

PEPTAN[®] FOR HEALTHY JOINTS AND BONES



Collagen Peptides for a Healthy Lifestyle

Peptan[®]

PRODUCED & MARKETED BY ROUSSELOT

DARLING
INGREDIENTS



Aging and more active lifestyles are pushing demand for joint and bone health nutrition

Demand for nutritional solutions offering joint and bone benefits is up. A healthy, active lifestyle is one of the great ideals of our time. This is leading consumers, old and young, not only to engage in more exercise, but also – and increasingly – to look for nutritional solutions that will help them sustain a physically active lifestyle for as long as possible. As more and more people look for ways to stay fit, awareness of the vital role of strong joints and bones is also on the rise. As a result of these developments, the market for nutritional solutions that can offer proven benefits to joints and bones is booming, and opportunities for manufacturers are huge.

Joint and bone health solutions matter to many different consumer groups today

Nutritional solutions aimed at healthier joints and bones are no longer a niche product. High-intensity exercise – a growing pastime among consumers worldwide – can place extreme pressure on joints, often causing joint discomfort and injury to connective tissue. Individuals with overweight also suffer joint strain. Another major driver in this market is the aging of populations. As the global population gets older, joint- and bone-related health concerns are becoming quite common.

Peptan: a natural answer to the mobility trend

Supporting healthy cartilage, joint function and strong, healthy bones

Collagen peptides are vital ingredients for healthy joints and bones. Collagen fibers make up 70 to 95% of our cartilage and 90% of organic bone mass. They are responsible for its structure and strength. In order to maintain healthy joints, our bodies need building blocks that will support tissue regeneration. Collagen peptides are a source of bioactive peptides, which offer benefits for our cellular metabolism. This means collagen peptides actively support healthy cartilage and joint function as well as bone health and strength.

Peptan, the world's leading collagen peptides brand

With Peptan – the world's leading collagen peptide brand – you have an outstanding joint and bone nutrition solution. Peptan collagen peptides have a unique amino acid profile, containing high levels of the amino acids glycine, hydroxyproline, proline, alanine and arginine – and thus providing specific nutritional benefits not found in other protein sources. Rapidly gaining popularity, our collagen peptides can be used alone or in combination with other ingredients. Peptan is widely used in dietary supplements and is easy to integrate in functional food and beverage products.

Scientific evidence of mobility benefits means long-term success

As this market expands, research into ingredients that will support consumers in their health and wellness pursuits has intensified. A growing understanding of physical fitness and wellbeing is leading manufacturers and consumers to place ever higher demands on the benefits as well as the quality, safety and natural origins of the ingredients they use – and on the science behind it all. Performing the science, in fact, is one of the secrets to dependable, lasting results in nutrition. With Peptan, you have a partner offering outstanding joint and bone health solutions with reliable scientific backing. Peptan is a natural, clean label food ingredient, free of additives and preservatives. It is the perfect solution for manufacturers seeking to serve customers in pursuit of an active, healthy and fit lifestyle.



Science's answer to joint health challenges

Consumers today, young and old, look for solutions that can alleviate current joint problems and help prevent future ones. Peptan offer such multiple benefits, -a natural and effective solution to move freely and maintain healthy and flexible joints.

How it works

Human cartilage contains cellular building blocks (chondrocytes). These produce our extracellular matrix, which consists of collagen and proteoglycans (mainly aggrecan). Collagen fibers make up 70-95% of cartilage and are responsible for its structure and strength, while proteoglycans lubricate and cushion our joints. Healthy cartilage relies on a finely balanced process that breaks down collagen and aggrecan and replaces them both with newly-formed matrix. If the process is disturbed, increased matrix breakdown leads to a loss of cartilage and joint function. Peptan collagen peptides are designed to keep this process in balance.

Proven joint benefits of Peptan

Several in vivo and randomized double-blind placebo-controlled clinical studies have proven that offering multiple benefits that you will not find combined in other joint health supplements.



Peptan can keep joints healthy by:

- Reducing joint discomfort and stiffness¹
- Acting as a cellular trigger to increase collagen and aggrecan production²
- Helping to prevent cartilage degeneration and support healthy joints³
- Uniquely helping to reduce joint inflammation³, a leading cause of joint discomfort

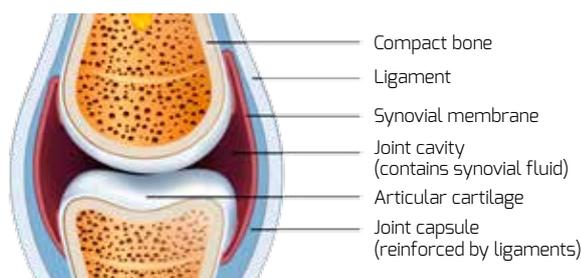
Additional facts highlighted by recent scientific studies:

- Subjects with the greatest joint deterioration benefited the most from the effects of collagen peptides^{4,5}
- Healthy athletes with reduced joint discomfort also benefited from collagen peptides when walking, standing or carrying objects⁶.



Highlights from scientific studies

As one of the most extensively researched collagen peptides brands available on the market today, Peptan's multiple benefits for joint health are well-documented. On these pages, we've presented some of the highlights from our scientific research.

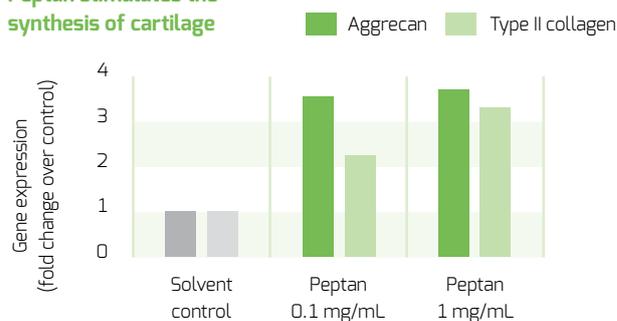


Peptan stimulates chondrocytes, boosting the production of matrix components

In an *in vitro* study², primary cartilage cells, or chondrocytes, were cultured in the presence of different concentrations of Peptan. The purpose was to demonstrate Peptan's ability to induce the production of the key cartilage components aggrecan and type 2 collagen.

Peptan treatment clearly stimulated the expression of aggrecan and type 2 collagen by the cartilage cells.

Peptan stimulates the synthesis of cartilage



Effect of different concentrations of Peptan on the gene expression of extracellular matrix components (aggrecan and collagen Type II) in chondrocytes.

Rousselot unpublished data 2011

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▪ **Less discomfort and stiffness with Peptan**

In a randomized, placebo-controlled, double-blind clinical trial¹, 94 women aged 40 to 70 with knee joint problems (osteoarthritis classification: 0-III) received 8g of Peptan or placebo daily for a period of six months. The efficacy of Peptan was assessed by two established and standardized questionnaires. The WOMAC score (the lower the better) measured joint pain and joint function in daily life, while the Lysholm score (the higher the better) evaluated knee joint function when limping, walking, jumping and stair climbing.

- Peptan treatment resulted in a statistically significant reduction of the WOMAC score by 24% linked to a 32% decrease in joint pain and a 44% improvement in stiffness (subscale scores).

Peptan reduces joint discomfort

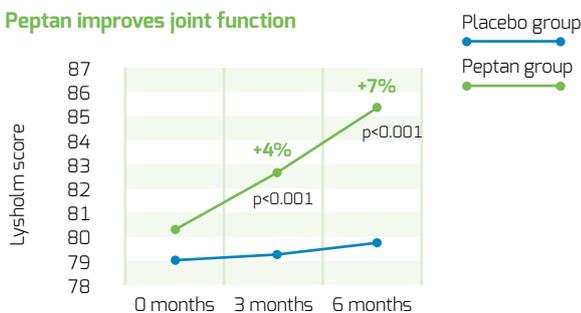


Development of the WOMAC score assessing joint discomfort (decreased score = improvement) after the intake of Peptan or placebo over the duration of 6 months.

Jiang, 2014

- Peptan treatment also resulted in a statistically significant increase of the Lysholm score by 7%, which demonstrates the improvements over time.

Peptan improves joint function



Development of the Lysholm score assessing joint function (increased score = improvement) after the intake of Peptan or placebo over the duration of 6 months.

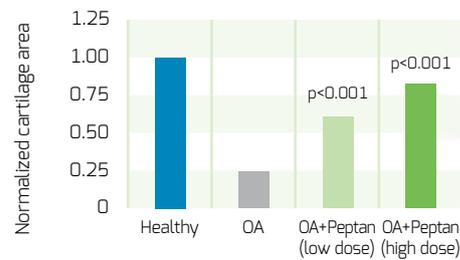
Jiang, 2014

▪ **Protecting cartilage and reducing joint inflammation with Peptan**

A new in vivo study confirms Peptan collagen peptides' role in supporting joint health by providing clear evidence of Peptan's ability to protect the cartilage and to reduce inflammation in mice³. Reporting a visible reduction of cartilage loss in response to osteoarthritis and injury. The research findings highlight Peptan's capacity to dose-dependently preserve cartilage and to stimulate the production of extracellular matrix proteoglycans, which are involved in joint lubrication and cushioning.



Peptan prevents cartilage degradation

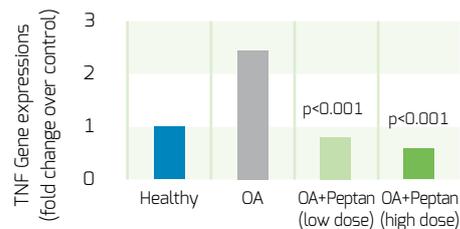


Osteoarthritis (OA) was induced by surgery in mice that received Peptan at two different dosages or a control twelve weeks after OA induction. Histology of the knee joints was performed and the area of the (tibia) cartilage was quantified.

Dar, 2016

A common symptom of joint inflammation is the thickening of the synovial membrane which surrounds the knee. This thickening and the presence of inflammation markers was significantly reduced in the Peptan-treated groups. These findings have since been presented at international scientific congresses, such as the Annual Meeting of the Orthopaedic Research Society and at the World Congress on Osteoarthritis.

Peptan improves joint inflammation



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

Dar, 2016

Science's answer to bone health challenges

With age, bones can become weaker and more fragile leading to risks of fractures. With Peptan you can offer consumers a reliable and natural nutritional solution for strong, healthy bones.

The building blocks for healthy bones

Bones are dynamic, living and growing tissues. Representing around 90% of organic bone mass, collagen is a protein that provides bones with their flexible framework. Calcium phosphate is deposited on this framework, adding strength and stabilizing the bone. In other words, collagen and calcium together give our bones their stability, flexibility and stress resistance.

Throughout a person's lifetime, old bone tissue is broken down (bone resorption) and new tissue is added to the skeleton (bone formation). This process is called bone remodeling, or bone turnover. In healthy adults, bone turnover replaces approximately 15% of our bone per year. As we age, bone resorption begins to exceed bone formation. We can help to preserve our bone health with regular exercise and a balanced diet that includes the right nutrients: along with vitamin D and calcium, protein is essential.

Proven bone benefits of Peptan

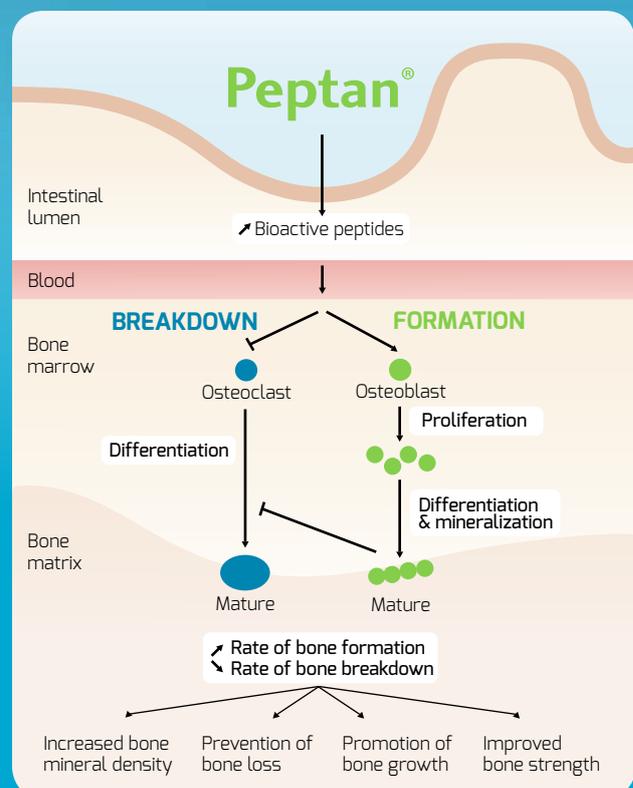
Several scientific studies have proven Peptan's numerous benefits for bone health^{7,8,9}:

- Peptan helps maintain bone mineral density (BMD) and thus prevent bone loss
- Peptan helps maintain bone strength and a healthy bone micro-architecture

- Peptan is efficiently digested (<90%) and absorbed into the blood stream in form of small peptides within one hour
- Peptan helps balance bone formation and bone breakdown
- Peptan actively stimulates bone building metabolism (proliferation, differentiation and mineralization of osteoblasts)
- Peptan slows down the activity of bone-degrading cells (differentiation and function of osteoclasts)

Peptan: the mechanism of action

Schematic summary of the effect of Peptan on bone metabolism, adapted from Daneault, 2015¹⁰



Studies show Peptan's positive effect on bone metabolism

On top of delivering the right 'building blocks' for healthy bones, Peptan contributes to improved modulation of bone metabolism, as the studies presented below demonstrate.

Improving bone quality

In a set of *in vivo* studies at a leading French academic research institute^{7,8} ovariectomized (Ovx) mice were used to mimic the loss of bone mineral density following the onset of menopause in women. The animals were fed a diet containing Peptan or control protein over a 12-week period. A group of healthy (non-ovariectomized) mice was also used as a control.

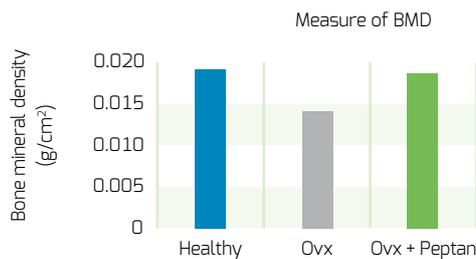
The study found that the group taking Peptan maintained the same bone mineral density (BMD) level as the non-ovariectomized

mice over the test period, showing that a daily intake of Peptan can restore bone mineral density. The daily intake of Peptan over a 12-week period was also shown to promote the restoration of bone size and increase bone strength and solidity. A follow-up experiment investigating the preventive effect of Peptan by starting the treatment one month before ovariectomy clearly demonstrated that Peptan can not only help restore, but can also protect against, bone loss.

Blending Peptan with other health ingredients

In an *in vivo* study the combined oral administration of collagen peptides with calcium citrate inhibited bone loss in ovariectomized mice¹¹, suggesting that the combination of collagen and calcium can create a synergistic effect on bone mineral density.

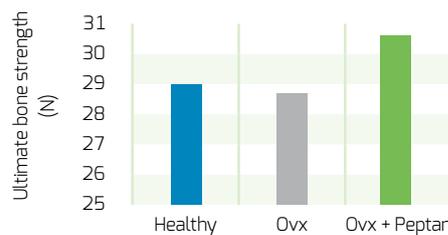
Peptan improves bone mineral density



Menopause was induced by ovariectomy (Ovx) in mice and the animals were supplemented with Peptan or a control for twelve weeks. Bone mineral density was measured by DEXA.

Guillerminet, 2010, 2012

Peptan increases bone strength



Menopause was induced by ovariectomy (Ovx) in mice and the animals were supplemented with Peptan or a control for twelve weeks. The ultimate bone strength was determined by the 3-point bending test.

Guillerminet, 2010, 2012

References

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A holistic approach to joint and bone health



Dairy



Powder drinks



Beverages



Tablets and capsules



Nutritional bars



Other applications

Peptan: easy to use, easy to digest

Research has shown that over 90% of collagen peptides are digested and quickly absorbed after oral ingestion – ready to deliver their benefits to the consumer^{12,13,14}. Manufactured by means of a unique enzymatic hydrolysis process, Peptan collagen peptides are broken down into smaller peptides that are easy for the body to absorb and put to use.

High protein content, neutral taste and odor

Containing more than 97% protein (dry weight basis), Peptan powder is neutral in taste, odor and color. It can be used alone as powder supplement or you can incorporate it in other supplements or functional foods and beverages.

Compatible with other minerals and vitamins for a synergistic effect

If you want to optimize the positioning of your joint and bone product, you can combine Peptan with other joint and bone health ingredients, such as vitamin D, K, calcium, magnesium etc. You can also blend Peptan with other proteins to target specific consumer groups, such as healthy agers and sports people.

Peptan is available in a wide range of product grades to match any formulation or product requirement. Adapted for dietary supplements, Peptan is for example perfect for tablets and capsules:

- Easy to handle during operations
- Fully adapted to tableting processes (direct compression and wet granulation)
- Can be used directly as dry powder at high dosage (99.5%)
- Consistency in powder specification



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

With Peptan, you will have a reliable, closely connected partner

Our global leadership in collagen peptides, combined with our worldwide presence and customer-centric culture, enables us to be a closely connected, reliable partner to you as a manufacturer.

We can help you with virtually any product requirement or innovation you have in mind. Here are some key benefits you will enjoy as you partner with Peptan.



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 is available to help you develop successful, marketable product innovations with Peptan – we are happy to co-innovate with you.

Join our Innovation Day 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 and Peptan are both brands of Darling Ingredients Inc. 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.

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

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