has shown promise in improving insulin sensitivity and managing complications of diabetes. It has been observed that GLA levels are lower in diabetic children during ketoacidosis but normalize after treatment. GLA improves nerve conduction velocity in diabetic patients, suggesting its role as a beneficial nutrient and adjunct in preventing diabetes complications. [13,15,31]

Pet Food

Atopic dermatitis manifests in dogs and cats causing dry, irritated, itchy skin and can lead to lesions that cause



discomfort and require treatment with glucocorticoids and/or antihistamines. Aside from unwanted side effects, Multiple studies have shown that polyunsaturated fatty acids (PUFAs), including gamma-linolenic acid (GLA), added to a pet's diet mitigates atopic dermatitis and supplants the use of medication. The addition of PUFAs restores healthy lipid composition and supports the skin's natural impermeability to irritants or genetic factors that trigger atopic dermatitis. GLA, when consumed with other PUFAs, improves skin health, corrects atopic dermatitis and can prevent discomfort in pets. [32-37]

In summary, GLA offers a range of health benefits, particularly in managing inflammation, improving skin health, and supporting conditions like diabetic neuropathy, cancer, and coronary heart disease. While further research is needed to fully understand its potential, GLA remains a valuable nutrient in both clinical and cosmetic applications.

GLA sources

The two primary dietary sources of GLA are evening primrose oil (EPO) and borage oil (BO), containing 10% and 20% GLA respectively. Black currant oil (BCO), with 15-20% GLA, is limited in availability. Hemp seed oil, though rich in ALA, contains only up to 5% GLA. Both evening primrose and borage are grown as identity-preserved specialty crops, which raises their production costs significantly.

The high cost and low concentration of GLA in these oils pose challenges for their use in nutraceutical and functional food products. For instance, a therapeutic dose of 2,000 mg of GLA would require 40 capsules of 500 mg evening primrose oil, making daily consumption expensive and cumbersome for consumers.

Moolec Science's GLASO™

The high-GLA safflower variety developed by Moolec Science (GLASO™) ensures optimal performance, leveraging safflower's agronomic advantages and eliminating interference from linolenic acid found in other oils.

GLASO™ offers a high-concentrate GLA solution derived from safflowers cultivated under stringent sustainable farming practices. With over 50% more GLA than other plant sources like evening primrose and borage, Moolec's oil is the most concentrated GLA available in the market, ensuring maximum efficacy.

Purity verified, FDA-recognized and free from gluten, allergens, and BSE/TSE, GLASO™ oil undergoes meticulous refining processes, guaranteeing top-notch quality.

With complete control over the production chain and robust stewardship measures, we ensure crop integrity and prevent unintended release. Safflower's favorable oil composition, and existing grower base further enhance its appeal, making GLASO™ the premier choice for those seeking a natural and effective source of GLA for their health and wellness needs.

Disclaimer

This report should not be interpreted as clinical trials or as an endorsement by Moolec Science S.A. It is intended solely as a literature review of the existing scientific evidence.

References

1. Van Hoorn et al. "A short review on sources and health benefits of GLA, The GOOD omega-6". OCL 2008 ; 15(4) : 262-264.
2. Fan et al. "Dietary gamma-linolenic acid suppresses aortic smooth muscle cell proliferation and modifies atherosclerotic lesions in apolipoprotein E Knockout Mice". J Nutr 2001 ; 131 : 1675-81.
3. Fukushima et al. "Investigation of gene expressions related to cholesterol metabolism in rats fed diets enriched in n-6 or n-3 fatty acid with a cholesterol after long-term feeding using quantitative-competitive RT-PCR analysis. J Nutr Sci Vitaminol (Tokyo) 2001 ; 47 : 228-35.
4. Hornych et al. "Effect of gamma-linolenic acid on plasma and membrane lipids and renal prostaglandins in old subjects". Br J Clin Pharma-col 1999 ; 48 : 869-70.
5. Rose et al. "Effects of arachidonic acid on systemic arterial pressure, myocardial contractility and platelets in the dog". Proc Soc Exp Biol Med 1974 ; 147 : 625-5.
6. Engler et al. "Effects of dietary gamma-linolenic acid on blood pressure and adrenal angiotensin receptors in hypertensive rats". Proc Soc Exp Biol Med 1998 ; 218 : 234-7.
7. Chobanian et al. "Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure". Hypertension 2003 ; 42 : 1206-52.
8. Muggli. "Systemic evening primrose oil improves the biophysical skin parameters of healthy adults". Int J Cosm Sci 2005 ; 27 : 243-9.
9. Nissen et al. "Borage oil: c-linolenic acid in the oil decreases skin roughness and TEWL and increases skin moisture in normal and irritated human skin. Cosmet Toilet 1995 ; 110 : 71-6.
10. Poncelet. "Unpublished information of bioriginal food and science corporation" i.c.w. 1999 ; (Dr. Poncelet MD).
11. Andreassi et al. "Efficacy of gamma-linolenic acid in the treatment of patients with atopic dermatitis". J Int Med Res 1997 ; 25 : 266-74.
12. Flider. "GLA: Uses and new sources". Inform 2005 ; 16 : 279-282.
13. Kapoor & Huang. "Gamma linolenic acid: an antiinflammatory Omega-6 fatty acid". Current Pharmaceutical Biotechnology 2006 ; 7 : 531-534.
14. Balch et al. "Effects of altering dietary essential fatty acids on requirements for non-steroidal anti-inflammatory drugs in patients with rheumatoid arthritis: a double blind placebo controlled study". Ann. Rheum. Dis. 1988 ; 47 : 96-104.
15. Decsi et al. "Polyunsaturated fatty acids in plasma lipids of diabetic children during and after diabetic ketoacidosis". Acta Paediatr. 2005 ; 94 : 850-55.
16. Sagar et al. "Cytotoxic action of cis-unsaturated fatty acids on human cervical carcinoma (HeLa) cells: relationship to free radicals and lipid peroxidation and its modulation by calmodulin antagonists". Cancer Lett. 1992 ; 63 : 189-98.
17. Mainou-Fowler. "Gamma-linolenic acid induces apoptosis in B-chronic lymphocytic leukaemia cells in vitro". Leuk. Lymphoma 2001 ; 40(3-4) : 393-403.
18. Watkins et al. "Increased levels of SPARC (osteonectin) in human breast cancer tissues and its association with clinical outcomes". Prostaglandins Leukot. Essent. Fatty Acids 2005 ; 72 : 273-78.
19. Menendez et al. "ω-6 Polyunsaturated Fatty Acid γ-Linolenic Acid (18:3n-6) Is a Selective Estrogen-Response Modulator in Human Breast Cancer Cells: γ-Linolenic Acid Antagonizes Estrogen Receptor-Dependent Transcriptional Activity, Transcriptionally Represses Estrogen Receptor Expression and Synergistically Enhances Tamoxifen and ICI 162,780 (Faslodec) Efficacy in Human Breast Cancer Cells" Int. J. Cancer 2004 ; 109 :949-54.
20. Das. "Occlusion of infusion vessels on γ-linolenic acid infusion" Prostaglandins Leukot. Essent. Fatty Acids 2004 ; 70 : 23-32.
21. Jiang et al. "The effects of n-6 polyunsaturated fatty acids on the expression of nm-23 in human cancer cells." Br. J. Cancer 1998 ; 77 : 731-38.
22. Jiang, W.G., Bryce, R.P., Mansel R.E. "Gamma linolenic acid regulates expression of maspin and the motility of cancer cells" Biochem Biophys Res Commun. 1997 ; 237(3) : 639-44.
23. Heard et al. "Preferential pi-pi complexation between tamoxifen and borage oil/gamma linolenic acid: transcutaneous delivery and NMR spectral modulation" Int. J. Pharm. 2005 ; 302 : 47-55.
24. Karia et al. "Simultaneous permeation of tamoxifen and gamma linolenic acid across excised human skin. Further evidence of the permeation of solvated complexes" Int. J. Pharm. 2004 ; 271 : 305-09.
25. Davies et al. "Effect of gamma-linolenic acid on cellular uptake of structurally related anthracyclines in human drug sensitive and multidrug resistant bladder and breast cancer cell lines" Eur. J. Cancer 1999 ; 35 : 1534-40.
26. Menendez et al. "Effects of gamma-linolenic acid and oleic acid on paclitaxel cytotoxicity in human breast cancer cells" Eur. J. Cancer 2001 ; 37 : 402-13.
27. Menendez et al. "Synergistic interaction between vinorelbine and gamma-linolenic acid in breast cancer cells" Breast. Cancer Res. Treat. 2002 ; 72 : 203-19.
28. Whitehouse et al. "Synergistic Activity of Gamma-Linolenic Acid and Cytotoxic Drugs against Pancreatic Adenocarcinoma Cell Lines" Pancreatology 2003 ; 3 : 367-73.
29. Cai et al. "Inhibition of angiogenic factor- and tumor-induced angiogenesis by gamma linolenic acid" Prostaglandins Leukot. Essent. Fatty Acids 1999 ; 60 : 21-29.
30. Menendez et al. "Effect of gamma-linolenic acid on the transcriptional activity of the Her-2/neu (erbB-2) oncogene" J. Natl. Cancer Inst. 2005 ; 97 : 1611-15.
31. Qi et al. "Altered cardiac fatty acid composition and utilization following dexamethasone-induced insulin resistance" Am. J. Physiol. Endocrinol. Metab. 2006 ; 291 : E420-E427.
32. Poppa et al. "Analysis of epidermal lipids in normal and atopic dogs, before and after administration of an oral omega-6/omega-3 fatty acid feed supplement. A pilot study." Vet Res Commun 2011 ; 35 : 501-509.
33. Sævik et al. "A randomized, controlled study to evaluate the steroid sparing effect of essential fatty acid supplementation in the treatment of canine atopic dermatitis." Veterinary Dermatology 2004 ; 15 : 137-145.
34. Smith. "Omega fatty acids: sources, effects, and therapeutic uses in dogs" 2017.http://www.drfsfoster-smith.com/pic/article.cfm?articleid=1063
35. Horrobin. "Essential fatty acid metabolism and its modification in atopic eczema." Am J Clin Nutr 2000 ; 71(suppl) : 367S-72S.
36. Seidel et al. "The influence of long-chain polyunsaturated fatty acids on total lipid/fatty acid composition of a canine mastocytoma cell line." J. Vet. Med. A 2005 ; 52 : 219-224.
37. Gueck et al. "Alterations of mast cell mediator production and release by gamma-linolenic and docosahexaenoic acid." Veterinary Dermatology 2004 ; 15 : 309-314.
38. Phinney et al. "Abnormal polyunsaturated lipid metabolism in the obese Zucker rat, with partial metabolic correction by g-linolenic acid administration". Metabolism 1993 ; 42 : 1127-1140.
39. Schirmer & Phinney. "γ-Linoleate reduces weight regain in formerly obese humans". American society for nutrition 2007 ; 137(6) : 1430-1435.
40. Phinney. "Arachidonic acid maldistribution in obesity". AOCs press Lipids 1996 ; 31 : S271-S274.
41. Phinney. "Exploring the benefits of Gamma-Linoleate in combination with a GLP-1ra as co-therapies for sustained weight loss". Unpublished draft
42. Xin Zhao et al. "GLP-1 Receptor Agonists: Beyond Their Pancreatic Effects". Frontiers in endocrinology 2021 ; 12 : 721155.
43. Huang & Ziboh. "Gamma Linolenic Acid: Recent advances in biotechnology and clinical applications" AOCs 2001 : 259 pages.
44. Gunstone & Dekker. "Structured and modified lipids" CRC press 2001 : 75-117.