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# FLAXSEED VS FISH OIL: A NEW LOOK AT BIO-UTILITY FOR PHARMA



In modern pharmaceutical and nutraceutical development, omega-3 fatty acids remain central to cardiometabolic and anti-inflammatory health. Fish oil has traditionally dominated because of its direct EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) content. However, emerging data suggest that flaxseed and flaxseed oil offer distinct advantages in terms of bio-utility, tolerability, and mechanistic impact—particularly in targeted populations.

## The Classic Rivalry

Fish oil provides long-chain omega-3 fatty acids EPA and DHA, which are well established for cardiovascular and neurological benefits. Flaxseed oil, on the other hand, supplies ALA (alpha-linolenic acid), a shorter-chain omega-3 that undergoes conversion in the body to EPA and DHA. Although the conversion rate is modest,

overall bio-utility depends on multiple physiological pathways absorption, tissue incorporation, gene regulation, and downstream inflammatory signalling not only on direct EPA/DHA content.

Within this broader framework, flaxseed oil's advantages become more pronounced when evaluated through markers related to inflammation, lipid metabolism, gene regulation, tissue incorporation, glycaemic control, and real-world patient outcomes.

## Plant-Based, Allergen-Friendly and Sustainable

Flaxseed oil provides a plant-derived, allergen-friendly alternative to marine oils. It is suitable for vegetarian and vegan populations, free of fish allergens, and avoids concerns related to marine contaminants such as heavy metals and persistent organic pollutants. In addition, flaxseed cultivation has a more predictable and scalable agricultural supply chain compared with vulnerable marine ecosystems, aligning with sustainability and ESG priorities for pharma and nutraceutical brands.

These attributes make flaxseed oil especially valuable in markets where clean-label, plant-based and ocean-friendly formulations are preferred.

## **Mechanistic Advantages in Cardiometabolic Health**

Within the cardiometabolic context, flaxseed oil can be positioned as having better Bioavailability (bio-utility) than fish oil in specific settings, as it not only delivers omega-3 precursors but also demonstrates superior performance on key functional markers in defined populations.

### **Preclinical data in diabetic models show that flaxseed oil:**

- More effectively improves red blood cell and plasma omega-3 levels compared with control diets,
- Up-regulates PPAR- $\alpha$  and down-regulates SREBP-1 in the liver- promoting fatty acid  $\beta$ -oxidation and reducing lipogenesis,
- Leads to improvements in triglycerides and other lipid parameters.

In type-2 diabetes and cardiometabolic models, flaxseed oil has also been associated with reduced hepatic steatosis, improved insulin sensitivity, and attenuation of low-grade inflammation.

Taken together, these outcomes indicate that beyond simple EPA/DHA content, flaxseed oil may offer higher practical Bioavailability through better metabolic, inflammatory, and gene-regulatory impact than traditional fish-oil formulations in specific therapeutic and nutraceutical settings.

## **Red Blood Cell Omega-3 Status**

In streptozotocin $\square$ nicotinamide-induced diabetic rats, diets enriched with flaxseed oil increased omega-3 levels in plasma and red blood cells while simultaneously modulating hepatic lipid-metabolism genes. This suggests that under insulin-resistant or diabetic conditions, ALA from flaxseed oil can be effectively elongated and desaturated, resulting in meaningful tissue-level omega-3 incorporation despite its precursor status.

These findings support the concept that metabolic context may determine how efficiently ALA is converted and utilized- potentially favouring flaxseed oil in diabetic and cardiometabolic populations where gene-expression patterns and enzyme activity are altered.

### **Clinical Impact on Inflammation and Insulin Regulation**

In specific populations with type-2 diabetes and coronary heart disease, flaxseed oil supplementation has been associated with:

- Greater reductions in fasting insulin compared with fish oil,
- Larger decreases in high-sensitivity C-reactive protein (hs-CRP), Improvements in composite cardiometabolic risk markers.

A retrospective study in T2DM patients with CHD found that

flaxseed oil was more effective than fish oil in reducing serum insulin and hs-CRP levels, supporting its positioning as a cardiometabolic adjunct rather than a mere plant-based substitute.

Meta-analyses and systematic reviews of flaxseed interventions further show significant reductions in inflammatory markers such as CRP and hs-CRP, particularly with flaxseed oil subgroups, reinforcing its anti-inflammatory potential.

These responses reflect a broader metabolic and inflammatory influence that aligns well with pharmaceutical objectives in metabolic syndrome, chronic inflammation, and secondary cardiovascular prevention.

### **Beyond EPA/DHA: Multi-Component Flaxseed Advantage**

While fish oil largely delivers EPA and DHA, flaxseed offers a multi-component matrix:

- ALA as the primary omega-3 precursor,
- Lignans with antioxidant and potential phytoestrogenic actions,
- Fibre (in whole or milled flaxseed) supporting glycaemic control and gut health.

Preclinical and early clinical work suggests that this combination may synergistically:

- Reduce hepatic lipid accumulation,

- Improve oxidative-stress parameters,
- Modulate gut microbiota in favour of anti-inflammatory profiles.

This multi-pathway activity strengthens the value proposition of flaxseed-based interventions for chronic cardiometabolic and inflammatory indications.

### **Compliance, Safety and Tolerability Advantages**

From a patient-centric and commercial standpoint, flaxseed oil provides several practical advantages over fish oil:

- No fishy aftertaste or regurgitation, improving long-term adherence.
- Lower risk of marine-origin contaminants when sourced from controlled agricultural systems.
- Favourable safety profile with routine doses, with fewer concerns around fish allergies.

For long-duration supplementation programs typical of cardiometabolic and preventive indications, these tolerability benefits can translate into better real-world effectiveness than formulations that are clinically potent but poorly adhered to.

### **Important Caveats**

#### **For scientific and regulatory accuracy:**

- ALA conversion to EPA/DHA in humans remains limited in absolute percentage terms, especially in the general population.
- Fish oil continues to have the largest evidence base for direct EPA/DHA delivery in cardiovascular outcomes.
- Flaxseed advantages are currently strongest in specific populations and controlled conditions rather than universal applications.
- Reported benefits vary across studies depending on dose, formulation (whole seed vs oil vs lignan extract), baseline diet, and disease status.

Bioavailability is multifactorial, influenced by absorption, tissue incorporation, metabolic pathways, immunomodulation, and gene regulation- not just plasma EPA/DHA.

### **Strategic Opportunities for Pharma and Nutraceutical Development**

#### **1. Positioning & Targeting**

Flaxseed-derived formulations can be positioned as:

- Sustainable, plant-based omega-3 sources,
- Suitable for allergy-sensitive, vegan, and environmentally conscious markets,
- Particularly relevant for metabolic syndrome, T2DM,

NAFLD and CHD adjunct management where multi-pathway benefits (lipids, inflammation, insulin) are desirable.

### **2. Biomarker-Focused Development**

Clinical studies centred around flaxseed oil should measure:

- Inflammatory markers (hs-CRP, IL-6, TNF- $\alpha$ ),
- Insulin, HOMA-IR, and glucose parameters,
- Omega-3 index or red-blood-cell incorporation,
- Gene-expression outcomes related to PPARs, SREBP-1, NF- $\kappa$ B and other lipid/inflammatory pathways.

Such designs will allow sponsors to showcase flaxseed's bio-utility beyond legacy EPA/DHA metrics.

### **3. Formulation Innovation**

**Opportunities include:**

- Micro-emulsions and advanced lipid carriers to enhance ALA absorption and stability,
- Antioxidant co-formulations (e.g., vitamin E, polyphenols) to limit oxidation,
- Hybrid blends combining flaxseed oil with algae-derived long-chain omega-3s to deliver both precursor and direct EPA/DHA in a fully plant-based system.

## 4. Compliance & Tolerability

Flaxseed oil avoids fishy aftertaste, offers flexible flavouring, and can be incorporated into softgels, functional foods, and medical-nutrition formats. These attributes are critical for chronic-use indications where real-world adherence is often the limiting factor.

### Conclusion

Fish oil remains the reference standard for direct EPA/DHA delivery and has a deep cardiovascular evidence base. Yet, flaxseed oil introduces powerful advantages in metabolic regulation, inflammatory control, gene-pathway modulation, tolerability, sustainability, and plant-based positioning.

In targeted therapeutic or nutraceutical settings- especially among cardiometabolic and diabetic populations- flaxseed oil may deliver higher practical Bioavailability than traditional fish-oil formulations, not by competing on EPA/DHA content alone, but by leveraging multi-pathway, multi-component mechanisms that align closely with modern pharma and nutraceutical objectives.

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