

Native Type II Collagen for Joint Health: Small Dose, Big Benefits

By Cai Berg

Collagens are the most abundant family of proteins in the extracellular matrix of connective tissues. They perform a variety of biological functions, the best known of which is providing the structural framework for tissues throughout the body. Based on their supramolecular organization, 26 different types of collagen have been identified, each with its own role and position in the body.

Type II collagen is the main structural protein in the cartilage. It provides tensile strength and toughness to the tissue. Joint disorders involving inflammation and cartilage erosion, such as arthritis, are often characterized by an autoimmune component in which the immune system acts against the body's own type II collagen.

Studies have shown that supplementing native (undenatured) type II collagen can help modulate the destructive immune response against endogenous type II collagen to support joint health and comfort.¹

Not All Collagens Are Equal

Collagen and collagen derivatives have been investigated and employed for joint nourishment for decades. Collagen products are defined by their degree of hydrolyzation and their molecular weight as either undenatured (native) collagen, collagen hydrolysate (hydrolyzed collagen) or gelatin. Undenatured (native) collagen has the highest molecular weight (300 kDa), while hydrolyzed collagen ranges from 2 to 9 kDa.

Unlike gelatin and hydrolyzed collagen supplements, which are intended to be absorbed to augment the collagen needs of various cells and tissues, native type II collagen supplements work through a mechanism known as oral tolerization. This immune-mediated process involves ingestion of an autoantigen (in this case, type II collagen) in order to suppress the immune response against endogenous tissue.



Oral Tolerization: A Unique Mechanism of Action

When taken orally, native type II collagen passes through the stomach without being denatured, reaching the small intestine intact. It is the presence of intact epitopes on undenatured collagen that allows for the process of oral tolerization.

In the small intestine, the undenatured collagen molecule interacts with the immune system through **Peyer's patches**, where it is recognized as native type II collagen. Peyer's patches are small nodules of lymphoid tissue found throughout the ilium of the small intestine. They are central to the mucosal immune system, monitoring the small intestine and signaling the activation or deactivation of relevant immune responses to foreign antigens.

In the Peyer's patch, orally ingested native type II collagen binds to specific immune cells, which then signal the greater immune system to stop its attack on the body's own type II collagen in joint cartilage. It's important to note that native type II collagen is not absorbed by the body. By simply binding to the immune

cells in the intestinal lumen, the molecule performs its function and is then excreted from the body.

Thanks to this specific mechanism of action, it takes just a small amount of native type II collagen to reduce inflammation and defend against collagen degradation. Whereas standard dosages for hydrolyzed collagen can be up to 10 grams per day, the standard dose of native (undenatured) collagen is just 10 mg once daily.

Clinical Evidence and Market Development

Use of native type II collagen for support of joint health was first investigated and reported in the early 1990s with a **breakthrough publication** in the journal *Science*.² More than two decades later, it remains an active field of study, although research has been limited by strong intellectual property concerns and commercial interests.

Originally developed by Harvard scientists with technology licensed to various entities over the years, the market for native (undenatured) type II collagen has been somewhat restricted. Now, advancements in extraction and manufacturing technologies have led to new clinical research and market competition.

Initial research with a specific form of native collagen type II followed the progress of 104 individuals with osteoarthritis of the hand, knee or hip for one year. Patients were treated with either glucosamine/chondroitin (1,000 mg each) or a combination of glucosamine/chondroitin and native collagen type II (2 mg).

Results showed a significant ($p < 0.05$) reduction in disease progression among the native type II collagen group as compared to baseline and those treated only with glucosamine/chondroitin. This was demonstrated both by radiologic score and by measurement of uCTX-1 and uCTX11 (markers of collagen breakdown).³

Subsequent animal studies found that native type II collagen induces significant analgesic effect (marking a reduction in joint pain) comparable to that achieved with 250 mg/Kg of glucosamine, and strongly reduced IL-1B and TNF-a plasmatic levels (marking reduction of inflammation).⁴

Further clinical studies found that just three months of supplementation with native type II collagen along with acetaminophen produced significant reduction in pain (VAS walking) for those with osteoarthritis of the knee compared to those taking only acetaminophen. The same study also found improvement of joint function as measured by WOMAC among those taking native type II collagen, while those taking only acetaminophen showed no such improvement.⁵

A Clear Opportunity

In a market enjoying high consumer demand, native type II collagen presents a clear opportunity. With a unique mechanism of action, clinical validation and flexibility to combine with established protocols, native type II collagen can be a valuable addition to any joint care program.

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