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High-Concentration Re-Esterified Triglyceride EPA+DHA Fish Oil: Formulation Characterization and Clinical Evidence for Triglyceride Homeostasis

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Abstract: Concentrated marine omega-3 products must retain polyunsaturated fatty acids during processing and deliver them in a form suitable for oral use. We characterized a mackerel-derived re-esterified triglyceride (rTG) fish oil developed as the BCLC® high-concentration EPA+DHA platform. Formulation measurements were considered together with published human evidence on triglyceride lowering. The process used low-temperature antioxidant pretreatment, enzymatic oil release under nitrogen, pH-salt demulsification, ceramic-membrane clarification, ethanolysis, two-stage molecular distillation and immobilized-lipase re-esterification. Final oils contained 68.9-71.4% EPA+DHA and 81.7-84.0% triglyceride-type lipids; residual ethyl esters were 7.9-10.6% and TOTOX values were 15.0-17.0. In the optimized reference process, EPA+DHA rose from 28.1% in refined mackerel oil to 72.8% in enriched ethyl esters and measured 70.6% after rTG conversion.

Human trials report triglyceride reductions with gram-level EPA+DHA, and rTG formulations have produced efficient omega-3 incorporation. Across randomized trials, the response varies with dose, baseline triglycerides and background lipid therapy. These formulation characteristics allow high-concentration rTG EPA+DHA to be evaluated at defined exposures for triglyceride and lipid homeostasis.

Keywords: EPA; DHA; re-esterified triglyceride; fish oil; triglycerides; omega-3 index; mackerel

Introduction

Circulating triglyceride concentrations reflect the balance between hepatic very-low-density lipoprotein production, intestinal lipid delivery and peripheral clearance. EPA and DHA can alter several parts of this balance, and their effects on serum lipoproteins have been studied for decades [1]. In a 14-week randomized trial in adults with mild-to-moderate hypertriglyceridemia, 2.0 g/day DHA+EPA lowered triacylglycerols relative to control [2]. A separate multicenter trial in Taiwanese adults found triglyceride reductions at both 2 and 4 g/day EPA+DHA [3]. Pooled randomized evidence likewise supports a triglyceride-lowering effect, while showing that the magnitude of change varies among trials and background therapies [4]. More recent work in type 2 diabetes illustrates the same point: omega-3 exposure can be studied alongside lipidomic and metabolic context rather than as a single uniform response [5].

The amount printed on a capsule label is not the only determinant of exposure. Concentrated marine oils are commonly processed through an ethyl-ester intermediate because this facilitates separation of EPA- and DHA-rich fractions. Re-esterification returns much of that material to a glycerol-based lipid structure before oral use. In a double-blind comparison, Dyerberg et al. reported higher relative EPA+DHA bioavailability from re-esterified triglycerides than from ethyl esters [6]. Neubronner et al. then followed identical EPA+DHA doses for six months and observed a larger rise in the omega-3 index with re-esterified triacylglycerides [7]. These studies make lipid form relevant to formulation performance, but they do not imply that ester structure is itself a clinical endpoint.

The clinical literature surrounding marine omega-3 fatty acids is broader than triglycerides. Randomized-trial meta-analyses have examined blood pressure [8], [9], and intervention studies have assessed endothelial function in metabolic syndrome [10] and peripheral arterial disease [11]. Large outcome trials have also evaluated purified EPA or mixed marine omega-3 preparations in populations with elevated cardiovascular risk [12]-[15]. Their designs, doses, comparators and entry criteria differ substantially. For the present study, those trials provide context for long-term exposure, whereas fasting triglycerides and related lipoprotein measures remain the most direct functional endpoints for a concentrated EPA+DHA formulation.

A second issue is chemical rather than clinical. EPA and DHA are highly unsaturated and can be damaged during concentration, ester conversion, heating and storage. A useful high-concentration oil therefore has to satisfy several conditions at once: enrichment should be reproducible, the intended triglyceride-rich structure should be restored after the ethyl-ester concentration step, residual ethyl esters should be limited, and oxidation should remain controlled. Peroxide value, p-anisidine value and TOTOX describe that manufacturing state; they should be read as quality attributes rather than as evidence of a physiological effect.

The BCLC® process was developed around those constraints using mackerel processing fractions as the lipid source. Low-temperature handling, antioxidant pretreatment and nitrogen protection were used before and during oil recovery. Ethanolysis and two-stage molecular distillation created an EPA+DHA-rich intermediate, after which immobilized-lipase re-esterification with glycerol and short-path polishing produced the final rTG oil. This sequence makes it possible to examine concentration, lipid class and oxidative quality in the same material rather than treating them as separate specifications.

Accordingly, the present work characterized EPA+DHA enrichment, triglyceride-type lipid content, residual ethyl esters and oxidation indices across optimized preparations. Published human studies were then used to place two formulation features in context: the relation between EPA+DHA dose and triglyceride response, and the effect of rTG/rTAG structure on achieved omega-3 exposure. The clinical evidence is used here as a translational framework; it is not presented as a substitute for direct testing of the complete BCLC® formulation.

Materials and Methods

2.1 Process framework. Mackerel processing fractions containing head, bone, skin, belly tissue and viscera were washed and minced at low temperature. Mixed tocopherols and rosemary extract were added before

proteolysis with neutral protease and papain under nitrogen. Oil separation used pH adjustment and sodium-chloride demulsification. The recovered oil was centrifuged, clarified by ceramic-membrane cross-flow filtration and dehydrated under vacuum at low temperature.

2.2 Concentration and rTG conversion. Refined fish oil was converted to fatty-acid ethyl esters under nitrogen and concentrated by two-stage molecular distillation. The enriched ethyl esters were combined with food-grade glycerol under vacuum in the presence of immobilized *Candida antarctica* lipase. Filtration removed the residual catalyst. Short-path distillation was used for final polishing before the oil was sealed under nitrogen.

2.3 Analytical endpoints. EPA and DHA were quantified by gas chromatography. Triglyceride-type lipid proportion and residual ethyl esters were measured chromatographically. Peroxide value (PV), p-anisidine value (p-AV), TOTOX, acid value, water content and turbidity were used to evaluate oxidative and physicochemical quality.

2.4 Clinical evidence synthesis. We searched PubMed and primary journal sources through August 2026.

Search terms combined EPA, DHA, fish oil, rTG/rTAG, ethyl ester, bioavailability, omega-3 index, hypertriglyceridemia and triglyceride. Randomized human studies and meta-analyses were retained when the EPA+DHA dose, trial duration and triglyceride outcomes were reported explicitly.

Results

3.1 Enrichment and structural conversion. Refined mackerel fish oil in the optimized reference sequence contained 28.1% EPA+DHA. After ethanolysis, the ethyl-ester intermediate contained 39.2%; two-stage molecular distillation raised this to 72.8%. The final oil retained 70.6% EPA+DHA after lipase-catalyzed re-esterification and short-path polishing. Triglyceride-type lipids accounted for 83.2% of the oil, and residual ethyl esters accounted for 8.8%.

3.2 Reproducibility across process conditions. EPA+DHA ranged from 68.9% to 71.4% in the three optimized preparations, and triglyceride-type lipids ranged from 81.7% to 84.0%. Residual ethyl esters were 7.9-10.6%.

PV was 3.2-3.6 meq O₂/kg, p-AV was 8.6-9.8 and TOTOX was 15.0-17.0. Oxidation indices therefore remained within a narrow range despite the concentration steps.

3.3 Human triglyceride-lowering evidence. Maki et al. studied 93 adults with mild-to-moderate hypertriglyceridemia for 14 weeks. Fish oil supplying 2.0 g/day DHA+EPA reduced triacylglycerols by 22.9%, compared with a 3.5% increase in controls [2]. In 253 Taiwanese adults with hypertriglyceridemia, triglycerides decreased by 29.7% at 2 g/day and 32.1% at 4 g/day with an EPA+DHA ethyl-ester preparation; placebo produced a 5.4% reduction [3]. A meta-analysis of 32 randomized studies and 15,903 participants calculated a 39.81 mg/dL mean triglyceride reduction with omega-3 monotherapy, with additional reductions when omega-3 was combined with statins [4].

3.4 Lipid form and omega-3 exposure. In the six-month comparison of rTAG and ethyl esters, both groups received identical EPA+DHA doses and both showed higher omega-3 index values. The increase was greater with rTAG at 3 and 6 months [7]. Lipid form in this setting is a delivery characteristic rather than a separate health outcome.

Table 1. Final quality profile of three optimized rTG fish-oil preparations

Preparation	EPA+DHA (%)	TG-type lipids	Residual EE (%)	PV	p-AV	TOTOX	Water (%)	Turbidity (NTU)
F1	70.6	83.2	8.8	3.2	8.6	15.0	0.19	4.8
F2	68.9	81.7	10.6	3.5	9.4	16.4	0.22	5.4
F3	71.4	84.0	7.9	3.6	9.8	17.0	0.24	5.9

Table 2. Representative human evidence for EPA+DHA exposure and triglyceride lowering

Study	Design / population	Exposure	Key triglyceride or exposure result
Maki et al. [2]	Randomized double-blind; 93 adults with TG 150-499 mg/dL; 14	Fish oil 2.0 g/day DHA+EPA	TAG -22.9% vs +3.5% control
Su et al. [3]	Multicenter randomized double-blind; 253	EPA+DHA EE 2 or 4 g/day	TG -29.7% and -32.1% vs -5.4% placebo
Yang et al. [4]	Meta-analysis; RCTs; 32 15,903	Omega-3 monotherapy / statin combinations	TG mean difference -39.81 mg/dL with
Dyerberg et al. [6]	Double-blind bioavailability study; 72 volunteers	~3.3 g/day EPA+DHA for 2 weeks	rTG relative bioavailability 124% vs natural fish oil; EE 73%
Neubronner et al. [7]	Double-blind placebo-controlled; 150 volunteers; 6 months	1.68 g/day EPA+DHA as rTAG or EE	Omega-3 index increase greater with rTAG at 3

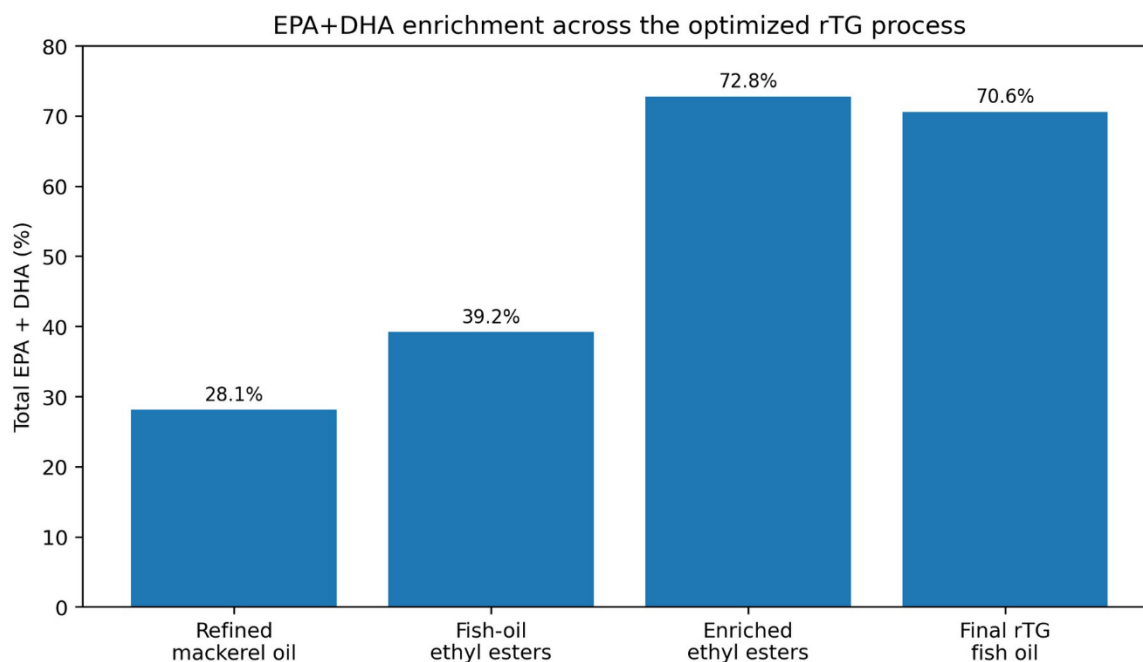


Figure 1. EPA+DHA concentration across the optimized reference process. Values are formulation-study measurements from refined mackerel oil through final rTG conversion.

4.

Discussion

The reference sequence concentrated EPA+DHA from 28.1% to 72.8% before re-esterification. Final rTG oil contained 70.6%, indicating limited dilution during structural conversion and polishing. More than 80% of the final lipid fraction was present as triglyceride-type lipids. The three optimized preparations also had similar oxidation indices, even after enrichment and conversion.

Clinical studies identify triglycerides as the clearest physiological endpoint for concentrated EPA+DHA.

Larger reductions generally occur at higher doses and in participants who begin with higher triglyceride concentrations. In the 2022 meta-analysis, omega-3 monotherapy reduced TG, VLDL-C and non-HDL-C [4]. Some DHA-containing formulations increased LDL-C in hypertriglyceridemic populations, so changes across the lipid fractions should be read separately rather than treated as a single uniform response.

Lipid form affects the exposure that precedes those metabolic responses. Dyerberg et al. measured a relative bioavailability advantage for re-esterified triglycerides over ethyl esters [6]. The longer rTAG trial found a greater omega-3-index increase at the same EPA+DHA dose [7]. For the BCLC® ingredient, the triglyceride-rich structure is therefore relevant to dose delivery and achieved EPA+DHA status.

Mackerel processing fractions supplied the starting oil for the concentrate. Their use shows that an existing seafood stream can yield a high-EPA+DHA ingredient when oxidation, water, impurities and ester structure are controlled during processing. This manufacturing consideration does not alter the nutritional identity of EPA and DHA.

Study

Considerations

and

Future

Directions

A practical next trial can compare several daily doses of the complete BCLC® ingredient. Fasting and postprandial EPA/DHA kinetics, omega-3 index, triglycerides and lipoprotein particles could be measured, with baseline triglyceride strata and dietary fat intake specified before enrollment. These measurements would connect the process profile with exposure and lipid responses in humans.

Conclusion

The low-oxygen enzymatic and molecular-distillation process produced mackerel-derived BCLC® rTG oil containing 68.9-71.4% EPA+DHA and 81.7-84.0% triglyceride-type lipids. Residual ethyl esters were low and oxidation indices remained controlled. Randomized trials and meta-analyses report triglyceride lowering with EPA+DHA, while bioavailability studies show efficient incorporation from rTG/rTAG formulations. The measured composition is appropriate for dose-specific evaluation of triglyceride and lipid homeostasis.

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