

Therapeutic use of Omega-3 + Eggshell Membrane

Applications and recommended use

Typical indications for EPA+DHA and eggshell membrane

- Joint support and cartilage maintenance
- Natural anti-inflammatory agents
- Muscle pain and stiffness after intense sporting (*delayed onset muscle soreness* or DOMS)
- Osteoarthritis, rheumatoid arthritis, low back pain, neck and shoulder pain
- Exercise-induced joint pain and stiffness in the elderly
- Additional benefit: positive impact on cardiovascular health (i.e. prevention of sudden cardiac death)

Interactions and precautions

No side effects are known when used correctly.

Scientific information

The omega-3 fatty acids **eicosapentaenoic acid (EPA)** and **docosahexaenoic acid (DHA)**, derived from fish, have well-known anti-inflammatory capacities since they are the precursors of inflammation-soothing compounds in the body. DHA is converted to resolvins, maresins and protectins. These are specialized pro-resolving mediators (SPM's) that are important in terminating an inflammatory response. EPA is converted to resolvins for real inflammation shutdown, and anti-inflammatory eicosanoids of the series 3 prostaglandins and series 5 leukotrienes for inhibiting inflammation.¹⁻³ Such anti-inflammatory potential is useful for healthy joint and muscle function.

A meta-analysis of 20 controlled clinical studies involving a total of 1288 patients with **rheumatoid arthritis** showed beneficial effects of omega-3 supplementation (± 3 g EPA+DHA/d) when taken for at least 3 months: grip strength improved, while complaints such as joint sensitivity, pain and early morning stiffness were reduced. Also, blood levels of the proinflammatory marker leukotriene B4 (LTB4) were reduced. LTB4 recruits white blood cells to the site of injury and sustains chronic inflammation.⁴

EPA+DHA supplementation has also been successfully used in the treatment of **discogenic pain (neck or low back pain)**. Patients (n=250) used 2,4 g EPA+DHA/d for 2 weeks, followed by 1,2 g EPA+DHA/d for on average 2 months, and were instructed to taper off of their prescription NSAID medications for pain over 1 to 2 weeks. At the end of the study the results were promising: 59% discontinued to take NSAIDs while 60% stated their overall pain and joint pain had improved.⁵

Omega-3 (EPA+DHA) likewise offers promise to improve the pain and discomfort that is characteristic of **delayed onset muscle soreness (DOMS)**, which is the pain and stiffness felt in muscles several hours to days after unaccustomed or strenuous exercise involving eccentric (muscle lengthening) contractions. This can occur involuntarily (e.g. when attempting to move a weight too heavy for the muscle to lift) or voluntarily (e.g. athletes on strength training).⁶

Moreover, EPA and DHA contribute to **cardiovascular health**, and are recognized by the American Heart Association for their usefulness in the secondary prevention of coronary heart disease and sudden cardiac death, and to reduce mortality and hospitalizations in patients with heart failure.⁷ This is why the **Omega-3 Index**, the percentage of EPA+DHA in the total fatty acid composition of the red blood cell membranes, is **preferably 8%**. Individuals with an Omega-3 Index of 4% or lower are 10 times more likely to have a sudden cardiac death than people with an Omega-3 Index between 8% and 11%.⁸ A recent study shows how the consumption of omega-3 fatty acids from **UnoCardio quality (2,23 g EPA+DHA/d)** improved the Omega-3 Index of elite soccer players **from ±5% to a safe 8% within 124 days**.⁹

Eggshell membrane is derived from the membrane that sits between the egg and eggshell. It is a natural source of glucosamine, chondroitin sulphate, hyaluronic acid, collagen (types I, V and X) and protein essential for maintaining healthy articular cartilage and connective tissues.

The eggshell membrane of patented **NEM® quality** underwent a positive safety evaluation¹⁰ and was **clinically tested** in individuals with **persistent joint pain** at their knees, hips, elbows, neck, shoulders, lower back, hands or feet (*open-label studies; n=39*)¹¹, in patients with **osteoarthritis** of the knee (*placebo-controlled study; n=67*)¹², and in postmenopausal women with **exercise-induced joint pain** and stiffness (*placebo-controlled study; n=60*)¹³.

- The participants with persistent joint pain of diverse origins experienced a 30% improved flexibility of the affected joint after 7 days of treatment. At 30 days of eggshell membrane treatment (500 mg NEM®/d) a pain reduction of 30 to 70% was reported.¹¹
- Of the patients with diagnosed osteoarthritis, those who used eggshell membrane (500 mg NEM®/d) for 8 weeks experienced a significantly 10% to 27% greater reduction of pain and stiffness than the placebo users. Rapid responses were noticed: after 10 days of supplementation mean pain and stiffness scores were reduced by 15.9% (p=0.036) and 12.8% (p=0.024), respectively. The researchers concluded that 1 out of every 5 patients should experience at least an 50% reduction in pain within 30-60 days of treatment with NEM® eggshell membrane, while nearly 1 out of every 2 patients would experience a 50% reduction in stiffness at 60 days.¹²
- Compared to placebo, NEM® eggshell membrane (500 mg NEM®/d) improved recovery from exercise-induced joint pain and stiffness in healthy postmenopausal women aged 40 – 75 years. The exercise comprised of 50–100 steps per leg utilizing an aerobics step. Moreover, a remarkable chondroprotective effect was demonstrated via a decrease in the cartilage degradation marker CTX-II (*C-terminal cross-linked telopeptide of type-II collagen*).¹³

Proposed mechanisms of action are a local reduction in proinflammatory substances (TNF α , PGE $_2$, LTB $_4$) as well as a general suppression of autoimmune responses towards cartilage components. About half of osteoarthritis patients have autoantibodies to type II collagen as a major driver of the immune-mediated cartilage destruction. Repeated ingestion of NEM is believed to teach gut-associated immune cells to better tolerate cartilaginous collagen II, a message that will consequently spread all over the immune system.¹³⁻¹⁵

References

1. Souza PR, Norling LV. Implications for eicosapentaenoic acid- and docosahexaenoic acid-derived resolvins as therapeutics for arthritis. *Eur J Pharmacol* 2016; 785:165-173.
2. Calder PC. Marine omega-3 fatty acids and inflammatory processes: Effects, mechanisms and clinical relevance. *Biochim Biophys Acta* 2015; 1851(4):469-84.
3. Caughey GE, James MJ, Proudman SM, Cleland LG. Fish oil supplementation increases the cyclooxygenase inhibitory activity of paracetamol in rheumatoid arthritis patients. *Complement Ther Med* 2010; 18(3-4):171-4.
4. Gioxari A, Kaliora AC, Marantidou F, Panagiotakos DP. Intake of ω -3 polyunsaturated fatty acids in patients with rheumatoid arthritis: A systematic review and meta-analysis. *Nutrition* 2018; 45:114-124.e4.
5. Maroon JC, Bost JW. Omega-3 fatty acids (fish oil) as an anti-inflammatory: an alternative to nonsteroidal anti-inflammatory drugs for discogenic pain. *Surg Neurol* 2006; 65(4):326-31.
6. Ochi E, Tsuchiya Y. Eicosahexanoic Acid (EPA) and Docosahexanoic Acid (DHA) in Muscle Damage and Function. *Nutrients*. 2018; 10(5).
7. Siscovick DS, Barringer TA, Fretts AM et al. Omega-3 Polyunsaturated Fatty Acid (Fish Oil) Supplementation and the Prevention of Clinical Cardiovascular Disease: A Science Advisory From the American Heart Association. *Circulation* 2017; 135(15):e867-e884.
8. Harris WS, von Schacky C. The Omega-3 Index: a new risk factor for death from coronary heart disease? *Prev Med* 2004; 39(1):212-20.
9. Rinderer M, Sohm M, Hämmerle M, Fink H, Passow A, von Schacky C. Omega-3 Index in 15 elite soccer players with and without EPA/DHA supplementation for 124 days: A pilot study. Poster presentation at the 13th Congress of ISFFAL, Las Vegas, 2018.
10. Ruff KJ, Endres JR, Clewell AE, Szabo JR, Schauss AG. Safety evaluation of a natural eggshell membrane-derived product. *Food Chem Toxicol* 2012; 50(3-4):604-11.
11. Ruff KJ, DeVore DP, Leu MD, Robinson MA. Eggshell membrane: a possible new natural therapeutic for joint and connective tissue disorders. Results from two open-label human clinical studies. *Clin Interv Aging* 2009; 4:235-40.
12. Ruff KJ, Winkler A, Jackson RW, DeVore DP, Ritz BW. Eggshell membrane in the treatment of pain and stiffness from osteoarthritis of the knee: a randomized, multicenter, double-blind, placebo-controlled clinical study. *Clin Rheumatol* 2009; 28(8):907-14.
13. Ruff KJ, Morrison D, Duncan SA, Back M, Aydogan C, Theodosakis J. Beneficial effects of natural eggshell membrane versus placebo in exercise-induced joint pain, stiffness, and cartilage turnover in healthy, postmenopausal women. *Clin Interv Aging* 2018; 13:285-295.
14. Benson KF, Ruff KJ, Jensen GS. Effects of natural eggshell membrane (NEM) on cytokine production in cultures of peripheral blood mononuclear cells: increased suppression of tumor necrosis factor- α levels after in vitro digestion. *J Med Food* 2012; 15(4):360-8.
15. Wedekind KJ, Ruff KJ, Atwell CA, Evans JL, Bendele AM. Beneficial effects of natural eggshell membrane (NEM) on multiple indices of arthritis in collagen-induced arthritic rats. *Mod Rheumatol* 2017; 27(5):838-848.