

NEM®

INTRODUCTION

Multiple clinical trials have shown that natural eggshell membrane (NEM) reduces joint pain and stiffness associated with osteoarthritis and caused by moderate-intensity aerobic exercise. NEM provides many bioactive nutrients associated with joint and connective tissue health. It has been shown to reduce both inflammatory signals as well as markers of cartilage degradation.

WHAT IS NEM?

NEM is a thin, film-like structure found in the space between the calcified shell and the albumin of chicken eggs. This protein-rich structure provides a natural source of many of the constituents of cartilage, including proteoglycans, dermatan sulfate and chondroitin sulfate, hexosamines such as glucosamine, and amino acids such as arginine, glutamic acid, histidine, cysteine, and proline, as well as hyaluronic acid and collagen type I.^{1,2} Many of these bioactive nutrients have key roles within the joint, such as preventing cartilage degeneration and reducing joint inflammation.³

MECHANISM OF ACTION

NEM is thought to reduce joint pain and stiffness at least in part by reducing the expression of several proinflammatory signals, such as interleukin-1 beta (IL-1β) and tumour necrosis factor-alpha $(TNF-\alpha)$.^{4,5} Evidence from a randomized and controlled clinical trial also indicates that NEM may reduce cartilage degradation. This study enrolled 60 postmenopausal women who received either a placebo or 500 mg of NEM per day for two weeks. It evaluated the effect of NEM on joint pain and stiffness immediately after moderate exercise, as well as up to 12 hours post-exercise. In addition to improved recovery from exerciseinduced joint pain and stiffness, researchers observed a reduction in the urinary levels of C-terminal cross-linked telopeptide of type-II collagen (CTX-II).6 CTX-II is a biomarker for cartilage degradation shown to be elevated in several joint diseases, including osteoarthritis and rheumatoid arthritis, as well as in response to strenuous exercise.⁶⁻⁸ This clinical trial suggests that NEM may also provide protection against cartilage degeneration/degradation, possibly by inducing immune tolerance to cartilage components.6

A reduction in clinical symptoms is observed relatively quickly following NEM supplementation. For example, controlled clinical trials have shown reductions in pain and stiffness associated with knee osteoarthritis within approximately 10 days of use. 9,10 Similarly, open-label trials have shown persistent improvements in pain and flexibility for multiple joint and connective tissue disorders, including knee, hip, and shoulder pain, within one week of supplementation. 11

ASSESSMENT

No known contraindications exist for NEM, other than an allergy to eggs and egg by-products. As reviewed above, controlled clinical trials have shown benefits for osteoarthritis of the knee, as well as joint pain following exercise, with open-label trials suggesting possible benefits for a wider range of joint and connective tissue disorders. Ruling out alternative sources of joint

pain, such as pain because of infection, should be considered before beginning treatment.¹²

GENERAL RECOMMENDATIONS AND DOSING

Take 1 capsule per day or as directed by a health care practitioner. Consult a health care practitioner for use beyond 8 weeks. Do not use if you have a known allergy to eggs or egg by-products. Consult a health care practitioner prior to use if you are pregnant or breastfeeding.

SUMMARY

NEM provides a natural source of bioactive nutrients associated with joint and connective tissue health. NEM has been shown to reduce inflammatory signals as well as markers of cartilage degradation, at least in response to exercise. Controlled clinical trials have shown that it reduces joint pain and stiffness caused by knee osteoarthritis and post-exercise, with clinical improvements observed within days of beginning supplementation.

REFERENCES

- Ruff, K.J., Winkler, A., Jackson, R.W., et al. (2009). Eggshell membrane in the treatment of pain and stiffness from osteoarthritis of the knee: A randomized, multicenter, doubleblind, placebo-controlled clinical study. Clin Rheumatol, 28(8), 907-14.
- 2. Mensah, R.A., Salim, K., Peszko, K., et al. (2023). The chicken eggshell membrane: A versatile, sustainable, biological material for translational biomedical applications. Biomed Mater, 18(4).
- 3. Oe, M., Tashiro, T., Yoshida, H., et al. (2016). Oral hyaluronan relieves knee pain: A review. *Nutr. J.* 15, 11.
- Benson, K.F., Ruff, K.J., & Jensen, G.S. (2012). 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, 15(4), 360-8.
- Ruff, K.J., & DeVore, D.P. (2014). Reduction of pro-inflammatory cytokines in rats following 7-day oral supplementation with a proprietary eggshell membrane-derived product. Mod Res Inflamm, 3(1), 19-25.
- Ruff, K.J., Morrison, D., Duncan, S.A., et al. (2018). Beneficial effects of natural eggshell membrane versus placebo in exercise-induced joint pain, stiffness, and cartilage turnover in healthy, postmenopausal women. Clin Interv Aging, 13, 285-95.
- Dam, E.B., Byrjalsen, I., Karsdal, M.A., et al. (2009). Increased urinary excretion of C-telopeptides of type II collagen (CTX-II) predicts cartilage loss over 21 months by MRI. Osteoarthr Cartil, 17(3), 384-9.
- O'Kane, J.W., Hutchinson, E., Atley, L.M., et al. (2006). Sport-related differences in biomarkers of bone resorption and cartilage degradation in endurance athletes. Osteoarthr Cartil, 14(1), 71-6.
- Brunello, E., & Masini, A. (2016). NEM® brand eggshell membrane effective in the treatment of pain and stiffness associated with osteoarthritis of the knee in an Italian study population. *Int J Clin Med, 7*, 169-75.
- Eskiyurt, N., Saridoğan, M., Senel K., et al. (2019). Efficacy and safety of natural eggshell membrane (NEM®) in patients with grade 2/3 knee osteoarthritis: A multi-center, randomized, double-blind, placebo-controlled, single-crossover clinical study. *I Arthritis*, 8(4), 1000285.
- 11. Ruff, K.J., DeVore, D.P., Leu, M.D., et al. (2009). Eggshell membrane: A possible new natural therapeutic for joint and connective tissue disorders. Results from two openlabel human clinical studies. Clin Interv Aging, 4, 235-40.
- 12. Arvikar, S.L., & Steere, A.C. (2022). Lyme arthritis. *Infect Dis Clin North Am,* 36(3), 563-77.
- 13. Baums, M.H., Aquilina, J., Pérez-Prieto, D., et al. (2023). Risk analysis of periprosthetic knee joint infection (PJI) in total knee arthroplasty after preoperative corticosteroid injection: A systematic review: A study performed by the Early-Osteoarthritis group of ESSKA-European Knee Associates section. Arch Orthop Trauma Sura, 143(5), 2683-91.