Omega-3 • Autoimmunity • Microcirculation

SJÖGREN + RAYNAUD

What changes when EPA+DHA enter the membranes,
the Omega-3 Index rises and the n-6:n-3 imbalance decreases.

OPERATIONAL TARGET: O3I ≈ 8%

RATIO: DIRECTION → LOWER

Sjögren: dry eye • dry mouth • saliva • inflammatory activity.
Raynaud: vasospasm • cold tolerance • digital perfusion.



OVERVIEW

Four lines of evidence converge.

From glandular manifestation to vascular response to cold.

1

SJÖGREN — RCT DIRECT

104 patients • 2 months

Dry eyes ↓ • Dry mouth ↓ • Increased saliva flow

2

BLOOD STATUS

108 patients

More DHA/mega-3 ↔️ lower ESSDAI and lower salivary CCL2

3

RAYNAUD — DIRECT RCT

32 patients

Time to vasospasm +49% • digital pressure +32 mmHg

4

VASCULAR BRIDGE

Endothelium + cold + platelets

FMD ↑ • NO ↑ • platelet aggregation ↓ in human studies

Studies that verified what this page presents: Al-Rawi 2025 PMID 40557177 • Castrejón-Morales 2020 PMID 32896265 • DiGiacomo 1989 PMID 2536517 • Hammer 2019 PMID 31262371.

METHOD

How this presentation was constructed

The same logic used in Lupus: biomarker → mechanism → function → benefit.

01

Measure

Omega-3 Index,
n-6:n-3,
EPA/AA

→

02

Confirm membrane

EPA+DHA enter
red blood cells and
alter the
PUFA profile.

→

03

Observe biology

chemokines,
eicosanoids,
NO, platelets

→

04

Measure function

Tear, saliva,
FMD, perfusion,
response to cold

→

05

Connect to the patient

sicca,
activity,
vasospasm

The central question is not "Did they take omega-3?". It is: Did the status change, did the membrane change, and did the function relevant to Sjögren/Raynaud respond?

BIOMARKERS

Why target an Omega-3 Index ≈ 8% — and monitor the ratio

8% is the target for incorporation; 3:1 is a reference zone, not an isolated goal.

OMEGA-3 INDEX

≈ 8%

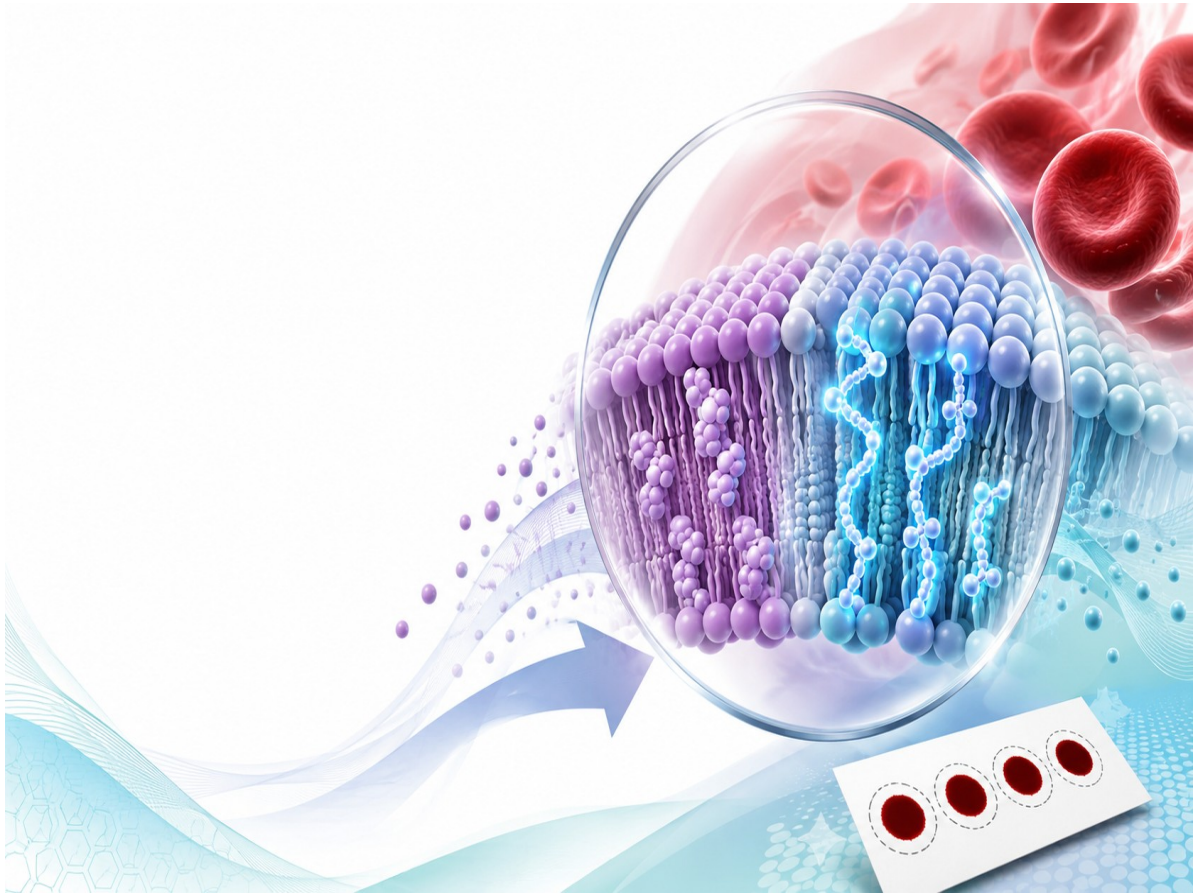
EPA+DHA incorporated into membranes

n-6:n-3 ratio

↓

The imbalance is losing magnitude.

- ATTICA: the plasma n-6:n-3 ratio showed the strongest positive correlations with hsCRP, IL-6, TNF-α, and fibrinogen.
- OMEGA-PAD: raising O3I from 5.1% to 9.0% reduced the n-6 content in red blood cells.
- In practice: O3I ≈8% is the primary target; the ratio serves as confirmation that the fatty-acid balance has also shifted.



Studies that verified what this page presents: Kalogeropoulos/ATTICA 2010 PMID 20097190 • Grenon/OMEGA-PAD 2017 PMID 28457318.

2025 — Dry eye: direct clinical improvement

Double-blind RCT • 104 patients • 2 months

START

10.44

average dry eye score

AFTER 2 MONTHS

4.85

omega-3 group

Approximately 54% reduction within the omega-3 group.

At the end: 4.85 vs 8.27 on placebo • p=0.001

In simple terms: eye discomfort dropped from a moderate level to a much milder one.



Study that verified what this page presents: Al-Rawi ZS et al. Mediterr J Rheumatol. 2025;36(1):92–99. PMID 40557177.

2025 — Dry mouth and saliva production

The same RCT measured symptoms and glandular function.

Xerostomia

2.83 → 1.91

Approximately 33% fewer symptoms.

SIALOMETRY

0.99 → 2.07

Approximately 109% more salivary flow

VS PLACEBO

2.07 vs 1.55

end salivary flow

- Dry mouth: 1.91 in the omega-3 group vs 2.35 in the placebo group • p=0.017.
- Salivary flow reached the normal range defined in the protocol.

The presentation goes beyond simply mentioning a "sensation of dryness": there is a measured functional signal from the salivary gland.



Study that verified what this page presents: Al-Rawi ZS et al. Mediterr J Rheumatol. 2025;36(1):92–99. PMID 40557177.

SJÖGREN

2020 — the blood tracked the disease activity.

108 patients • serum fatty acids + ESSDAI + chemokines in saliva and tears

DHA ↑ **ESSDAI ↓**

Higher DHA levels were associated with lower systemic activity.

OMEGA-3 ↑ **Salivary CCL2 ↓**

more favorable local inflammatory environment

AA ↑ **CXCL9 lacrimal ↑**

major inflammatory sign in tears

INGESTION ≠ STATUS **The blood mattered more.**

The reported intake did not match the serum levels.

Key message: In Sjögren, measuring the biological status of omega-3s adds information that declared intake does not provide.

Study that verified what this page presents: Castrejón-Morales CY et al. Clin Exp Rheumatol. 2020. PMID 32896265.

CLINIC BRIDGE

Sjögren and Raynaud: the meeting point is the endothelium.

Raynaud is part of the Sjögren spectrum, and vascular function is already altered.

FMD IN SJÖGREN

7%

vs 12% in controls

ANOTHER STUDY

3.0%

vs 4.2% in controls

- Endothelium-dependent vasodilation was reduced in Sjögren.
- The dysfunction was especially evident in patients who presented with Raynaud phenomenon.

This creates the biological bridge: sicca and autoimmunity on one side; microcirculation and cold response on the other.



Studies that verified what this page presents: Akyel A et al. West Indian Med J. 2012. PMID 24020226 • Piridar T et al. Rheumatol Int. 2005. PMID 15965638.

Fish oil: cold tolerance and vasospasm

Double-blind RCT • 32 patients • EPA 3.96 g + DHA 2.64 g/day

TIME UNTIL RAYNAUD

31.3 → 46.5 min

Approximately 49% greater cold tolerance.

uninduced attack

45.5%

5 of 11 in primary Raynaud

PRESSURE

+32

mmHg at 10°C



In simple terms: the fingers withstood the cold for longer and maintained higher blood pressure before vasospasm.

This study is the one most directly aligned with the functional problem of Raynaud.

Study that verified what this page presents: DiGiacomo RA, Kremer JM, Shah DM. Am J Med. 1989;86:158–164. PMID 2536517.

COLD + MICROCIRCULATION

2026 — Lowering the ratio accompanied better recovery from the cold.

126 adults with cold sensitivity • 12 weeks • ALA 1.27 or 2.03 g/d

n-6:n-3 ratio

8.34 → 7.34

largest group ALA

EPA:AA

Up

significant change

OMEGA-3 INDEX

≈ 7.4%

virtually stable

- Blood flow to the hand recovered more quickly after immersion in water at 15°C.
- In participants with baseline FMD <6%, endothelial function improved.

This study shows that the direction of the ratio also carries functional information, even when the O3I hardly changes.



Study that verified what this page presents: Ando N et al. Front Nutr. 2026;13:1878148. PMID 42601880 • DOI 10.3389/fnut.2026.1878148.

HUMAN MECHANISM

Endothelium, nitric oxide, and platelets

Three human studies show what changes inside the circulatory system.

FMD

+3.7%

vs −0.5% placebo • 3 months

Nitric oxide

+62.2%

2 g/day • 3 months

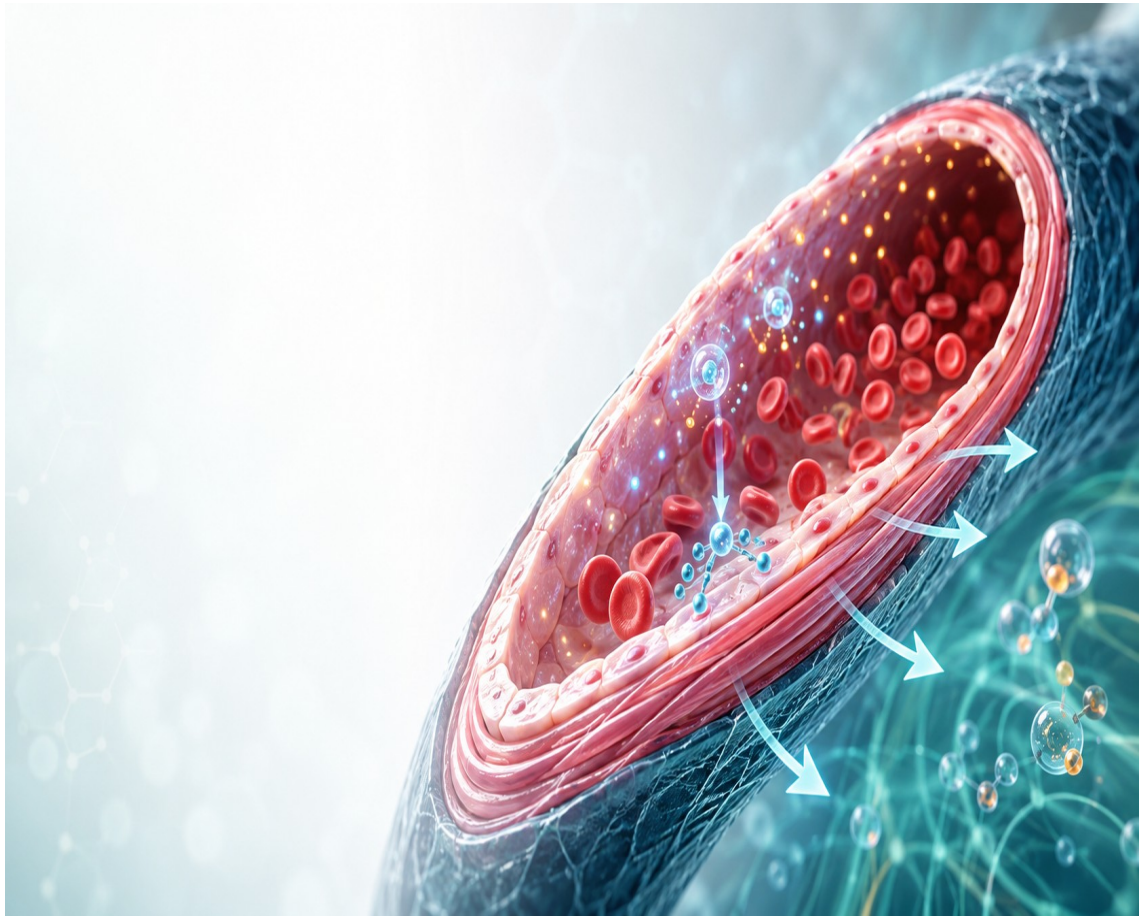
PLATELETS

-11.8% / -14.8%

EPA / DHA • 4 weeks

- EPA/DHA shifted the eicosanoid pattern: EPA/DHA-derived mediators increased and AA-derived LTB4 decreased.
- Reduced platelet aggregation and activation diminishes an additional component of the vascular response.

For Raynaud, this combination is especially relevant: better endothelium + more NO + lower platelet reactivity.



Studies that verified what this page presents: Hammer 2019 PMID 31262371 • Yuan 2021 PMID 33041091 • Phang 2013 PMID 23390192 • McEwen 2013 PMID 23329646.

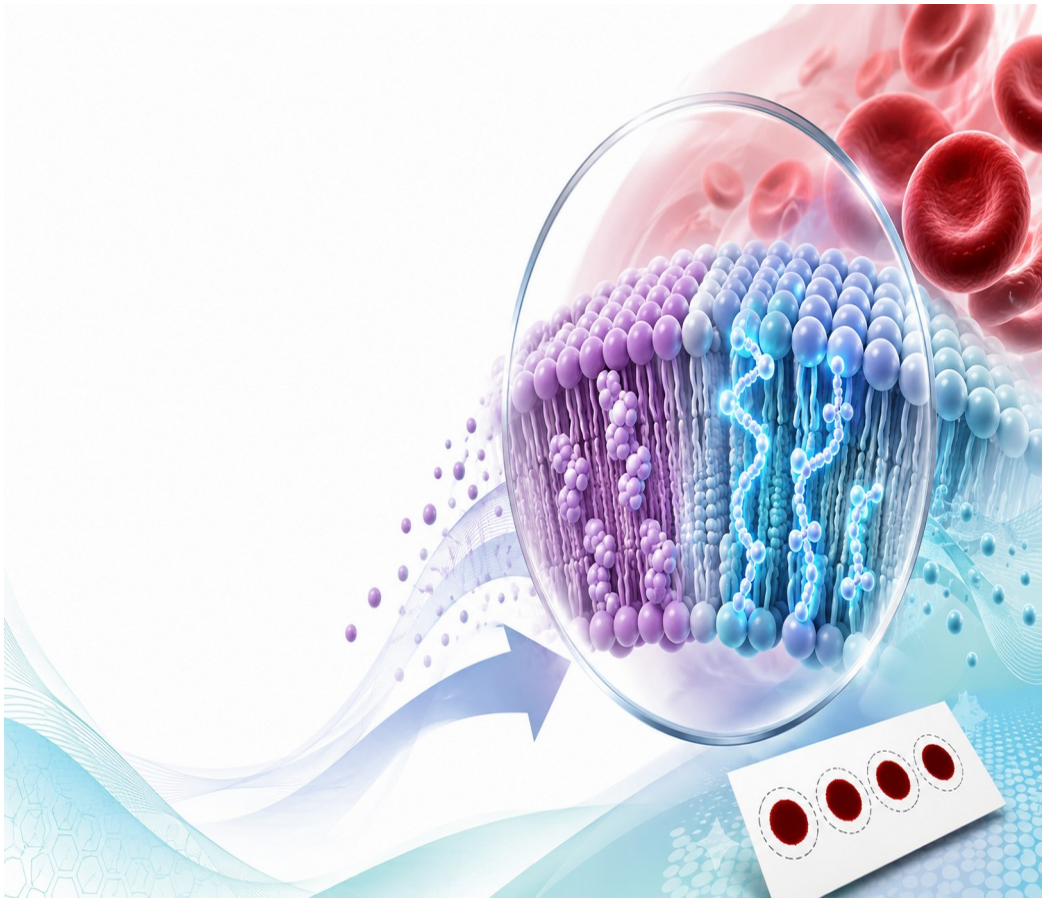
BIOLOGICAL LOGIC

How are the changes linked?

From the membrane to glandular symptoms and microcirculation.

1. **O3I ↑** — EPA and DHA enter the membranes.
2. **n-6:n-3 ↓** — less relative predominance of AA
3. **Signs change** — eicosanoids • NO • chemokines
4. **Function changes** — tear • saliva • endothelium • flow
5. **Patient feels** — less dryness • more cold tolerance

O3I ≈8% is proof that the first step — cellular incorporation — actually happened.



PMID 28457318 • PMID 33041091 • PMID 32896265 • PMID 2536517

IN PRACTICE

What do these findings mean for Sjögren + Raynaud?

Benefits observed directly or sustained by a human physiological bridge.

1 Dry eye

Symptoms decreased in approximately 54% of the RCT.

2 Dry mouth

Xerostomia ↓ ~33%

3 Saliva

flow ~doubled

4 Sjögren activity

DHA/ω-3 ↑ ↔ ESSDAI ↓

5 Raynaud

+49% time until vasospasm

6 Cold infusion

digital pressure +32 mmHg

7 Endothelium

FMD improved in RCTs

8 Inflammation linked to the profile

high ratio ↔️ hsCRP/IL-6/TNF-α

Key message: Correcting the EPA+DHA status simultaneously addresses the glandular, inflammatory, and vascular dimensions of the problem.

PMID 40557177 • PMID 32896265 • PMID 2536517 • PMID 31262371 • PMID 20097190

STRATEGY

Test → Correct → Retest → Connect to patient

An objective way to transform supplementation into a measurable intervention.

1

TEST

O3I • n-6:n-3 / AA:EPA + symptoms and function

Dry drop of blood + baseline

2

TO CORRECT

EPA+DHA + nutrition suitable for the case.

change the substrate of the membranes

3

RETEST

12–16 weeks confirm O3I and ratio

prove incorporation and displacement

4

CONNECT

Dry eye/mouth • saliva Raynaud • cold • perfusion

Let's see if biology has turned into something beneficial.

Reading rule: O3I ≈8% is the primary target; the ratio is the companion biomarker that confirms the direction of equilibrium.

REFERENCES

Scientific references — 1/2

Key human studies used for the narrative of Sjögren, Raynaud, and biomarkers.

1. Al-Rawi ZS et al. Mediterr J Rheumatol. 2025;36(1):92–99. PMID 40557177.
2. Castrejón-Morales CY et al. Clin Exp Rheumatol. 2020;38 Suppl 126(4):34–39. PMID 32896265.
3. Akyel A et al. West Indian Med J. 2012;61(9):870–872. PMID 24020226.
4. Pirildar T et al. Rheumatol Int. 2005;25(7):536–539. PMID 15965638.
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6. Ando N et al. Front Nutr. 2026;13:1878148. PMID 42601880.

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Scientific references — 2/2

Human studies used for endothelium, platelets, inflammation, and Omega-3 Index.

7 Hammer A et al. Br J Nutr. 2019;122(6):698–706. PMID 31262371.

8 Yuan M et al. Clin Nutr. 2021;40(2):445–459. PMID 33041091.

9 Phang M et al. J Nutr. 2013;143(4):457–463. PMID 23390192.

10 McEwen BJ et al. Semin Thromb Hemost. 2013. PMID 23329646.

11 Kalogeropoulos N et al. Clin Chim Acta. 2010;411:584–591. PMID 20097190.

12 Grenon SM et al. J Vasc Surg. 2017. Predictors of change in Omega-3 Index. PMID 28457318.

Technical summary: the set links fatty acid status → membrane → inflammation/endothelium → glandular symptoms and vascular response to cold.