

HARNESSING NATURE'S True potential

AHIFLOWER PRACTITIONER EDUCATION



ESSENTIAL CLINICAL INSIGHTS

Clinicians are currently facing several crucial issues when prescribing omega 3 fatty acids, the most important of which is the environmental impact of industrial fishing. This issue has created a situation where other avenues must be explored to reduce the environmental footprint that this essential nutrient is having on both our food chain and our oceans. The Omega market is now a \$5.2 billion dollar industry which is highly fragmented and lacking in innovation. The vegan portion of the market is missing a champion and has a large space between traditional marine/algal oils and plant-based oils. In addition, new research has uncovered the exciting fact that Omega 3 fatty acids have more value than just their EPA and DHA content.



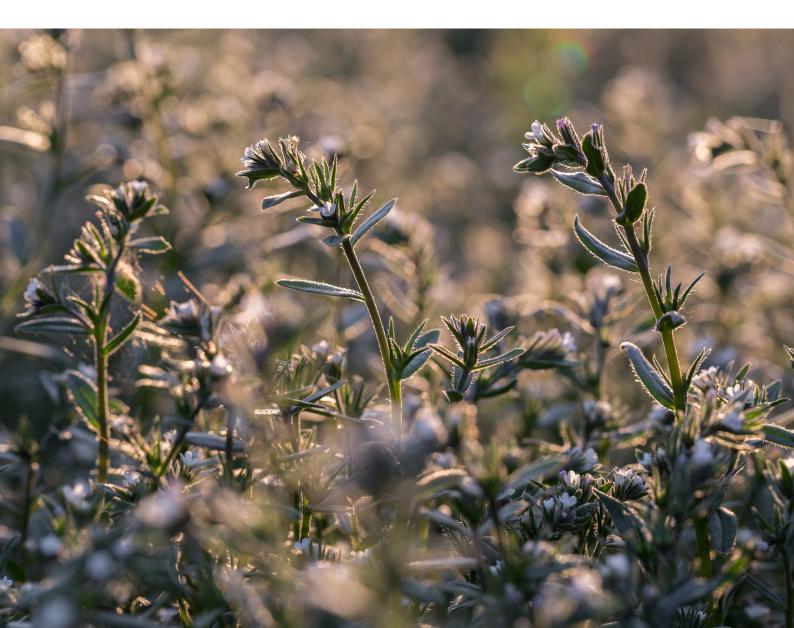


CLINICAL EVALUATION OF OMEGA 3 FATTY ACID REQUIREMENTS

100% of humans need both Omega 3 and 6 but research shows that less than 20% obtain sufficient omegas from their diets. Most consumers take fish oil, but a growing minority consume plant-based omega fatty acids like flax and chia oils. One of the biggest reasons for deciding on a source of omega oil is taste, followed by sustainability concerns with many consumers preferring a plant-based source over marine based. While fish, krill and sea algae form the majority of market share, the growth of land plant-based oil supplements such as flax is steadily growing. Omega 3 and 6 oils must be ingested and are essential for joint health, central nervous system (CNS), immune system and brain development. They also help with inflammation management, hair and skin health and hormonal regulation. The western diet has approximately 20-40 times more omega 6 than omega 3 which is an issue as the biological optimum is between 1:1 and 3:1 (Meyer 2016). Approximately 90% of people eating a western diet are therefore deficient in omega 3 and eating an excess of proinflammatory omega 6 oils (Gabbs et. Al 2015).

Both Omega fatty acids - Linoleic Acid (LA) and Alpha-linolenic (ALA) rely on and compete to use a rate limiting enzyme Delta-6-Desaturase (D-6-D) termed the "Omega gatekeeper". D-6-D is singularly responsible for our ability to convert ALA and LA into the longer chain fatty acids (FA) such as EPA and DHA. Even if your omega 3 intake is adequate, excess LA from Omega 6 oil consumption 'drowns out' much of the omega 3 by preventing conversion to the longer chain beneficial compounds SDA, ETA and EPA, as well as increasing the amount of LA that gets converted to pro-inflammatory Arachidonic Acid (AA) (Welch et al 2010).

EPA and DHA are among the best-known Omega 3 poly-unsaturated fatty acids (PUFAs) and are abundant in marine lipids from wild forage fish species such as anchovies, sardines, and wild krill. Not only is fishing decimating our fish stocks, but fish can contain microplastics (Sharma & Chatterjee 2017), dioxins, PCB's and heavy metals (Turenen et al. 2010, Berntssen et al 2010). According to the European Food Safety Authority, wild marine fish and fish oil have the highest PCB contamination. Another study found that fish oil may increase prostate cancer risk (Brasky 2013).



THE ECOLOGICAL IMPACT OF FISHING

70% of the microplastics in the ocean come from fishing gear, in fact 46% of the infamous Great Pacific Garbage Patch is made up of fishing nets whereas plastic straws make up only 0.03% but are a much larger focus especially in the media. Bycatch is responsible for 40% of the removal of marine wildlife from our seas. The Seaspiracy Movie claims 300,000 dolphins, whales and porpoises are killed globally per year by the fishing industry and that 40% of the global catch is bycatch, roughly equivalent to 30 million tonnes. Some experts predict if things continue as they are, we can expect virtually empty oceans by 2048 (Worm et al 2006).

For each metric tonne of fish biomass harvested only 10kg of commercial EPA/ DHA is produced. 25 million tonnes of oily fish are harvested each year – that is approximately 60 sardines for every human on the planet. This is a finite resource and what we take we deny to animals and birds who rely on them for food. The amount of omega rich oil required globally for human supplements can be grown sustainably on just 480,000 acres each year and provide valuable biodiversity for bees and butterflies (for perspective, US soybean acres in 2018 = 90 million).



EPA AND DHA – ARE THEY AS IMPORTANT AS BELIEVED?

We know we need these crucial fatty acids, but is raising blood levels of EPA and DHA the ultimate end game? One study by Metherel et al in 2019 showed that substantial amounts of EPA can be converted into DHA. Most of the scientific support for EPA and DHA comes from their role in ameliorating various health issues like cardiovascular disease, cognition, anxiety and depression, but they are often prescribed after elevated disease risk factors have already set in. Many of these health issues are caused by chronic inflammation which can be avoided with the correct supplementation and dietary changes before they occur. Both ALA and LA are precursors to lipid mediators that actively participate in the resolution of inflammation and are associated with the prevention of inflammatory diseases (Serhan & Pertassis 2011). In addition, omega 3 PUFAs can modulate gene expression of cytokines and adhesion molecules by interacting with the lipid binding transcription factor - peroxisome proliferator-activated receptor (PPAR) and thus also contribute to the modulation of immune and inflammatory responses (Lefort et al 2016).

Emerging research is showing that some dietary plant lipids can enrich tissues with long chain omega 3 and 6 PUFAs simultaneously – presenting the body with a more balanced, adaptive response to inflammation than fish or algal oils can provide. It has recently been shown that stearidonic acid (SDA) is the richest dietary source for synthesizing eicosatetraenoic acid (ETA). In addition, elevated DGLA formed from botanically derived GLA has been shown to inhibit pro-inflammatory AA formation (Metherel et al 2019).

Only certain plant derived omega 3-6-9 fatty acids bypass the body's rate limiting delta-6-desaturase enzyme, which provides an efficient platform from which the body can address both acute and chronic inflammation via parallel omega 3 and 6 metabolic processes.

Notably certain plant derived oils like AHIFLOWER combine high levels of ALA, SDA and gamma-linolenic acid (GLA) not just EPA and DHA thereby providing a more complete and balanced lipid profile.

AHIFLOWER oil is acknowledged as the richest combined ALA/SDA/GLA source.

SUPPLEMENTING WITH LONG CHAIN OMEGAS

When we supplement with long chain omegas like DHA we actually block the conversion of short chain omegas. Those who do not consume long chain fatty acids (FA) have an up-regulated conversion of short chain to long chain FA by epigenetic control of converting enzymes (Welch et al 2010). Vegans were shown in one large study to have a higher ratio of DHA levels to precursor product than meat eaters following supplementation of PUFAs. Furthermore, a study on supplementing with algal DHA showed it did not improve previously predicted cognition as (Benton et al 2013). It is thought that supplementing with DHA can switch off the conversion from EPA thereby altering natural metabolism, leading to a build-up of EPA which has been associated with higher rates of prostate cancer (Brasky et al 2011). It seems metabolism is intended to move in a singular direction from SCFA omega 3 to the LCFA omega 3 – the body intelligently converting what is needed within its tissues (Metherel 2019).

There is evidence that DHA synthesized from ALA can meet brain DHA requirements as animals fed ALA only diets have brain DHA concentrations similar to DHA fed animals. In humans, brain DHA uptake is estimated to be only 2.4-3.8mg/day (Domenichiello et al 2015) and vegans who do not consume fish and obtain DHA from ALA sources do not have higher neurological disease rates than in omnivores, indicating vegans are converting what they need. Dietary ALA has also been shown to restore brain DHA in rats and non-human primates following DHA depletion in utero. Research indicates that there may be other pathways to DHA synthesis including Alpha-8-desaturase and elongation of DPA catalysed by ELOVLYL 2.

DHA synthesis is also shown to be higher in women – thought to be linked with higher hepatic expression of alpha 5 & 6 desaturase (Domenicheiello et al 2014, Igarashi et al 2007, Makrides et al 1994).



WHAT IS THE CORRECT RATIO?

It is thought that the correct ratio and amount of EPA and DHA is individualized to age, gender and health condition based on conflicting studies into the health impacts of different ratios of EPA/DHA (Abu Mweis et al 2021). As it appears our need fluctuates, why not let the body determine how much omega 3 it needs to covert and metabolize by providing the correct precursors like ALA and SDA? Current recommendations are between 200-3000mg of EPA/DHA, while PET scans show the brain uptakes DHA at just 2.4–3.8mg per day. The rate of DHA uptake is assumed to be replacing DHA that is consumed and even a small amount of DHA synthesis from ALA is sufficient (Harris et al 2009, Barcelo-Coblijn 2009).

OXYLIPINS

Oxylipins derived from PUFAs are the main mediators of their beneficial effects in the body. They are formed via COX, LOX and cytochrome P450 pathways resulting in the formation of prostaglandins, thromboxanes, mono/di/tri hydroxy fatty acids, epoxy fatty acids, lipoxins, eoxins, hepoxilins, resolvins, protectins and maresins. Oxylipins from LA and ALA constitute half of those in tissues and while they have essential roles they can also have detrimental effects. For instance, oxylipins from omega 6 fatty acids have greater activity and more inflammatory, vasoconstrictory and proliferative effects (Gabbs et al 2015).

While acute inflammation evolved to be protective and permit repair of affected tissues, it was thought to be a passive process. However a series of elegant studies in the Harvard University laboratory of Charles Serhan showed that resolution is actively turned on. This led to a paradigm shift towards the understanding and identification of a new family of specialized pro-resolving mediators or SPM's – resolvins, protectins and meresins which all derive from EPA, DHA and DPA and following their consumption these longer chain PUFA's are preferentially incorporated into cellular membrane phospholipids where they participate in the proper functioning of membrane lipid bilayers and are precursors of these SPM's.

AHIFLOWER, when consumed supplies a more diverse array of anti-inflammatory oxylipin substrates. Both ETA and DGLA derived from vascular plant sources can serve as substrates for potential formation of SPM's, which is significant as historically conventional sources of EPA, DHA and DPA tend to derive from only fish, krill or algal sources. Plant based dietary sources of immediate ETA and DGLA precursors have far greater sustainability, scalability, and versatility in a range of foods and beverages.

AHIFLOWER										
Omega-3 Fatty Acids										
Alpha-linolenic Acid	ALA	42-48%								
Stearidonic Acid	SDA	17-21%								
Omega-6 Fatty Acids										
Linoleic Acid	LA	9-15%								
Gamma-linolenic Acid	GLA	4.5-8%								
Omega-9 Fatty Acid										
Oleic Acid	OA	6-14%								

ALA, SDA and ETA (all omega 3 precursors to EPA) and DGLA (omega 6) produce similar and potent anti-inflammatory metabolites that 'resolve' inflammation. A study in 2017 showed circulating ALA, SDA and ETA levels are predictors of fluid intelligence, total grey matter and frontal neocortex brain integrity in healthy seniors rather than EPA or DHA (Zamroziewicz et al 2018).



STEARIDONIC ACID (SDA) IS COMPARABLE TO DHA

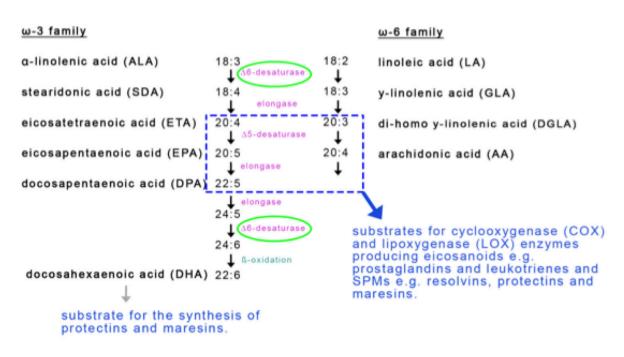
This 18-carbon omega 3 fatty acid is the immediate product following conversion of ALA catalysed by delta-6-desaturase. As this enzyme is rate limited it is not very efficient in humans which is the reason why consumption of ALA often results in little tissue accumulation of longer chain omega 3 PUFAs like ETA, EPA, DPA and DHA. Another anti-inflammatory prostaglandin PGE2 is also limited, and studies have shown that PGE2 inhibition, along with excess AA formation can precede chronic inflammation. Because SDA bypasses this rate limited step, the consumption of oils rich in SDA can result in an enrichment of tissues with longer chain PUFA like EPA and DPA. Preliminary research from University of Toronto indicates that Ahiflower readily converts to DHA in mice (Lefort et al 2016).

SDA inhibits nitric oxide produced from inducible nitric oxide synthase (iNOS) comparably with DHA. Researchers also found SDA and DHA similarly inhibited LPS-stimulated NFkB expression in macrophages (where NFkB is well -researched as a key immune and proinflammatory cell-signalling mediator) (Sung et al 2017). Further, SDA and DHA comparably inhibited mitogen-activated protein kinase (MAPK) phosphorylation, which is posited to be the underlying mechanism of SDA's anti-inflammatory effects. The researchers concluded that SDA is "as effective as DHA against inflammatory response in LPS-stimulated macrophages". Another human dietary study showed AHIFLOWER oil consumption increased IL-10 -(Interlueukin 10 – an anti-inflammatory cytokine) by 45% compared to baseline. It is noteworthy that IL-10 can predict the severity of several inflammatory diseases with low circulating IL-10 suggesting a greater disease severity. People with low levels of circulating IL-10 have also been shown to have higher severity of immune disease, for example athletes who engage in high intensity or extreme cardio fitness workouts are known to have higher susceptibility to upper respiratory tract infections, due to reduced auto-immune defence mechanisms during recovery.

ETA – EICOSATETRAENOIC ACID

A novel anti-inflammatory metabolite metabolized from SDA by the enzyme elongase, ETA is catalysed by a species of lipoxygenase (5-LO) which produce bioactive lipid mediators of inflammation including leukotrienes and prostaglandins. Authors of a 2018 study found two 5-LO dependant metabolites of ETA; one (Delta-17-8,15-diHETE) was novel and showed pronounced inhibition of human polymorphonuclear (PMN) cell leukotriene B4 (LTB4). They commented that such natural leukotriene antagonists "may be released at inflammatory sites when the diet is supplemented with SDA and could be of benefit in individuals with inflammatory diseases" (Gagnon et al 2018). They also observed that other ETA metabolites could possess analogous pro-resolving activity like SPM's derived from EPA, DHA and DPA. This is significant as AHIFLOWER is the richest available natural source of ETA's immediate precursor SDA – thus including AHIFLOWER in a cohort of omega 3 oils that warrant further investigation as a potential substrate for enhanced formation of SPM's.

Figure 1. Omega-3 and Omega-6 Metabolic Pathways.



AHIFLOWER has ALA, SDA, LA and GLA. It is the single richest available dietary source of combined SDA and GLA which can provide the body with an optimally rich substrate for channelling lipid metabolites including ETA and DGLA, as and where needed to various tissues in the body. This improves cellular support in a healthy inflammatory response due to dietary, lifestyle, immune and environmental factors. While AHIFLOWER is not a direct source of EPA or DHA it is the most versatile omega 3-6-9 dietary oil available. It allows the body to utilise a wider range of lipid metabolites dynamically to which every organ system - skin, brain, immune, eyes, CVS, or MSK that requires them. A truly on-demand oil, it is uniquely supportive of a more proactive approach to health and wellness in omega nutrition.

AHIFLOWER HUMAN STUDIES

Lefort and her colleagues in their 2017 placebo-controlled trial showed a dose dependant enrichment of plasma and circulating mononuclear cells (MNC) with ETA, EPA and DPA following consumption of AHIFLOWER oil. A dose as low as 3g per day of AHIFLOWER resulted in significant plasma and MNC enrichment with EPA after only 4 weeks of dietary supplementation. AHIFLOWER oil consumption was also associated with an increased production of IL-10, harnessing the body's natural anti-inflammatory mechanism for achieving greater immune and exercise fitness benefits.

This was the first investigation of an immune response following consumption of SDA containing oil and indicates oils such as AHIFLOWER may share immune modulating properties typically associated with marine oils. Further studies should be conducted to determine the potential impact of such dietary oils on the biosynthesis of pro-resolving mediators of inflammation.

In human clinical trials, AHIFLOWER also demonstrates up to 400% more effective conversion to EPA than flaxseed oil (Lefort et al. 2016). In addition, AHIFLOWER supplementation also demonstrates an up to 16% increase in DGLA – the anti-inflammatory omega 6 compound associated with longevity.



GLA – GAMMA LINOLENIC ACID

Often extracted from Evening Primrose, blackcurrant and borage seed oils, GLA has a very strong and loyal customer base specially to support women's health. It also skips the delta-6-desaturase and readily converts to DGLA. DGLA is the only omega 6 fatty acid positively associated with increased longevity and is a highly potent anti-inflammatory omega 6 not found in any marine oils. In studies with AHIFLOWER oil, DGLA increased 16% following consumption, whereas in studies with flax oil, DGLA decreased 14% following consumption (Sergeant et al 2016). Botanical sources of GLA combined with ALA and SDA "markedly increase circulating levels of DGLA and have little impact on circulating AA levels.. suggest(ing) that botanical omega 3 PUFAs not only enhance conversion of dietary GLA to DGLA but also inhibit further conversion of that DGLA to AA" (Sergeant et al 2016). GLA levels have been strongly linked to reductions in cardiovascular disease and increase in longevity. The higher the circulating GLA in red blood cells, the lower the risk for all-cause and cardiovascular mortality (Von Schacky 2014).

Species	Omega-3 (g/100 g oil)			Omega-6 (g/100 g oil)		Ratio	Total Omega	Ad- justed total	Basis	Ahiflower % higher in combo	Notes	
	ALA	SDA	Total	LA	GLA	Total	n3:n6	3+6	omega 3+6*	20313	omega 3+6	
Ahiflower [8]	39,8	18,2	58,0	11,3	5,6	16,9	3,4	74,9	111,3	w/w typical		Richest, most effective combined omega 3-6 source from a non-GM plant
Flaxseed [12]	49,9		49,9	13,3		13,3	3,7	63,2	63,2	w/w typical	76,0%	no GLA; no SDA = less efficient conversion to EPA
Camelina [5]	38,1		38,1	16,9		16,9	2,3	55	55	w/w typical	102,4%	no GLA; no SDA = less efficient conversion to EPA
Hemp [14]	19,6	1,8	21,4	49,8	3,6	53,4	0,4	74,8	78,4	w/w typical	42,0%	Very little SDA, ~40% lower GLA = less efficient conversion to EPA
Chia [6][11]	53,9		53,9	17,6		17,6	3,1	71,5	71,5	w/w typical	55,6%	no GLA; no SDA = less efficient conversion to EPA
Sacha Inchi [4]	42,5		42,5	31,8		31,8	1,3	74,3	74,3	w/w typical	49,7%	no GLA; no SDA = less efficient conversion to EPA
Perilla [3]	57		57	15,1		15,1	3,8	72,1	72,1	w/w max	54,4%	no GLA; no SDA = less efficient conversion to EPA
Echium [10]	27,3	11,4	38,7	13,7	10,2	23,9	1,6	62,6	85,4	w/w typical	30,3%	Ahiflower has >60% more SDA than this previously best known source
Blackcurrant seed [9]	11,7	2,9	14,6	40,2	15	55,2	0,3	69,8	75,6	w/w typical	47,2%	Ahiflower has >6x more SDA and significantly higher total omega 3+6
Evening primrose [9]			0	64,3	8,0	72,3	0,0	72,3	72,3	w/w typical	53,9%	Only a n-6 source, no n-3 content
Borage [9]	0,2		0,2	32,9	20,5	53,4	0,0	53,6	53,6	w/w typical	107,6%	Primarily n-6 source, miniscule n-3 content
Sea Buckthorn seed[15]	20		20	23,4		23,4	0,9	43,4	43,4	w/w typical	156,5%	no GLA; no SDA = less efficient conversion to EPA

* 'Adjusted total omega 3+6' – Content of SDA is multiplied by 3 to allow for the increased conversion to EPA relative to ALA per Krul et al.

THE BODY'S INNATE INTELLIGENCE

Fixating on marine or algal EPA/DHA supplementation has obscured the fact that the human body co-evolved over millions of years in various environments where plant-based omega rich foods sources were far more predominant and balanced in terms in of their omega 3:6 ratio.

AHIFLOWER helps to restore the balance in the many cellular membrane systems of the body by providing an optimally balanced full spectrum of omega 3-6-9 precursor PUFAs. Not only do these substrates control inflammation management but a host of other critical metabolic functions pertaining to cognition, digestion, RNA transcription and repair, wound healing and mental health.

"The stakes are high. The ocean can't provide even the most conservative daily dose of EPA+DHA for each human being." GOED, 2022

"With lower intake of marine-derived fish and environmental chemical pollutants, SDA-rich oil may safely and expediently increase the concentration of serum EPA or other long-chain n-3 PUFAs to play their beneficial roles." NHANES 2021

"The unique omega-3 PUFA composition (high SDA) of Ahiflower oil may provide DHA to blood and tissues at a rate similar to DHA and faster than flaxseed oil despite no differences in DHA levels." Professor Adam Metherel

AHIFLOWER IS SUSTAINABLE

Each acre of regeneratively cultivated AHIFLOWER crop produces the equivalent amount of omega-3 rich oil as from 450,000 anchovies. AHIFLOWER requires significantly less fertilizer or chemical inputs than most other farmed commodity crops. Natures Crops International, Ahiflower's exclusive producer, are a B-Corp certified company, verifying the highest possible standards of accountability and earth-friendly supply chain elements.

SUMMARY

AHIFLOWER is the highest in ALA/SDA of any commercially available plant and provides a 4:1 ratio of omega 3 to omega 6. It is a complete omega unlike fish/algal oils and compares superiorly to flax, chia or sacha inchi which contain no SDA or GLA. AHIFLOWER provides 10 times more SDA and twice as much omega 3 as hemp. Marine oils only contain EPA/DHA not ALA, SDA, GLA or omega 6 & 9. AHIFLOWER boosts live probiotic survival up to 2x into the small intestine. It supplies the most diverse array of anti-inflammatory oxylipin precursors from complementary omega 3-6 pathways and contains recognized anti-inflammatory substrates including ETA, EPA, DPA, DGLA and biosynthesized DHA.

Consumers want and need plant-based omega solutions for optimal wellness. No other omega fatty acid source including marine sources can supply such a complete, balanced, and clean tasting source of functional omegas.

AHIFLOWER is the cleanest, greenest, most regenerative, and traceable supply chain of any omega rich oil!

DELIVERY AND FORMULATIONS

Minimum intake is 2-2.5g per day based on WHO guidelines for EPA of 200-250mg/day. For those who are omega 3 deficient, you can increase to 4-5g per day. It has demonstrated safety at 10g daily in adults. Ahiflower contains 42-48% ALA, 17-21% SDA, LA of 9-15% and GLA of 5-8%.

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