

Peptan[®] IIm

HYDROLYZED COLLAGEN TYPE II MATRIX

BRINGING JOINT HEALTH A STEP CLOSER



Protects cartilage

Provides cushioning
and lubrication

Reduces
inflammation

Collagen Peptides for a Healthy Lifestyle

PRODUCED & MARKETED BY ROUSSELOT

Peptan[®]

DARLING
INGREDIENTS



How consumer needs are fueling demand for effective joint health supplements

Today's consumers desire lifelong mobility

More and more consumers today want to stay active and enjoy maximum mobility for as long as possible in life. For some, this active means running marathons and going on strenuous mountain biking rides, using fitness trackers and smart devices to monitor their performance; others are less ambitious and simply want to enjoy walking the dog or feel comfortable going up and down the stairs.

Many people are affected by joint stiffness and discomfort

Whatever the level of intensity, physical activity puts our bodies under pressure. Like aging, engaging in high-impact movement or sports, even for younger people, can result in stiffness, discomfort and locking in the knees, hips, fingers, shoulders and lower spine region. Many people are affected. According to CDC¹, by 2040, an estimated 78 million US adults ages 18 years (26%) or older are projected to have medically-diagnosed arthritis.

Effective health supplements are in high demand

More and more consumers are recognizing our ability to move freely and efficiently requires healthy joints that function smoothly and recover well after exercise. The combination of an aging population and rising demand for preventative nutrition opens exciting possibilities for effective joint health supplements. According to a publication in *Complementary Therapies in Medicine*², for example, 62.5% of arthritis sufferers reported taking at least one dietary supplement over the past 30 days. With numerous joint health supplements available on the market, active consumers are increasingly looking for supplements with specific characteristics:

- ingredients from natural sources;
- proven efficacy in relieving joint discomfort and improving joint function;
- proven efficacy in protecting cartilage and preventing future problems.

¹ Center for Disease Control and Prevention https://www.cdc.gov/arthritis/data_statistics/arthritis-related-stats.htm

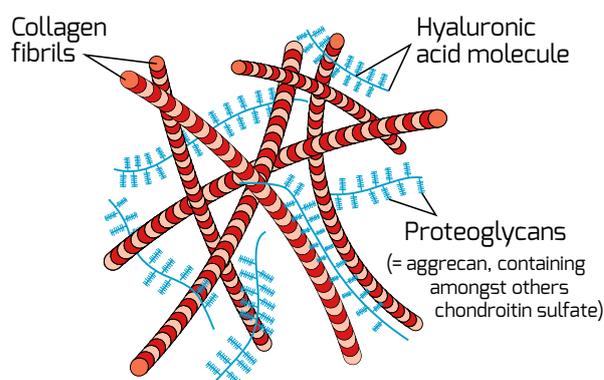
² Wilson, P. B., 2016, Dietary supplementation is more prevalent among adults with arthritis in the United States population. *Complementary Therapies in Medicine*, 29, 152-157. doi:10.1016/j.ctim.2016.10.004

Understanding joint health in order to take it further

Free motion joints are the keys to our mobility

As humans, we have about 350 joints in our bodies. Among them are our synovial joints, a special subgroup that exists in different parts of our bodies such as shoulders, elbows, knees and more.

They are also called free motion joints, as they facilitate a wide range of movements. Of all the types of joints in our bodies, our synovial joints are most often affected by the negative impact of exercise.



Cartilage provides the cushioning

A joint consists of at least two movable parts, or bodies. At the point at which they meet, bones are covered with hyaline cartilage, which provides cushioning and reduces friction as they slide over or against each other. Approximately 60% of cartilage consists of a substance called collagen type II and 40% the other matrix elements.

The matrix that protects and supports our joints

The hyaline cartilage in synovial joints is a very firm gel-like substance that has a specific form and function. This cartilage contains water and a specific build-up of molecules.

The predominant matrix elements are:

- **Collagen type II fibers:** these are the main structural component of cartilage, providing structure, firmness and resistance to compression;
- **Glycosaminoglycans (GAGs):** these are part of proteoglycans, the most important in cartilage being aggrecan. Chondroitin sulfate and hyaluronic acid are GAGs, building blocks of aggrecan. GAGs are essential components for maintaining a cushioned and lubricated environment allowing for easy joint movement.

This duo is responsible for protecting and supporting the hyaline cartilage that keeps our joints working the way we want them to.

New insights on the most common joint problem, osteoarthritis

The most common chronic condition of the joint is osteoarthritis (OA), also known as degenerative joint disease or 'wear and tear' arthritis. OA patients suffer pain, swelling, tenderness and warmth in the joints. Traditionally, OA was seen as an inevitable consequence of cartilage wear and tear. Today, researchers and medical doctors acknowledge that a (local) inflammation of the joint is a key driver of the disease³. The breakdown of cartilage matrix triggers an inflammation in the cartilage, the synovial membrane and even the underlying bone. The tissues release inflammatory mediators, pro-inflammatory cytokines, that accelerate the breakdown of cartilage matrix. The matrix breakdown products for their part attract inflammatory cells to the joint, driving the inflammation forward⁴. The joint inflammation leads to an increased volume of joint fluid. This causes joint swelling, damages cartilage and bone, and may result in muscle loss. Nerves in the joints are activated, causing pain. The inflammatory cytokines may also directly activate pain receptors, worsening the pain⁵.

³ Chevalier, X. et al., 2012, Nature Reviews

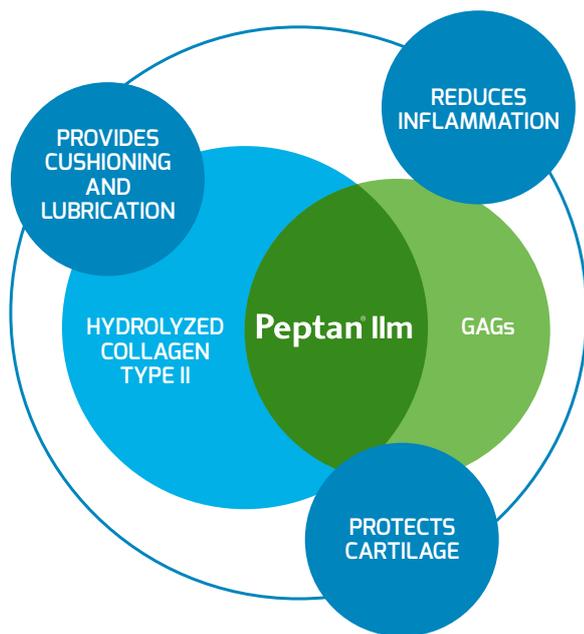
⁴ Lieberthal, J. et al., 2015, Osteoarthritis and Cartilage, 23: 1825-1834

⁵ Lange-Brokaar, B. et al., 2015, Arthritis & Rheumatology, 67(3): 733-740, Rheumatology 9(7): 400-410

Peptan Ilm, hydrolyzed collagen type II matrix delivering multiple joint health benefits

A single matrix ingredient with multiple joint health benefits

Extracted from natural sources, Peptan Ilm is a unique hydrolyzed cartilage matrix that contains hydrolyzed collagen type II in the form of bioactive peptides and glycosaminoglycans, so called GAGs. Its unique composition contains the same matrix ingredients, found in human cartilage as well. Its effects on users: Peptan Ilm provides multiple joint health benefits, including reduction of joint inflammation.



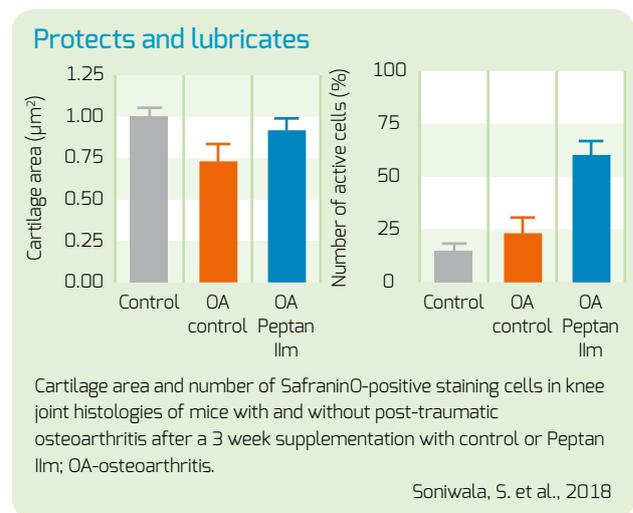
Peptan Ilm's effects on joint health, as demonstrated in scientific studies

Peptan Ilm has been shown to be an effective joint health ingredient in a recent set of *in vivo* studies⁶. Its efficacy was demonstrated in the context of injury-related osteoarthritis, as well as a combined mouse model of post-traumatic and obesity-induced osteoarthritis.

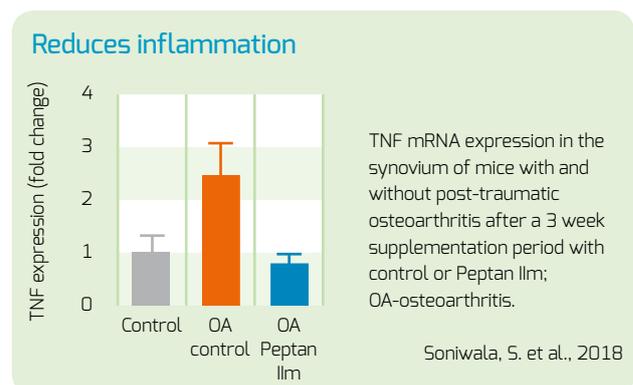
⁶ Soniwalla, S. et al., 2018. Oral Hydrolyzed Type 2 Collagen Protects Against the OA of Obesity and Mitigates Obese Gut Microbiome Dysbiosis. Poster presentation at ORS 2018 and OARSI 2018

In a model for post-traumatic osteoarthritis, joint injury induces the loss of cartilage (matrix and cells) and a strong local inflammation of the knee joint. Supplementation with Peptan Ilm at a low dose clearly demonstrated the following:

- Protection of the cartilage from degeneration (normalization of cartilage area, blue bar) and promotion of lubrication through the stimulation of proteoglycan synthesis in chondrocytes (increase in % of active cells, blue bar).



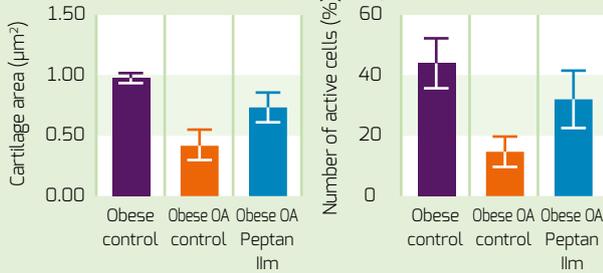
- Promotion of anti-inflammatory action in the knee joint (reducing local expression of inflammation markers in the synovial membrane, blue bar).



In a model for obesity-associated osteoarthritis combined with injury, the loss of cartilage (matrix and cells) and local inflammation of the knee joint were induced in an even shorter time. Peptan Ilm supplementation at a low dose resulted in a preventative effect helping to:

- Protect the cartilage from degeneration (normalization of cartilage area, blue bar) and promote lubrication by stimulating proteoglycan synthesis in chondrocytes (increase in % of active cells, blue bar) in animals rendered obese by means of a high-fat diet.

Protects & lubricates in obesity-associated OA



Cartilage area and number of SafraninO-positive staining cells in knee joint histologies of HFD-fed mice with and without post-traumatic osteoarthritis after a 3 week supplementation period with control or Peptan Ilm; OA-osteoarthritis.

Soniwala, S. et al., 2018

- Efficient protection of the knee joint from local, synovial inflammation in animals rendered obese by means of a high-fat diet.

Reduces inflammation in obesity-associated OA



TNF immunohistochemistry in knee joints of HFD-fed mice with and without post-traumatic osteoarthritis after a 3 week supplementation period with control or Peptan Ilm; OA-osteoarthritis; M-meniscus, F-femur, T-tibia.

Soniwala, S. et al., 2018

Brown staining, as indicated by the arrows, represents inflammation. In the obese OA – control image, the staining is apparent, while in the obese OA – Peptan Ilm image, there is no staining.

Highly bioavailable

Studies⁹ have shown Peptan Ilm has a high absorption rate, indicated by high levels of hydroxyproline after one hour of ingestion.

Efficient absorption



Serum hydroxyproline in mice 1h after ingestion of a Peptan Ilm bolus, after a supplementation period of 3 weeks and 12 weeks respectively.

Soniwala, S. et al. 2018.





Using Peptan II^m to uniquely position your joint health supplement in the market

Your answer to consumers in pursuit of an active, healthy lifestyle

If you are a nutraceutical manufacturer seeking to serve consumers who are in pursuit of an active, healthy lifestyle, Peptan II^m offers you the perfect solution.

- **An all-natural, bioactive and safe ingredient**

Peptan II^m is a unique hydrolyzed cartilage extracted from natural sources, it contains hydrolyzed collagen type II in the form of bio-available peptides and glycosaminoglycans (GAGs) of which chondroitin sulfate and hyaluronic acid. Peptan II^m is absorbed by the body, works on location and simultaneously delivers triple joint health benefits.

- **Low daily dosage for maximum convenience**

Consumers today want joint health supplements that offer convenience. Peptan II^m supports joint health at a low daily dosage (1-3 g/day), feasible for tablets and capsules, allowing consumers to easily ingest the product.



- **Designed for use in tablets and capsules, while being cold water-soluble**

Having a good flowability and consistent powder specification, Peptan II^m is fully adapted for tableting processes and can be encapsulated. While, at the same time, it has excellent cold water solubility, allowing incorporation in functional food and beverage solutions, such as liquid shots. It is also possible to formulate in nutritional confectioneries.

- **FDA-notified GRAS* and clean label**

Peptan II^m is a natural, clean label, non-drug nutraceutical ingredient, free of additives and preservatives.

*The FDA had no questions in response to the GRAS (Generally Recognized as Safe) notification for Peptan II^m.



Benefit from our (co-)innovation, commitment & world-class expertise

1. Trustworthy, up-to-date science

Peptan offers proven efficacy in extensive *in vitro*, *in vivo* and double blind, placebo controlled clinical studies and is recognized worldwide for its unrivalled scientific backing.

We'll help you communicate the science, too.

2. Quality & safety

Peptan is manufactured in-house in state-of-the-art certified plants which meet the highest international food quality standards and ensure traceability of products and processes. A premium quality collagen peptide, Peptan is free from preservatives or additives.

Full control from source to final product.

3. Formulation optimization

Peptan Application centers develop new product formulation concepts and share ideas and recipes. We facilitate the optimal use of Peptan in your applications.

We can help get your product faster to market.

4. Co-innovation

Global network of experts are available to help you develop successful, marketable product innovations with Peptan.

We are happy to co-innovate with you.

Join our Innovation Days to gain insights of the latest marketable innovations.

5. Brand development

We also offer outstanding brand development support. You can benefit from endorsement by Peptan branding and the opportunity to list Peptan as one of the ingredients used in your product.

Contact us to know more about our co-branding program.

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About Rousselet and Peptan:

Rousselet is the global leader¹ of gelatin and collagen peptides. Rousselet'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. Rousselet and Peptan are both brands of Darling Ingredients Inc.

¹ Global Industry Analysts, Inc, Gelatin a Global Strategic Business report, Nov 2016

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