Arthred™

Nutrition for healthy joints

Totally Derma®

Joint problems – one of the leading risks of disability

Early protection of cartilage is very important to ensure its health over time. Everyone is at risk of decreasing joint health as a result of the natural ageing process, environmental influence, and congenital or inherited factors. Individual lifestyles that may influence joint health include obesity and strenuous physical activities, e.g. professions involving activities, exercises, or sports that continually stress joints or cause injury. Proper nutrition, lifestyle choices to maintain or achieve a healthy body weight, and protection from abrasion with exercise, rest, and relief from stress are important factors in maintaining joint health [1, 2]. In addition, cartilage should be stimulated to regenerate itself as much as possible [3].

What is Arthred™ hydrolysed collagen?

Arthred™ hydrolysed collagen is produced by enzymatic hydrolysis of collagen from cattle under controlled conditions [4]. Hydrolysed collagen or hydrolysed gelatin is a special type of gelatin with a much lower molecular weight (MW). This enzymatic hydrolysis process yields short-chained peptides having a low mean MW of approximately 3 kilodaltons (kDa) (mean chain length of 25 - 30 amino acids). Upon further processing, the product is spray-dried into an agglomerated form which offers excellent solubility. Because it is sourced from animal collagen, the amino-acid composition of the peptides resembles that of collagen in human articular (joint) cartilage. The product has a high content of the amino acids hydroxyproline and hydroxylysine as is characteristic of collagen. The predominant amino acids in Arthred™ hydrolysed collagen – glycine, proline, hydroxyproline, lysine, and hydroxylysine – comprise approximately 50% of the substance, by weight.

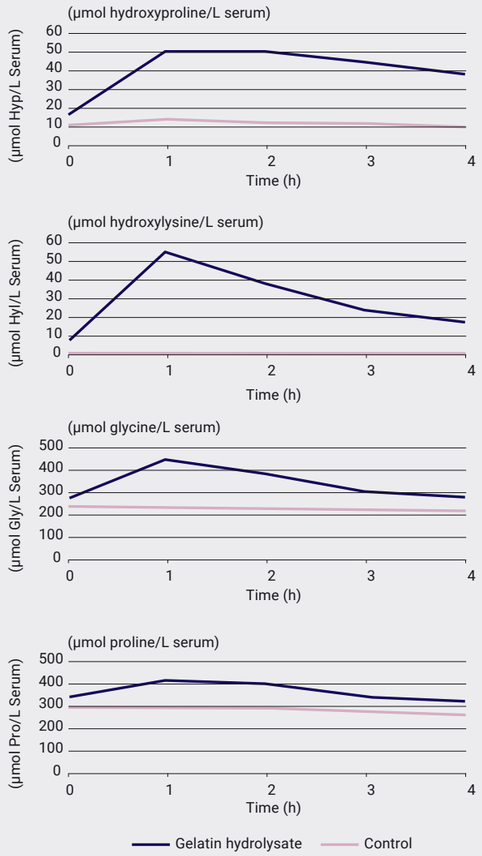
Bioavailability of Arthred™ hydrolysed collagen

The term bioavailability describes the degree to which a substance can be absorbed and is available to interact in metabolism. The bioavailability of protein from protein fragments is influenced mainly by size and amino-acid composition. Absorption and distribution of Arthred™ hydrolysed collagen clearly differs from that of free amino acids and, due to its low mean MW (2-3 kDa), from that of conventional collagen (30-90 kDa). As a concentrated source of typical collagen amino acids (glycine, proline, hydroxyproline, lysine, and hydroxylysine) and peptides, Arthred™ hydrolysed collagen helps to supply them to collagen-containing tissues, such as cartilage, throughout the body [3].

Clinical studies

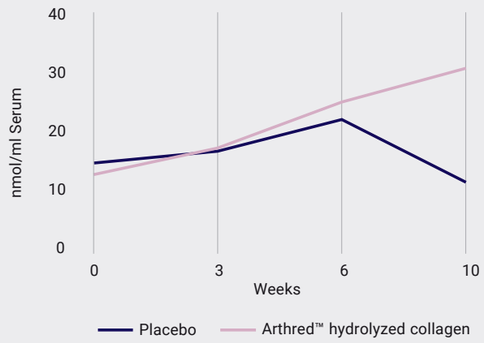
Hydroxyproline is one of the main components of Arthred™ hydrolysed collagen and is therefore a good marker whose uptake can be quantified in blood serum [10]. The absorption of short-term orally-administered hydrolysed collagen was measured by a single supplementation of 10g Arthred™ hydrolysed collagen. When compared to a standard diet control without hydrolysed collagen, supplementation resulted in a significant increase in collagen characteristic amino acids like hydroxyproline, hydroxylysine, glycine, and proline in blood serum [9] (see chart, right).

Amino acid concentration in serum after oral administration of gelatin hydrolysate



Beuker et al. (1993) conducted a double-blind, placebo-controlled clinical trial involving 52 student athletes (aged 21 to 27 years) to investigate amino acid concentrations in serum following long-term oral administration of Arthred™ hydrolysed collagen or a standard diet without hydrolysed collagen (placebo) during exercise [10]. The athletes performed one hour of physical training three times a week during a period of four months. The collagen-specific amino acid hydroxyproline concentration in plasma was continuously and significantly elevated during supplementation with hydrolysed collagen providing evidence that collagen was absorbed into the bloodstream. The placebo had no effect on hydroxyproline levels in the blood (see following chart).

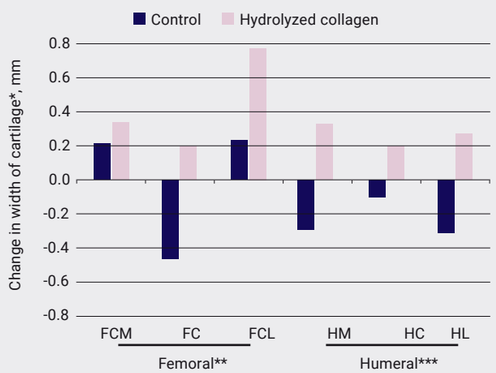
Hydroxyproline concentration during supplementation with Arthred™ hydrolysed collagen in humans



The most recent clinical studies provide the first indication of the ability of hydrolysed collagen to support more normal joint function and cartilage homeostasis. This clinical research has been conducted among generally healthy athletes providing preliminary evidence that hydrolysed collagen may help in the maintenance of healthy cartilage homeostasis.

Among healthy, competitive Spanish male mountain bikers (n=16) and female basketball players (n=10), Fernandez and Perez (1998) examined the effect of hydrolysed collagen (also called hydrolysed gelatin) on shoulder and knee joints. Subjects consumed hydrolysed collagen (10g/day) enriched with magnesium, vitamins B1, B2, B6 and pantothenic acid for a six-month period [11]. After supplementation, biometric ultrasound values of the cartilage showed statistically significant increases of cartilage thickness in supplemented athletes while control subjects exhibited either no change or decreasing cartilage thickness (see chart, below). This indicates that enriched hydrolysed collagen may help maintain cartilage homeostatis and joint health among athletes whose joints have been stressed through competitive athletic performance.

Effect of hydrolysed collagen on cartilage thickness



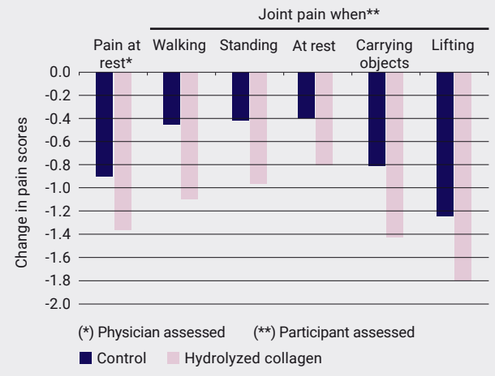
* Change in width of cartilage following 6 months of supplementation

** Femorotibial cartilage: medial condylar (FCM), intercondylar notch (FC), lateral condylar (FCL)

*** Cartilage of the humeral head (HM), central (HC), lateral (HL)

Clark et al. (2008) investigated the effects of collagen hydrolysate on generally healthy and physically active subjects (n=97) competing in varsity or club sports and complaining from joint pain or discomfort [13]. Athletes were excluded from the study population if they 1) did not have joint pain or discomfort, 2) had an acute injury or inflammatory process, 3) consumed chondroitin, glucosamine, or other dietary supplements indicated for joint health, or 4) were likely to increase their dose of analgesics due to severe symptoms of arthalgia. In this 24-week, randomized, double-blind, placebo controlled study, subjects received either 10g collagen hydrolysate per day in a 25 ml liquid formulation or a placebo that contained xanthan. Physician and participant-assessed joint pain measures assessed by visual analogue scales were improved (clinically and statistically significant) with supplementation of collagen hydrolysate (see chart, below). The improvement in pain was more pronounced in a sub-group of subjects with knee pain. These results from clinical studies in generally healthy and physically active subjects provide preliminary indication that collagen hydrolysate may promote the healthy functioning of joints under conditions that may be associated with increased catabolic or degenerative processes in cartilage homeostasis.

Effect of hydrolysed collagen on cartilage thickness

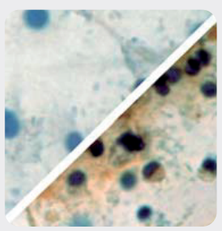


Mode of action of hydrolysed collagen

The functional integrity of cartilage is dependent on maintenance of the extracellular matrix, a process controlled by articular chondrocytes as previously described. Oesser and Seifert (2003) investigated the effect of hydrolysed collagen on the formation of type II collagen by articular chondrocytes in a cell culture model [3]. Chondrocytes were cultivated over a period of eleven days. In the presence of collagen hydrolysate (0.5mg/mL) and type II collagen, the articular chondrocytes were able to stimulate type II collagen biosynthesis over the 11-day period. (See chart, below).

Enhancement of type II collagen biosynthesis by hydrolysed collagen

Without hydrolyzed collagen



With hydrolyzed collagen

The control, containing native type I and type II collagen in a collagen free hydrolysate, failed to show any effect (see chart, previous page). These results indicate a stimulatory effect of hydrolysed collagen on type II collagen biosynthesis of chondrocytes and suggest the need for further testing to determine the mechanisms that regulate collagen biosynthesis. This study and other work by Oesser (Bello and Oesser, 2006 [14]; Oesser et al., 1999 [8]) suggest that collagen hydrolysate is absorbed from the intestine in its high molecular weight form, preferentially accumulates in the cartilage, and is able to stimulate chondrocyte metabolism. Oesser and colleagues speculate that collagen hydrolysate may be useful as an oral supplement to activate collagen biosynthesis in human chondrocytes in conditions where cartilage is stressed and joints are painful. They further identify individuals who may experience joint stress, discomfort, or pain as including individuals age 50 and older, active and vigorous athletes, individuals engaging in repetitive motions, and individuals who are overweight, sedentary, or have a familial history of joint disease. These conditions correspond to those that are known to shift cartilage homeostasis to a more catabolic state.

Safety and regulatory considerations

The raw material for Arthred™ hydrolysed collagen is sourced from cattle. Raw materials used in the production of Arthred™ hydrolysed collagen originate from healthy animals that have been approved for human consumption by the relevant regulatory authorities. The manufacturing process for hydrolysed collagen is well-controlled leading to a product that meets food grade specifications. The FDA recognizes hydrolysed collagen (gelatin) as GRAS (Generally Recognized as Safe) when used in accordance with Good Manufacturing Practices [15,16,17]. In addition, the Scientific Committee on Food of the EU (European Union) confirmed in 2002 that gelatin (hydrolysed collagen) is safe for human consumption provided it is manufactured according to good hygiene practices [18]. Additionally, the European Food Safety Authority (EFSA) confirmed the safety of hydrolysed collagen or gelatin from cattle [19].

Summary

- Arthred™ hydrolysed collagen has short-chain peptides of low mean MW of approximately 3 kDa (mean chain length of 25 - 30 amino acids).
- Due to its source, the amino-acid composition of Arthred™ hydrolysed collagen resembles that of collagen in articular cartilage which is characterized by a high proportion of hydroxyproline and hydroxylysine.
- Arthred™ hydrolysed collagen is well-absorbed and the results of a study in mice suggests it accumulates in cartilage tissue.
- Preliminary results on the biometry of cartilage of competitive athletes indicate that hydrolysed collagen, such as Arthred™ hydrolysed collagen, might support joint maintenance in generally healthy, physically active individuals.
- In vitro studies indicate a possible stimulatory effect of Arthred™ hydrolysed collagen on the type II collagen biosynthesis and secretion in chondrocytes.
- A 10 g intake of Arthred™ hydrolysed collagen per day is suggested based on the available data.
- Arthred™ hydrolysed collagen is stable and readily soluble by stirring into cold or warm water. It does not gel in concentrated solutions.
- Hydrolysed collagen is confirmed as GRAS by the FDA and safe for human consumption by the Scientific Committee on Food of the European Union.

The statements in this brochure have not been evaluated by the Food and Drug Administration or EU regulatory authorities. This product is not intended to diagnose, treat, cure, or prevent any disease.

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