

WHITE PAPER

UNRAVELLING THE MECHANISMS BEHIND THE JOINT HEALTH EFFECTS OF COLLAGEN PEPTIDES



A new publication in the PLOS ONE scientific journal has confirmed the role of Peptan collagen peptides in supporting joint health. The study provides scientific documentation of the mechanisms behind cartilage regeneration and joint inflammation reduction. The study was carried out in collaboration with leading scientists at the University of Rochester, NY, and performed in an in vivo model for osteoarthritis.

By Dr. Janne Prawitt, Principal Scientist – Nutrition, Peptan. August 2017.

Collagen Peptides for a Healthy Lifestyle

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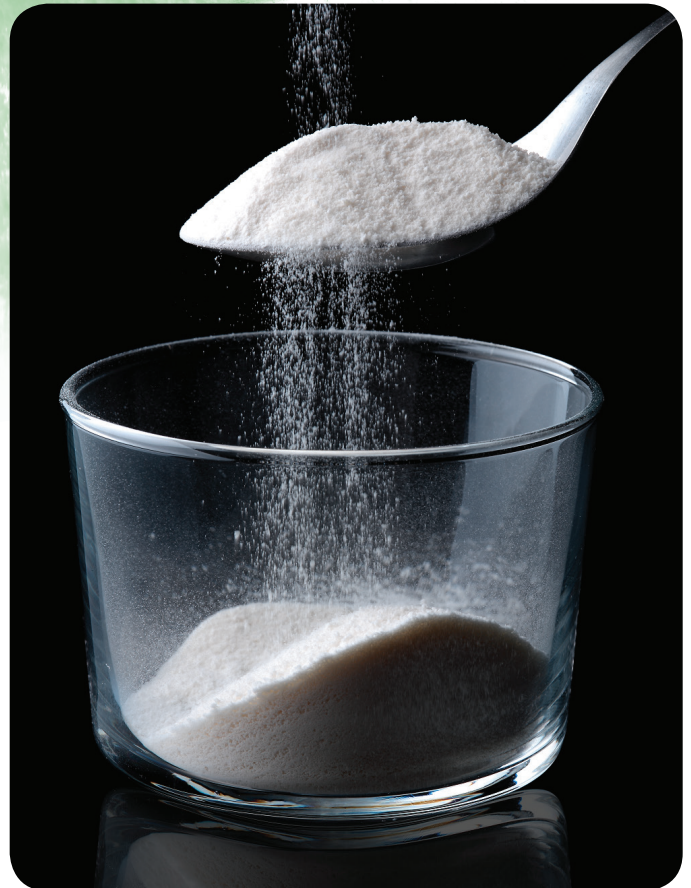
Peptan[®]

DARLING
INGREDIENTS

INTRODUCTION

A growing body of scientific evidence demonstrates the effectiveness of collagen peptides in supporting joint structure and function. Collagen peptides' bioactive properties have been shown in a clinical study to reduce joint discomfort, improve joint function and joint flexibilityⁱ, and to support the formation of cartilage matrix components.ⁱⁱ Multiple clinical trials further reported that subjects with joint deterioration benefited from the effects of collagen peptides.ⁱⁱⁱ Remarkably, a recently-published study unravels the mechanisms of how collagen peptides can deliver benefits for joint health.^{iv}

The study described in this paper aimed at investigating the impact of orally delivered collagen peptides on the joint degenerative process focussing on mechanisms of action. Results based on close observation of cartilage structure, chondrocyte number and synovial change revealed significant chondroprotective and anti-inflammatory effect in injured joints.



DR. JANNE PRAWITT

Dr Janne Prawitt is the Principal Scientist – Nutrition at Rousselot where she is responsible for the Nutrition and Health Science portfolio supporting Peptan[®], Rousselot's collagen peptides brand. A nutritional scientist by education she has spent 10 years in academic research in Germany and France, investigating mechanisms that contribute to the development of metabolic diseases such as obesity and diabetes. Janne joined Rousselot in 2013, where her main interest is to understand the benefit of collagen peptides for musculoskeletal health and skin physiology, and to develop related products for the global market.

ⁱ Jiang, J.X. et al., 2014. Collagen peptides improve knee osteoarthritis in elderly women: a 6-month randomized, double-blind, placebo-controlled study. *Agro FOOD Industry Hi Tech*, 25:19-23

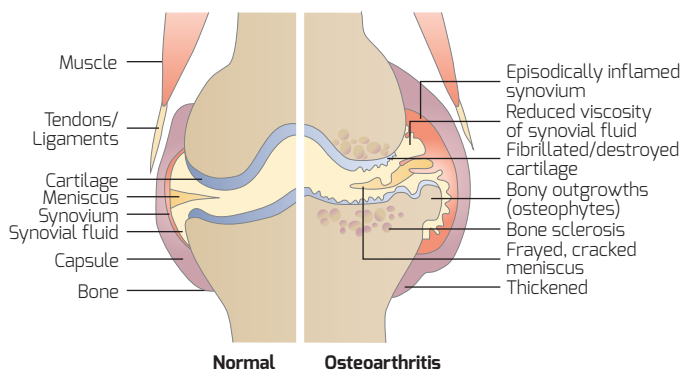
ⁱⁱ Kiani, C. et al., 2002. Structure and function of aggrecan. *Cell Research*, 12(1):19-32

ⁱⁱⁱ Henrotin, Y. et al., 2011. Nutraceuticals: do they represent a new era in the management of osteoarthritis? – a narrative review from the lessons taken with five products. *Osteoarthritis and Cartilage*, 19:1-21

^{iv} Dar, Q. et al., 2017. Daily oral consumption of hydrolyzed type 1 collagen is chondroprotective and anti-inflammatory in murine posttraumatic osteoarthritis. *PLoS ONE* 12(4):e0174705

COLLAGEN PEPTIDES' BENEFITS FOR JOINT HEALTH

Arthritis stands for 'joint inflammation'. Osteoarthritis (OA) is a degenerative joint disease, the most common type of arthritis associated with the breakdown of cartilage tissues. Inflammation of the joint or synovium is recognized to play an active role in driving the disease at an early stage of OA. OA often occurs with previous injury, excessive stress or an underlying disorder of cartilage. OA causes the cartilage in a joint to become stiff and lose its elasticity, making the joint susceptible to damage and decrease in its ability to act as shock absorber.



The concept that oral consumption of matrix components from cartilage and connective tissue may have a positive impact on the symptoms of degenerative joint diseases such as arthritic conditions have been debated for decades, with glucosamine and chondroitin sulfate being the most recognized and widely studied ingredients. However, conflicting reports on their effectiveness have created an opportunity for new ingredients such as collagen peptides.^v In addition, recent reports have also highlighted the active role of synovial inflammation in the progression of the disease, on which collagen peptides can have a beneficial effect, as shown below.

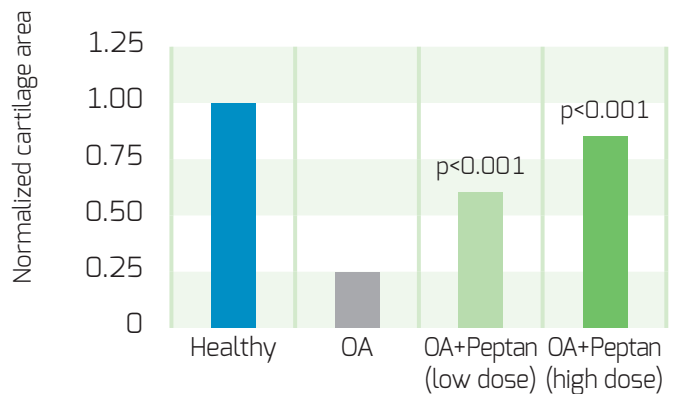
Recently, the mechanisms of how collagen peptides can support joint health were explained.^{vi} Oral consumption of type I collagen peptides in animals were reported to stimulate chondrocyte cells, promote the synthesis of new cartilage matrix and to reduce joint inflammation. Collagen peptides were administered daily at either low (LD) or high dosage (HD), corresponding to around 0.7g and 7 g /day in a human, while a separate group received a control. Four weeks after the start of supplementation, post-traumatic osteoarthritis (PTOA) was induced by administering injury to the meniscus and medial collateral ligament in the knee of the right hindlimb (MLI).^{vi}

PROTECTION FROM CARTILAGE DEGENERATION

Subsequent assessment showed significant joint cartilage loss at 12 weeks after injury in control animals (by 75%). The beneficial supplementation with collagen peptides had a dose-dependent effect on cartilage loss, with the LD protecting from cartilage loss, and the HD to an extent that cartilage was thickness comparable to healthy animals, clearly showing that dietary supplementation with collagen peptides had a cartilage protective effect during the progression of PTOA.

Osteoarthritis is characterized by progressive loss of articular cartilage that eventually leads to degradation of various components of the cartilage matrix, including collagen. Collagen degradation by matrix metalloproteinase 13 (MMP13), is considered a key step in the loss of structural and functional integrity of cartilage. As expected, control MLI mice had high levels of MMP13, Mice supplemented with HD collagen were protected from MLI induced MMP13 activity in the cartilage, giving a mechanistic explanation of how collagen peptides can inhibit matrix degeneration (as shown by protection from cartilage loss, refer to Fig 5 in publication^{vi}).

Peptan prevents cartilage degradation



Osteoarthritis (OA) was induced by surgery in mice that received Peptan at two different dosages or a control twelve weeks after OA induction. Histology of the knee joints was performed and the area of the (tibia) cartilage was quantified and compared with healthy animals.

Dar, 2017

^vClegg, D.O. et al., 2006. Glucosamine, Chondroitin Sulfate, and the Two in Combination for Painful Knee Osteoarthritis. N Engl J Med 2006 354(8): 795-808

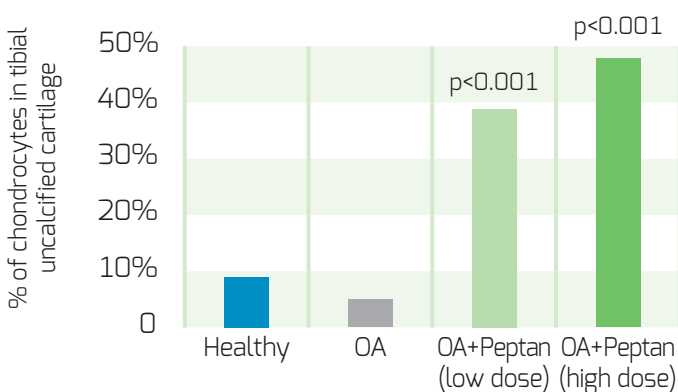
^{vi} Dar, Q. et al., 2017. Daily oral consumption of hydrolyzed type 1 collagen is chondroprotective and anti-inflammatory in murine posttraumatic osteoarthritis. PLoS ONE 12(4):e0174705

CHONDROREGENERATION

In addition to protecting from cartilage loss, collagen peptides supplementation led to an increased number of chondrocytes in the cartilage. This effect was again dose-dependent. Chondrocyte apoptosis was reduced three weeks post-MLI in mice supplemented with collagen peptides, suggesting collagen-linked protection earlier in the process.

Interestingly, collagen peptide supplementation also resulted in a higher number of active cells. The number of chondrocytes that were actively producing aggrecan, one of the major constituents of cartilage matrix, was significantly increased under HD treatment.

Peptan increases the number of proteoglycan-secreting chondrocytes



Twelve weeks after OA induction cartilage architecture was evaluated to determine the percentage of chondrocytes in the tibial uncalcified cartilage.

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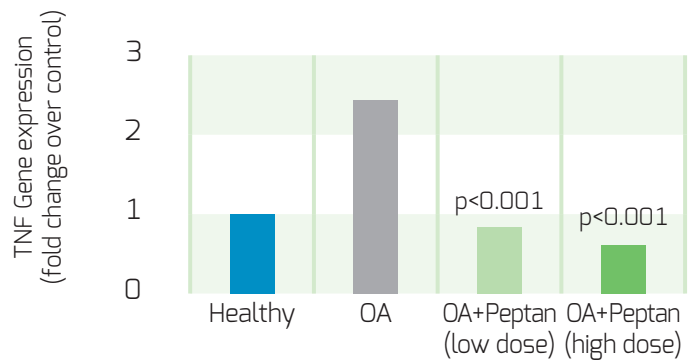
INFLAMMATION REDUCTION

At both three and twelve weeks post-MLI, the synovium, the membrane that encases the joint, showed strong signs of inflammation, which is today considered to be one of the main drivers of OA disease progression. Unexpectedly, supplementation with collagen peptide completely eliminated

the inflammation of the synovium. At three weeks synovial scores of the collagen supplemented mice trended towards a reduction with even clearer results at twelve weeks, when the synovium from mice in the HD group showed significantly lower inflammation levels evidenced by lower expression levels of the pro-inflammatory molecule tumor necrosis factor (TNF), clearly indicating an anti-inflammatory effect of collagen peptide supplementation.

Mice from both the HD and LD group showed significantly reduced level of (TNF) three weeks post-injury. Note that inflammation is especially at an early stage of the disease. This statistically significant effect persisted up to twelve weeks in the HD group.

Peptan improves joint inflammation



Three weeks after OA induction the joint synovium was analyzed for the gene expression of inflammatory markers (TNF).

Dar, 2017

CONCLUSION

The efficacy of nutraceuticals comprised of cartilage matrix components in supporting joint health is a hot topic in the industry. For the first time, these novel results unravel the mechanisms of action of collagen peptides. They demonstrate that demonstrates that daily consumption protects against cartilage loss, stimulates the production of proteoglycan by chondrocytes and inhibits synovial inflammation in the context of post-traumatic osteoarthritis. Overall, these results suggest that collagen peptides are chondroprotective, chondroregenerative and anti-inflammatory, putting collagen peptides in a leading position for joint health within the supplement sector. The collagen peptides used in Dar, 2017 the study discussed in this whitepaper is Peptan, produced and marketed by Rousselot.



Your Rousselot and Peptan sales contact information

About Rousselot. Reaching Further Together.

Rousselot and Peptan are both brands of Darling Ingredients Inc. Rousselot is the global leader* of gelatin and collagen peptides. Rousselot's wide range of collagen peptides are marketed under the Peptan brand. We work in partnership with our customers all over the world, delivering innovative and advanced ingredient solutions manufactured through state of the art operations. We help our customers achieve their goals, enabling them to create world class pharmaceutical, food and nutritional products to inspire and excite today's demanding consumers.

**Source: Global Industry Analysts, Inc., Gelatin a Global Strategic Business report, Nov 2016*

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