
# Understanding Omega-3 SDA Metabolism, IL-10 Upregulation & Modulating Inflammatory Phenotypes

Community Hub Presentation

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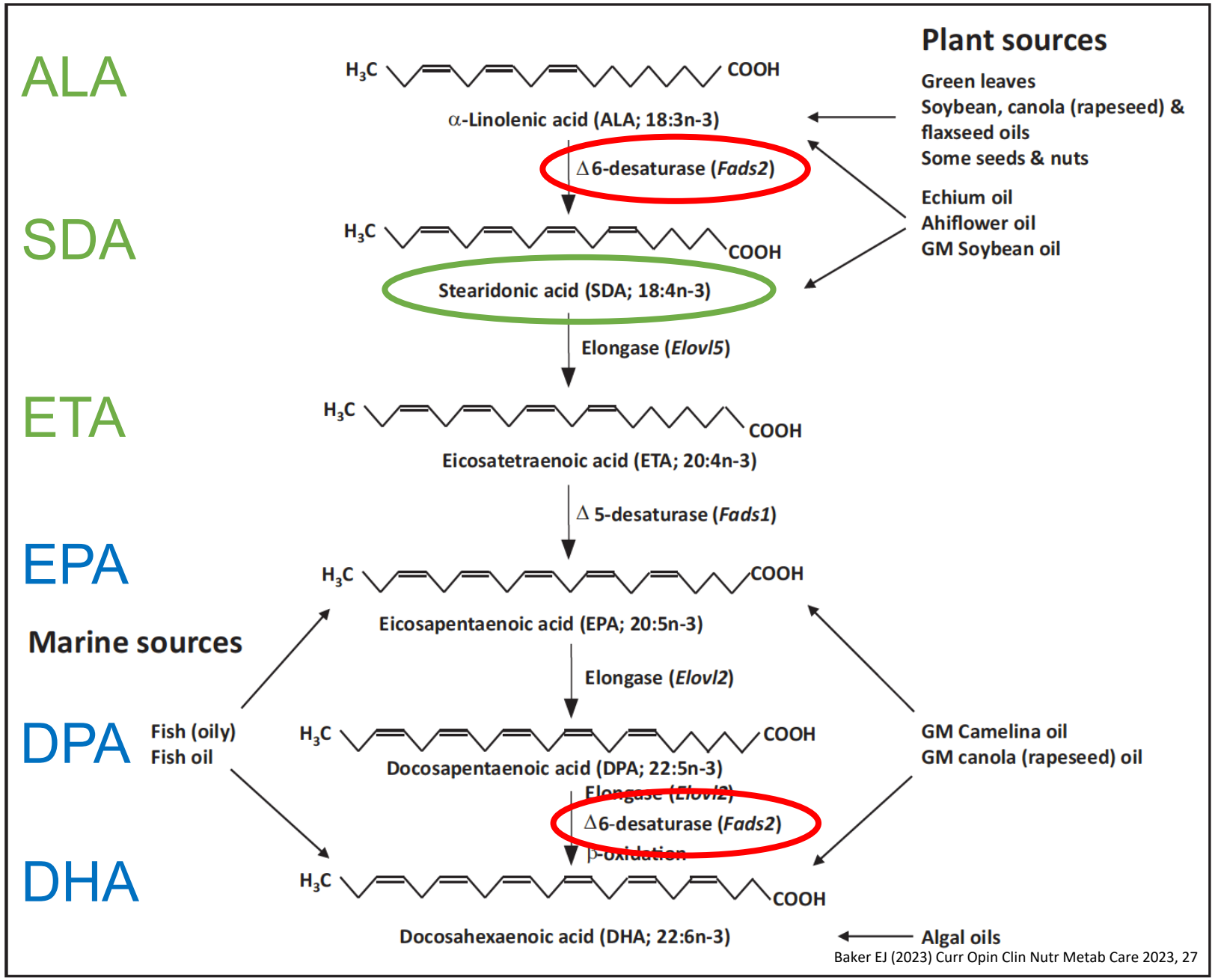
# Omega-3 PUFA Metabolism

ALA converts less efficiently to EPA/DHA due to Δ6D rate-limiting enzyme & high background omega-6 LA in the Western diet.

SDA is ALA's next omega-3 metabolite and by-passes this rate-limiting step. SDA converts to EPA ~5x more efficiently.



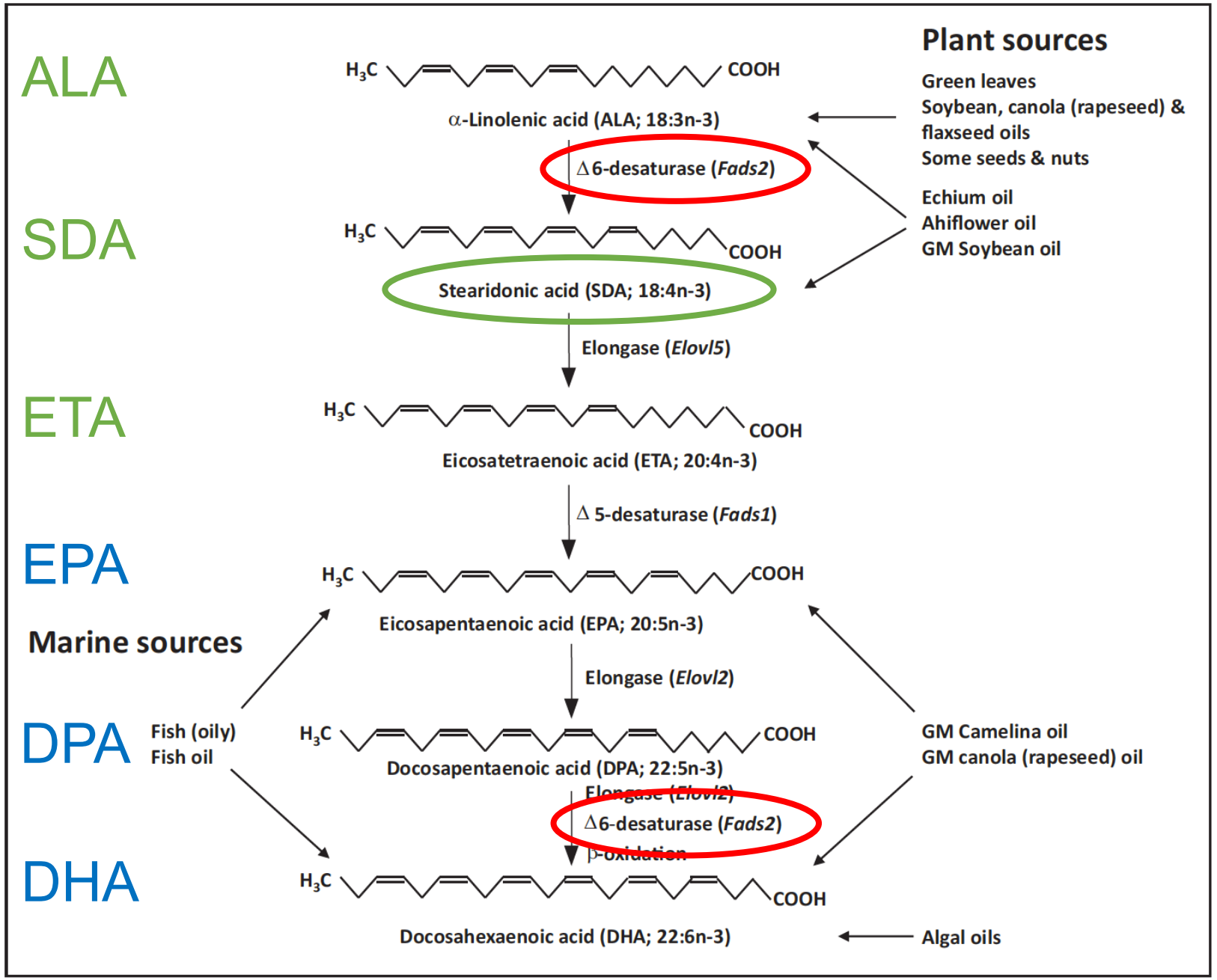

Baker EJ (2023) Curr Opin Clin Nutr Metab Care 2023, 27

# Omega-3 Index: % (EPA + DHA) in red blood cells

In humans and mammals, circulating DHA levels dominate EPA levels by 3-4x

O3I more sensitive to flux in circulating DHA, which does not 'retroconvert' to EPA

ALA —> EPA metabolic pathway under-represented



# Stearidonic acid (SDA) occurs in some readily available dietary omega-3 oils led by Ahiflower

The body's first metabolite of omega-3 ALA — found in:

- Ahiflower (18-21%) — highest available non-GM source
- *Calanus* zooplankton (7-8%)
- Black Currant (3%)
- Hemp (2%)
- Krill (2%)

Ahiflower *(Buglossoides arvensis)*
under cultivation in the UK

# Common omega-3 rich dietary sources

| FATTY ACIDS BY OIL WITH COMPARATIVE METABOLIC EFFICIENCY SCORING INDEX | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Score per Double Bonds* | | 6 | 5 | 4 | 3 | 3 | 2 | 1 | |
| Oils | Total % PUFA's | DHA | EPA(+ DPA) | SDA | ALA | GLA | LA | OA | Total Score |
| Ahiflower (*Buglossoides arvensis*) | 83 | 0 | 0 | 20 | 45 | 6 | 12 | 10 | **267** |
| Algal DHA (*Schizochytrium* spp) | 41 | 40 | 1 | 0 | 0 | 0 | 0 | 0 | **245** |
| Flax / Linseed | 71 | 0 | 0 | 0 | 57 | 0 | 14 | 16 | **215** |
| Chia | 72 | 0 | 0 | 0 | 54 | 0 | 18 | 8 | **206** |
| Hemp | 75 | 0 | 0 | 2 | 20 | 3 | 50 | 13 | **190** |
| Echium | 63 | 0 | 0 | 12 | 27 | 10 | 14 | 0 | **187** |
| Nutriterra GMO Canola* | 36.5 | 9 | 1.5 | 0 | 19 | 0 | 7 | 45 | **179** |
| Krill (phospholipid/TG form) | 33 | 11 | 19 | 2 | 1 | 0 | 0 | 0 | **172** |
| Soya | 68 | 0 | 0 | 0 | 13 | 0 | 55 | 18 | **167** |
| Fish | 30 | 12 | 18 | 0 | 0 | 0 | 0 | 0 | **162** |
| Camelina | 55 | 0 | 0 | 0 | 38 | 0 | 17 | 15 | **163** |
| Canola | 30 | 0 | 0 | 0 | 10 | 0 | 20 | 60 | **130** |
| Calanus (waxy ester)* | 19 | 4 | 5.8 | 7 | 1.4 | 0 | 0.7 | 1.6 | **88** |

- Higher carbon double bond occurrence equates with degree of polyunsaturation & efficiency of uptake
- Higher total omega-3 PUFA & lower LA (C18:2n-6) intakes assist in hepatic processing efficiency
- Triglyceride (TG) form readily metabolized & predominant PUFA form found in human and mammal diets.



**EPA+DPA. Fatty acid composition literature citations available upon request*

# Marine EPA/DHA oils are recognized as unsustainable[1, 2] even by the omega-3 trade association (GOED)

- Closures of the Peruvian anchovy fishery caused real disruption in the marine omega-3 industry
- Signficant FO price increases & supply chain woes
- Highlights vulnerability of wild-harvested marine supply chain to climate change & supply/demand factors


Alternative sustainable sources must scale to meet practitioner needs, consumer preference & recommended intakes for omega-3 LC-PUFA



[1]Baker EJ, Curr Opin Clin Nutr Metab Care 2023, 27. [2]http://tinyurl.com/wsyb7863 (15Dec2023 GOED interview)


# Recent SDA clinical support

Multiple published human clinical trials, plus supporting animal science shows:

- Demonstrated anti-neuroinflammatory synergist + improved brain function
- Most efficient non-GM plant-based EPA accrual, raising Omega-3 Index in 28 days
- Increased IL-10 production supporting immune & gut microbiome balance
- Aligns with naturally evolved omega-3 metabolic needs in cell membranes
  - ✓ Forms anti-inflammatory ETA, EPA, DPA, & DHA dynamically, as & when needed
- Matches preformed DHA for efficient DHA biosynthesis in the brain
- Exerts an overall anti-inflammatory phenotype via ↑ IL-10 & ↓ O6:O3 (AA:EPA)
- Comparable and/or superior anti-inflammatory activity vs FO or EPA/DHA

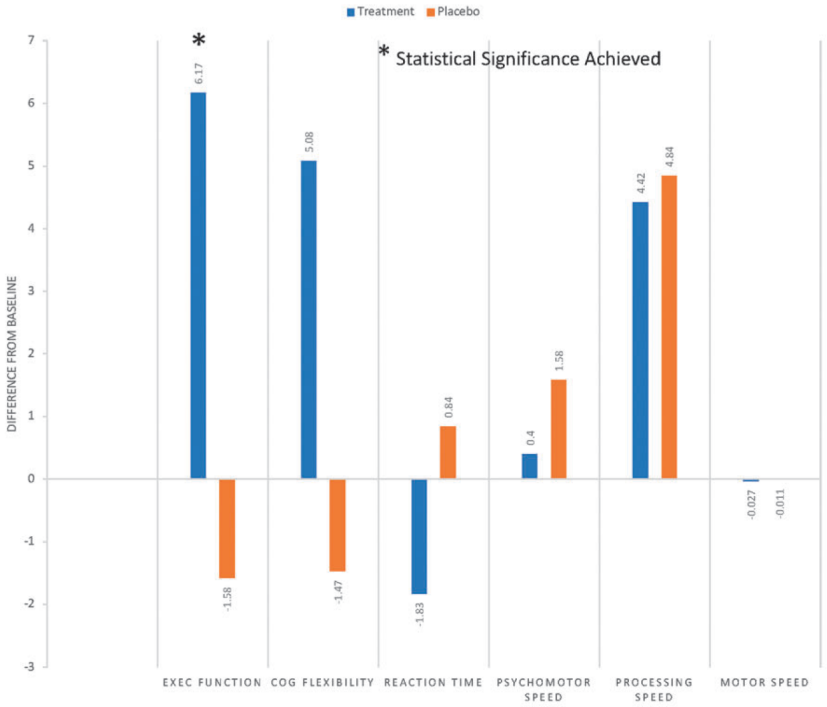
**Emerging science in SDA-rich omega oil demonstrates plant-based solutions can balance and deliver the body's needs for essential fatty acids. But instead of supplying EPA/DHA in arbitrary amounts, SDA lets the body determine how much & when they are needed — naturally & adaptively.**

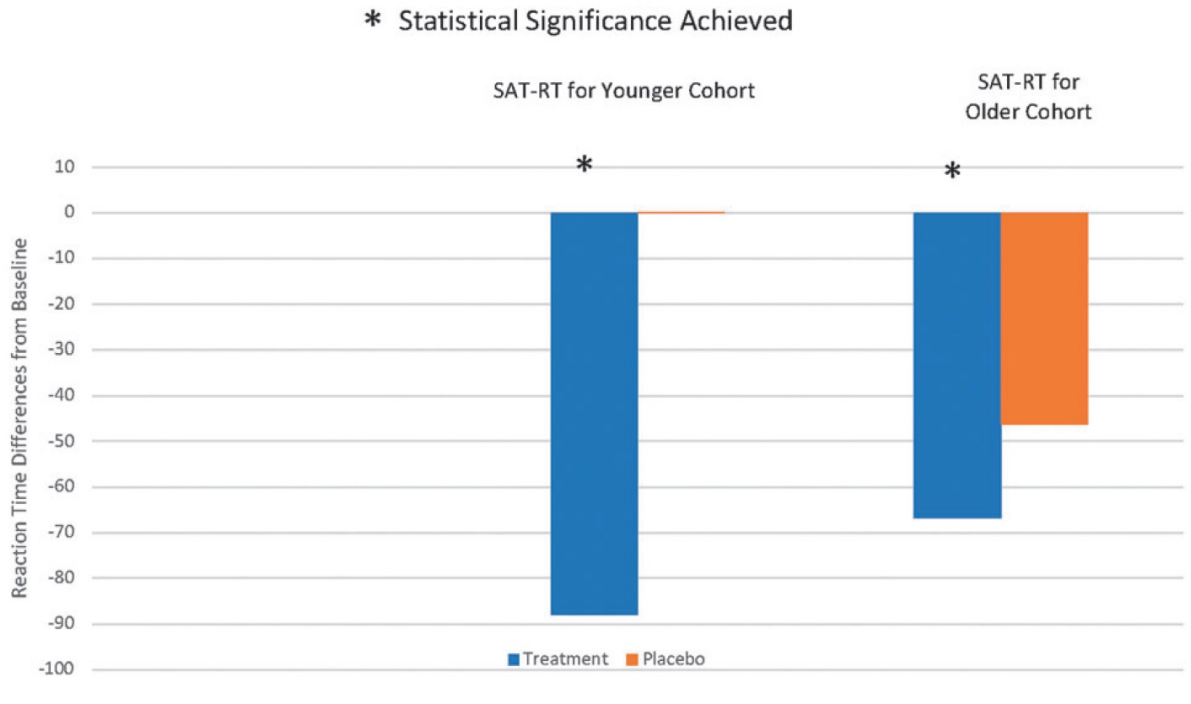
Integrative Healthcare SYMPOSIUM

**A Randomized, Placebo-Controlled Clinical Trial of a Novel Dietary Supplement (Braini) on Standardized CNS Vital Signs Cognitive Performance Parameters in Adults**

Amy Joy Lanou, PhD,[1] Aubrey C. Mast, MPH,[1] Benjamin D. Hill, PhD,[2] Sung-Su Kim, PhD,[3] and Patrick Hanaway, MD[4]

# Neuroprotection & improved brain function




R-DBPC trial in young adults (n=31) and healthy seniors (n=29) after 28 days at 250 mg/day Ahiflower oil in proprietary blend. Lanou (2022) JICM DOI: 10.1089/jicm.2022.0543

Ahiflower oil shows statistically significant anti-neuroinflammatory synergist effects in microglial RAW264.7 cells[1]

Circulating ALA+SDA status drives highest fluid intelligence & frontal neocortex brain mass in healthy seniors, not circulating EPA/DHA status.[2]

[1]US Patent #11,707,497 B2, p. 101. [2]Zamroziewicz M et al. (2017) *Nutritional Neuroscience* DOI: 10.1080/1028415X.2017.1324357

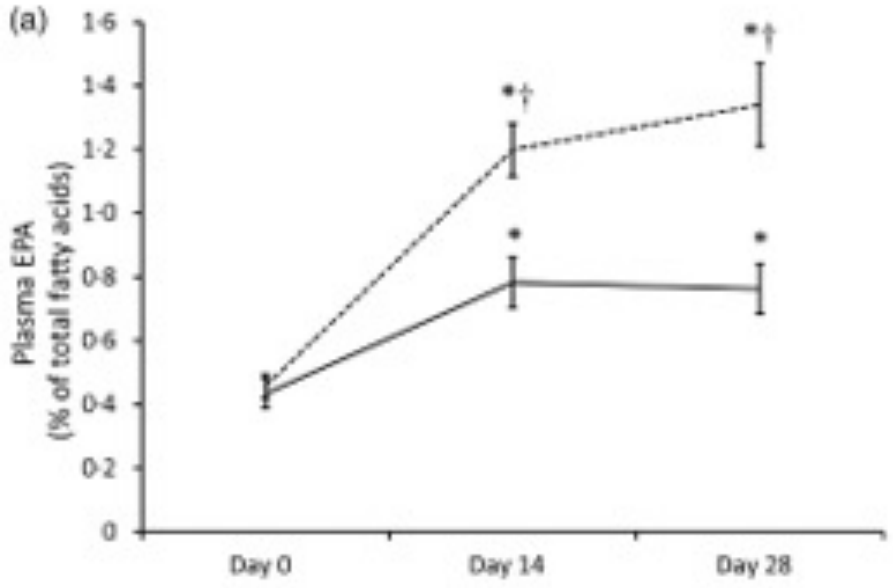
# Superior EPA Conversion vs Flax in Humans

Ahiflower oil accrues circulating **EPA** up to 4X more efficiently than flaxseed oil — plus GLA, DGLA

EPA plays a major role in:

- Cardiovascular health
- Brain DHA formation
- Immune function & anti-inflammatory cell signaling

Lefort (2016) *J Nutr Sci* 5:e2;1-12



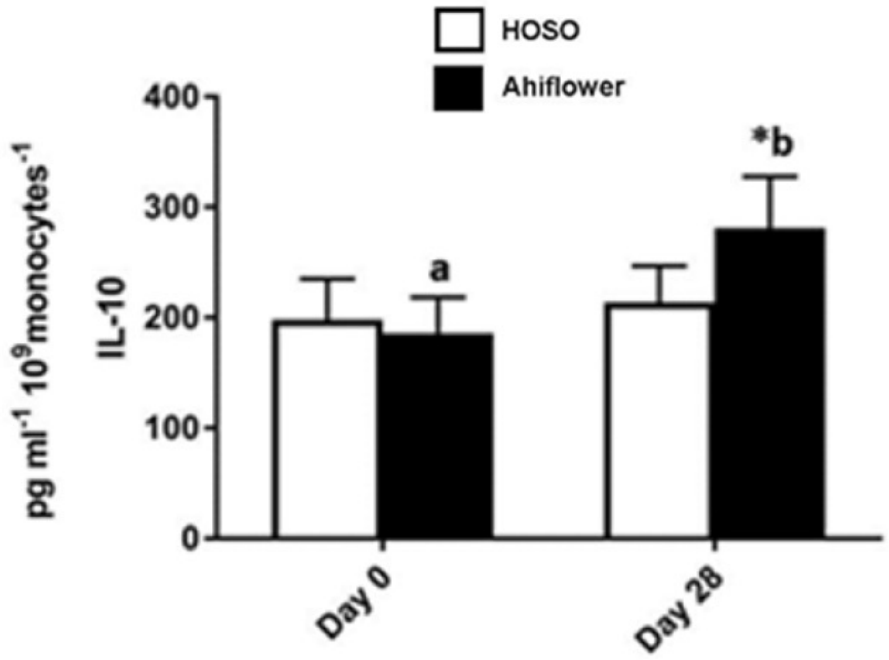

Flaxseeds & flaxseed oil — darker than Ahiflower oil

**Actions**

Boosts circulating EPA up to 4x better than flaxseed oil in humans & raises O3 Index in 28 days.
Helps exert an anti-inflammatory phenotype via lowered AA:EPA ratio

# ↑ LC-PUFA & IL-10 — ↓ n-6/n-3 ratio (AA:EPA)

- 2nd human trial confirmed **significant EPA** (c20:5) increase in white blood cells and plasma after only 28 days with **excellent linear dose response**.
- Significant increases in **omega-3 ETA** (c20:4) and **DPA** (c22:5) also found at all dose levels — both have recognized anti-inflammatory oxylipins
- Significant **increase (+40%) IL-10** in immune monocyte cells in whole blood after only 28 days.
- **Reduced n-6/n-3 ratio** in plasma (-66%), RBCs (-43%) and mononuclear cells (-57%) (via AA:EPA, C20 metabolites)



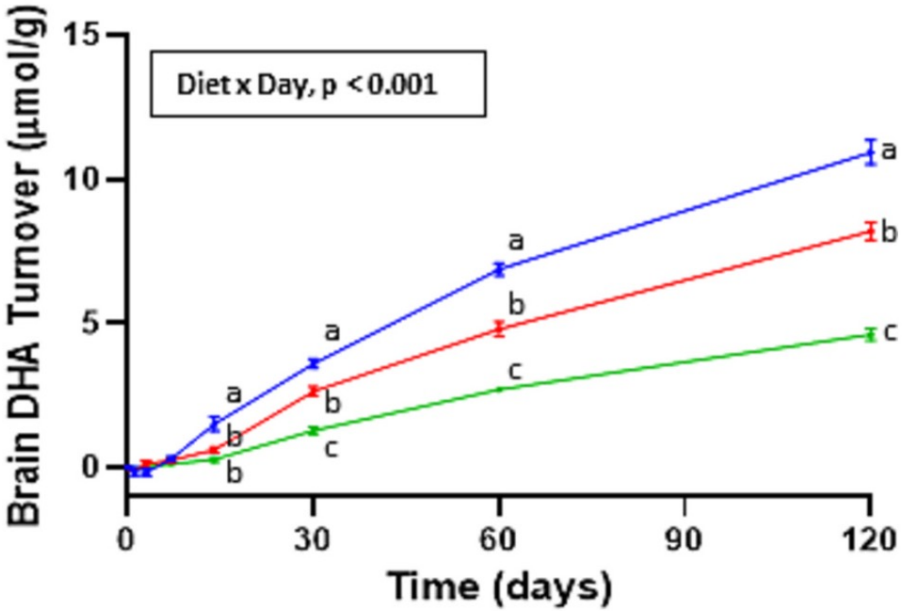

Lefort (2017) *Nutrients* 9:261

**Action**

**Supports a healthy inflammatory & immune response** fostered by boosting IL-10

# New C-isotope ratio MS method shows SDA-rich oil forms DHA in brain & liver tissues with comparable efficiency as pure marine DHA.

UNIVERSITY OF TORONTO




**Brain (Mice)** — All values statistically significant

DHA — Ahiflower — Flaxseed

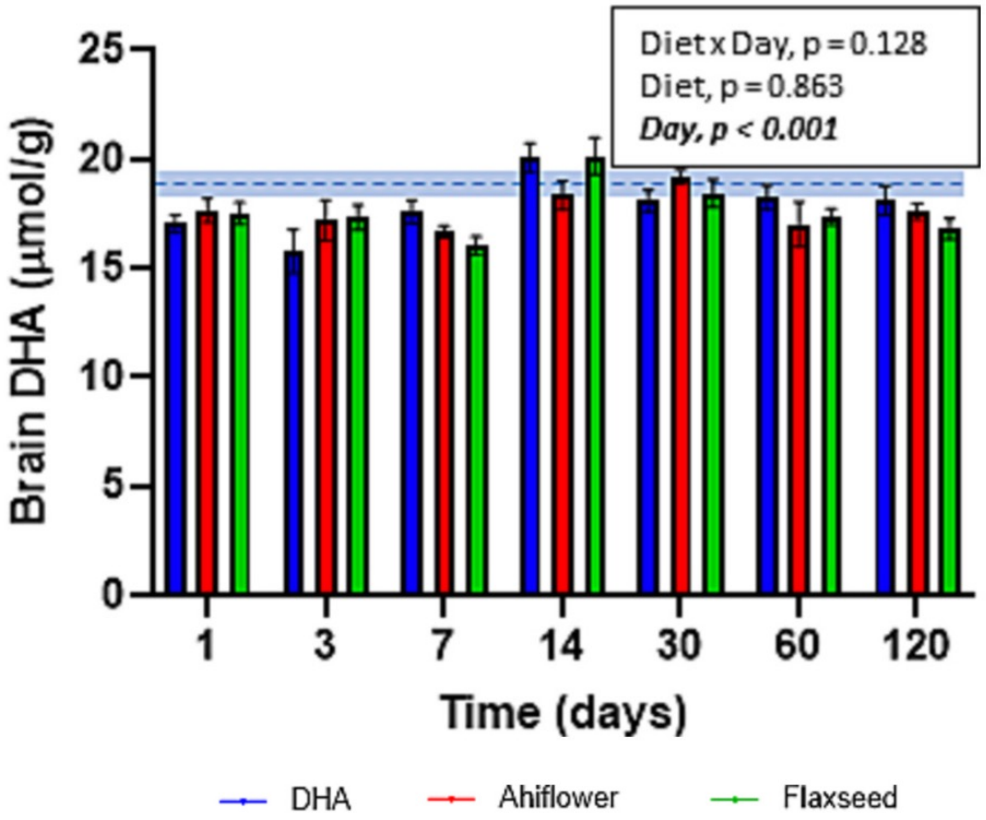
"Our findings indicate that Ahiflower oil may be a useful plant-based dietary source for maintaining tissue DHA turnover comparably to dietary DHA."

— Profs Adam Metherel & Richard Bazinet, Principal Investigators



Metherel AH, BBA - Molecular and Cell Biology of Lipids 1869 (2024) 159422

# ALA or ALA+SDA maintain comparable brain DHA levels despite no DHA intake over 120 days at equimolar PUFA intakes.




Indicates the **mammal brain does not need any preformed DHA** in the diet to maintain adequate brain DHA levels.



Metherel AH, BBA - Molecular and Cell Biology of Lipids 1869 (2024) 159422

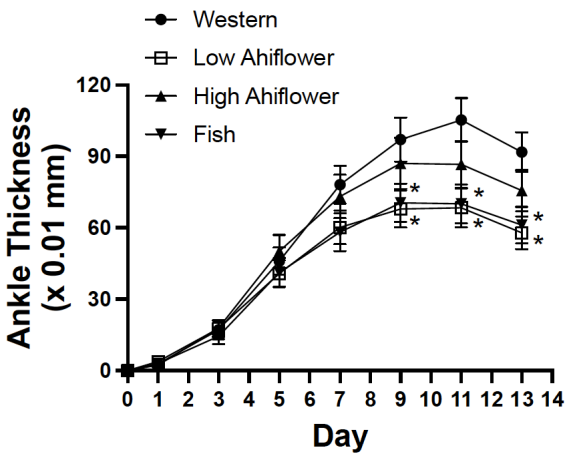

# The findings that SDA oil enriches EPA and forms DHA in key tissues as needed points to limitations of O3I as an accurate gauge of omega-3 tissue status

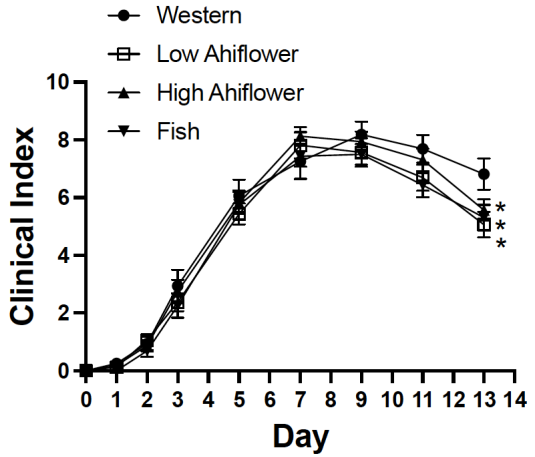
- In humans, Ahiflower oil raised EPA levels 0.9% in plasma & 0.3% in RBC's after only 28 days in humans, but not circulating DHA levels.
- Dr Metherel has found whole body (including liver, adipose) DHA accrual rates from dietary ALA are up to 30-40x higher than in circulating cells.
- Liver and adipose DHA stores — which the body deploys to other tissues as & when needed — **are not measured in the omega-3 index**.
- Metabolically, circulating DHA levels go up because the body isn't using them.
- Not so for all DHA precursors: SDA, ETA, EPA, DPA which SDA-rich oils raise significantly in humans.

"Ahiflower oil feeding can supply DHA to tissues at similar rates compared to DHA feeding alone, and once again reveals a limitation of considering DHA levels only as a marker of DHA status in tissue." — Profs Richard Bazinet & Adam Metherel, University of Toronto

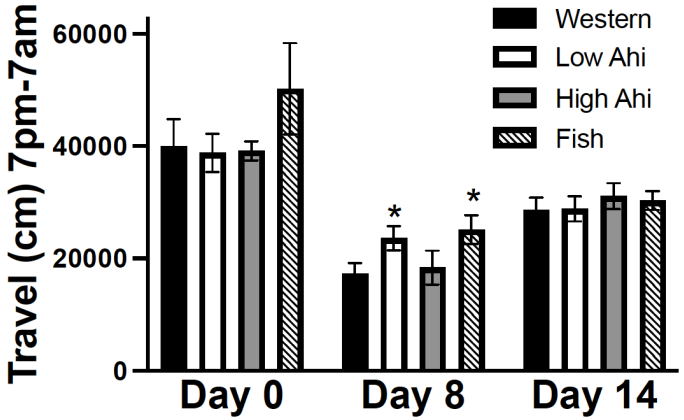
# Buglossoides oil has comparable anti-inflammatory activity to fish oil in a pre-rheumatoid arthritis mouse model

## Diets Have Impact on Paw Inflammation




## Locomotor Activity Affected by Diets and Time After Induction of Arthritis




| ANOVA Table | F (DFn, DFd) | P value |
|---|---|---|
| Interaction | F (6, 70) = 1.336 | P=0.25 |
| Day | F (2, 70) = 48.70 | P<0.0001 |
| Diet | F (3, 70) = 2.728 | P=0.05 |

Low dietary intakes = 3.3% of energy; High = 10% of energy. Arthritis induced on Day 0 after 3 weeks of dietary equilibration.

"Changes in ankle thickness were smaller in the low dose B. arvensis and FO groups compared to controls ($p<0.05$)."

"On a background diet based on human equivalent western diets, low dose B. arvensis oil or dietary fish oil equivalent to human consumption of 7g/day impacted on tissue fatty acid profiles, alleviated joint inflammation and increased activity levels in this animal model."



Doucet MR & Laevski AM, results In publication, presented at ISSFAL 2023 (3-6 July, Nantes, FRANCE)

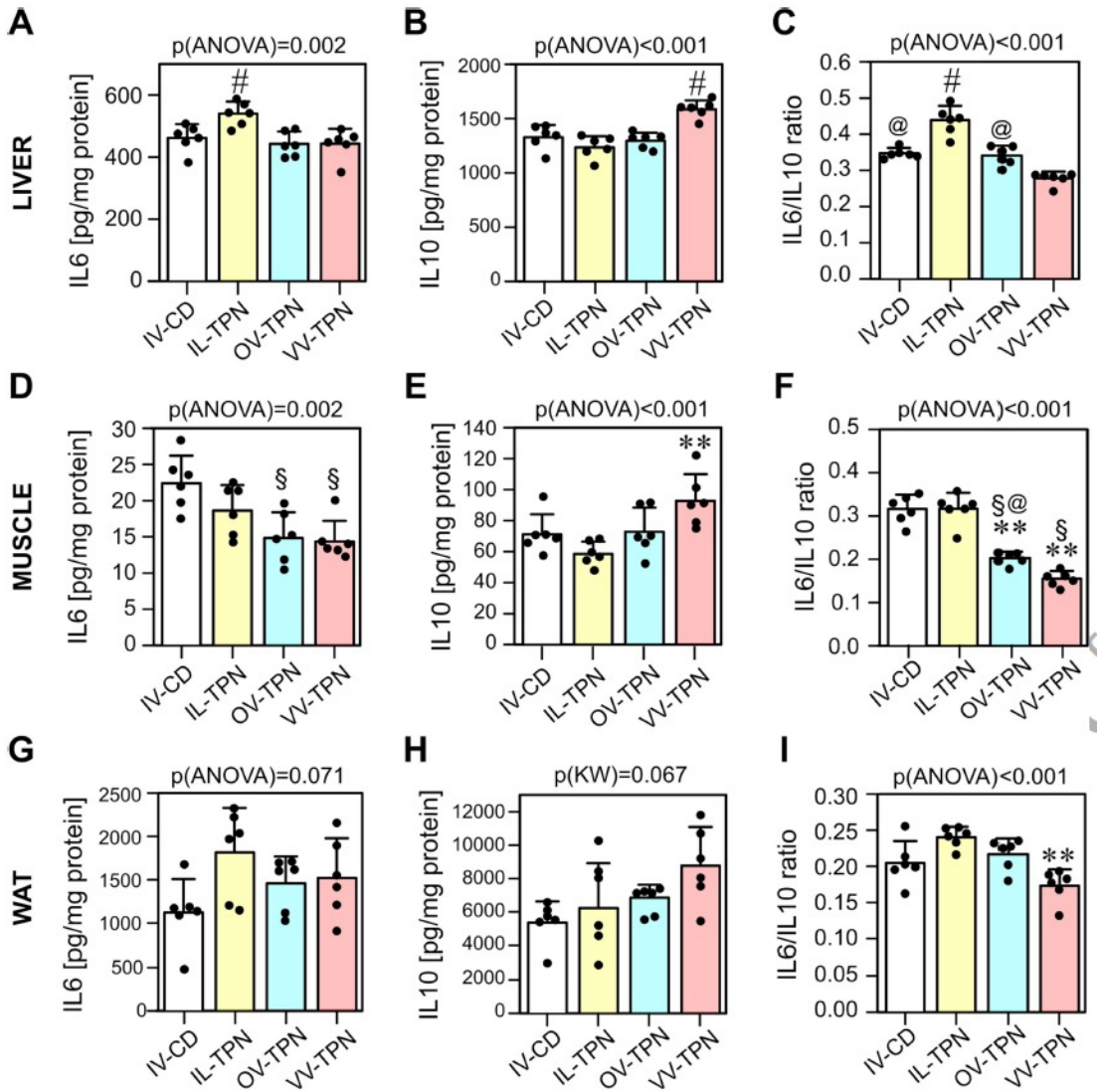
# SDA Raises IL-10 Systemically in TPN in Mice

Comparing Vegaven (VV) TPN emulsion to Intralipid (IL) and Omegaven (OV) in plasma and key insulin sensitive tissues:

- IL-10 significantly up
- IL-10:IL-6 ratio significantly up
- Effected an anti-inflammatory, insulin sensitizing, and immune-enhancing response while promoting host defense against bowel-invasive Akkermansia.

> "Remarkably, the effects of the Ahiflower oil containing lipid emulsion were **greater than those of the fish oil** emulsion. Liver and muscle interleukin 10 and the ratio of interleukin 10 to interleukin 6 were higher with Ahiflower oil than with either soybean oil or fish oil."

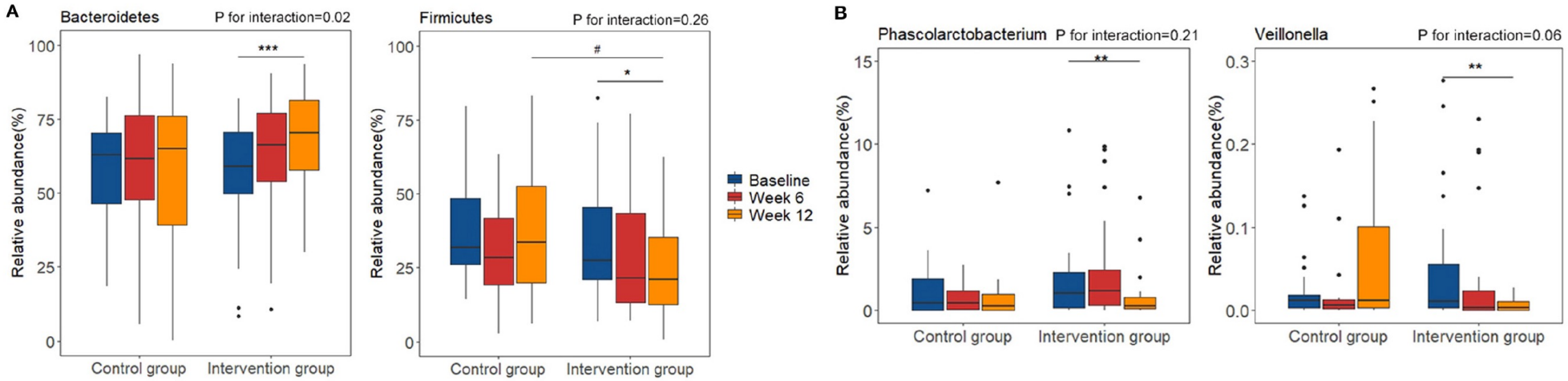
— Ella Baker, PhD (Curr Opin Clin Nutr Metab Care 2023, 27)




Lucchinetti (2022) *Am J Clin Nutr* 0:1–15

# Dietary ALA/SDA/GLA lowered cholesterol & balanced microbiome

## A plant oil blend with similar FA levels as Buglossoides oil balanced Bacteroides>Firmicutes & lowered total cholesterol (-7.4%) in humans




Daily intake equivalent to ~2-3 g Ahiflower oil (1.2 g ALA + 0.4 g SDA). Placebo = corn oil. R-DBPC 12-week trial carried out in marginally hyperlipidemic adults in China where Ahiflower oil is not yet available. Higher gut microbiome *Veillonella* is associated with higher levels of gut inflammation, and the development of colitis.

"ALA/SDA-rich natural oils have the potential to provide a useful plant-derived dietary resource for increasing tissue concentrations of long-chain n-3 fatty acids in humans… Plant derived n-3 PUFA supplementation **significantly decreased the TC concentration** in subjects with marginal hyperlipidemia after the 12-week intervention… **The imbalance in microbial communities linked with hyperlipidemia** seems to be corrected by plant-derived n-3 PUFA supplementation."



Liu H et al (2022) Effect of Plant-Derived n-3 Polyunsaturated Fatty Acids on Blood Lipids and Gut Microbiota: A Double-Blind Randomized Controlled Trial, *FNutr* v9 (#830960). doi: 10.3389/fnut.2022.830960

# Ahiflower oil boosts live probiotic survival 2x vs probiotics alone

## Supports gut microbiome balance & gut-brain axis function

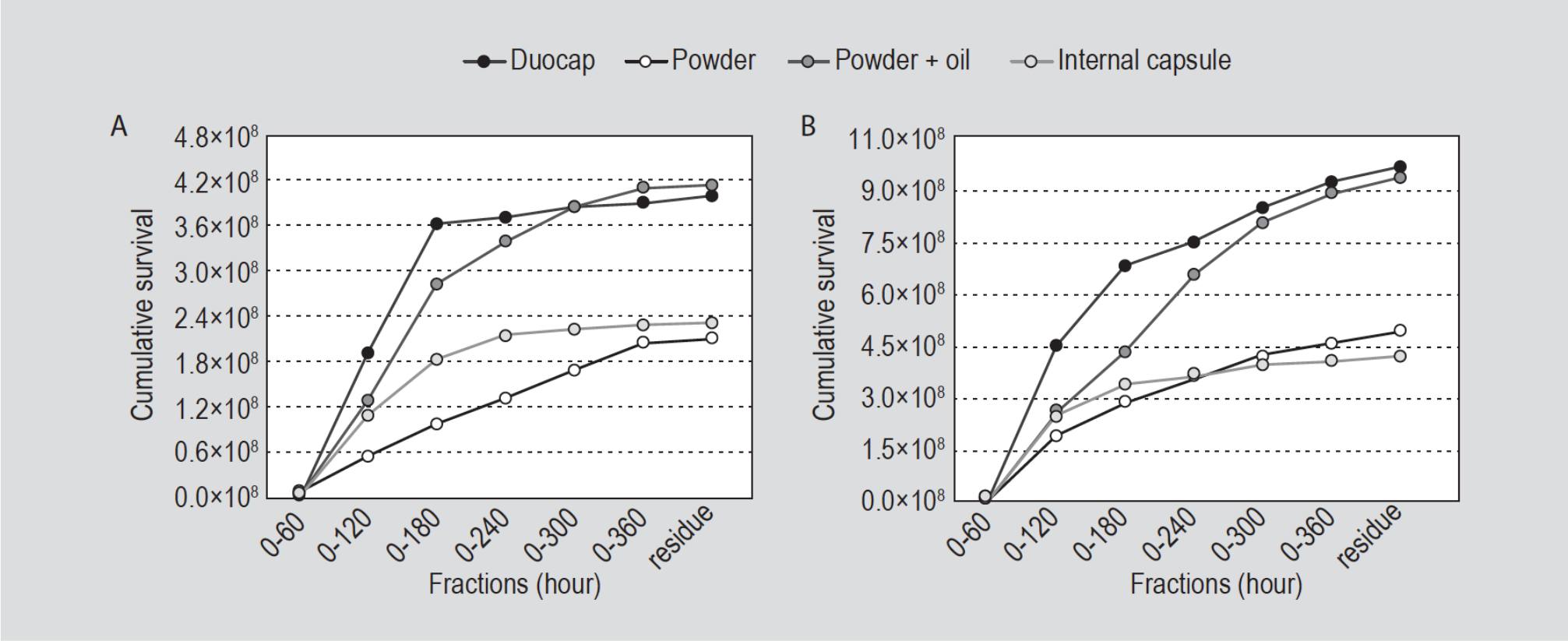



**Figure 2. Cumulative survival for the two genera during transit through the complete TIM-1 system simulating adults. (A) Survival of the combined *Lactobacillus* strains; (B) survival of the combined *Bifidobacterium* strains.**



Venema (2020) *Beneficial Microbes*; 11(4): 403-409. doi: 10.3920/BM2019.0209


# What this means:

- High dietary SDA omega-3 sources can meet the body's intracellular DHA requirements efficiently, notably in the brain.
- Ahiflower oil, now recognized in peer-reviewed literature, is a regenerative plant-based omega-3 alternative to unsustainable marine EPA/DHA sources
- O3I is dominated by DHA in RBCs yet does not correlate with tissue and intracellular DHA status — notably in liver, adipose, and brain.
- Metabolically, high circulating DHA means the body isn't using it to meet intracellular needs.
- ALA and especially SDA-rich sources elevate ETA, EPA & DPA which are deployed dynamically to support all cell membrane & signaling functions — including DHA biosynthesis as & when needed.

"SDA has qualitatively similar effects to EPA and combinations of EPA and DHA… greater than the effects of ALA (at the same intake level)."

— Dr Ella Baker



Baker EJ, Curr Opin Clin Nutr Metab Care 2023, 27

# THANK YOU

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