DISCUSSION

Type II Collagen

Type II collagen (CII) is the most abundant structural protein in cartilage. It provides tensile strength and toughness to the tissue. In some individuals, immune responses to endogenous CII may impact joint cartilage integrity and joint comfort. However, researchers have discovered that a repetitive low dose of chicken or bovine CII—when taken orally and in its native form—is able to support a naturally balanced and healthy joint environment in such individuals.[3-5] This is accomplished through a natural mechanism called oral tolerization (or “oral tolerance”), which supports the body’s desensitization process to a specific antigen—in this case, CII.[3] Oral tolerization using CII essentially works as follows:

- Orally administered native CII enters the Peyer’s patches (immune surveillance structures) in the gut-associated lymphoid tissue (GALT).*
- Dendritic cells in the GALT take up the CII and present it to T-cells to produce regulatory T-cells.*
- Regulatory T-cells change specific systemic immune responses via the production of certain regulatory cytokines (e.g., TGF-beta 1, IL-10 and IL-4).*
- Systemic immune tolerance to CII is induced by the body and endogenous CII is naturally protected.*

Human trials have been conducted to study the effects of oral CII in joint health.[4,6] In a multicenter, double-blind, placebo-controlled trial, 205 individuals were enrolled at six different sites and randomized to receive a placebo or an oral dose (20, 100, 500, or 2,500 mcg) of CII for 24 weeks. Efficacy was assessed monthly, and responses were analyzed utilizing three sets of criteria. Positive effects were observed at the lowest dose of CII, and no side effects were detected.[5] Trentham et al found beneficial effects on the size and comfort of joints in a randomized, double-blind, placebo-controlled trial involving 60 patients who were given 100-500 mcg/d of chicken CII for three months.[5] Aussar et al found beneficial effects in 90% of the subjects who received 0.5 mg/day of CII for 12 weeks.[6] Conversely, another 12-week study found no significant difference in benefit between three groups (placebo, 10 mg/d of CII, 1 mg/d of CII). There was, however, a higher prevalence of responders in the CII groups. Conversely, another 12-week study found no significant difference in benefit between three groups (placebo, 10 mg/d of CII, 1 mg/d of CII). There was, however, a higher prevalence of responders in the CII groups.[7] Researchers have noted that differences in study results may be related to the dose, species, and formulation of the CII.[6,8]

b-2Cool®

B-2Cool is a specially developed native CII that is extracted from chicken sternums. Its manufacturing process is strictly controlled to preserve the triple helix structure of the molecule and the specific epitopes of the native protein that are thought to account for maximum effectiveness.*

Human Study

Bakilan et al demonstrated a superior effect, compared to baseline, of b-2Cool (40 mg/d) combined with a standard intervention (acetaminophen (AC)) versus the standard intervention alone. In this three-month clinical study (n = 39), statistically significant results in comfort and mobility were achieved in the group taking the combination. The researchers reported, “the results suggest that native type II collagen treatment combined with acetaminophen is superior to acetaminophen alone for symptomatic treatment of patients with knee osteoarthritis.”[9][10]

Hesperidin

Free radicals that are released by activated neutrophils and produced by other biochemical pathways can play a significant role in joint cartilage changes. As a citrus bioflavonoid, hesperidin (HES) has been studied for its positive effects on free radical production, COX-2 gene expression, and cytokine balance.[11-13] HES is often combined with other natural and standard joint health agents.[14,15] Animal models have demonstrated that administration of hesperidin leads to significant improvements in biochemical and histological features of experimentally challenged joint tissues.[14,15] Hesperidin administration is associated with the suppression of T-lymphocyte proliferation and IL-2 production as well as downregulation of IL-1, IL-6, and tumor necrosis factor-alpha.[10]

Xanthohumol

Research suggests that hop extract, particularly xanthohumol (XN), helps support eicosanoid and cytokine balance and joint health.[16-20] Specifically, XN has been found to be superior to other hops-derived compounds (including isoxanthohumol) for inhibiting hyaluronic acid export, supporting proteoglycan and collagen homeostasis, and supporting cytokine balance in bovine chondrocytes.[18] XN appears to suppress production of nitric oxide, IL-1 beta, and TNF-alpha; induce nuclear translocation of Nrf2 (nuclear factor erythroid 2-related factor 2); and increase cellular glutathione.[21] Furthermore, XN appears to confer additional support for cytokine balance by downregulating cellular toll-like receptor 4 (TLR4) protein content.[22]

Available in 60 vegetarian capsules

CLINICAL APPLICATIONS

- Supports Joint Comfort and Mobility*
- Has a Protective Effect on Endogenous Type II Collagen*
- Modulates Immune Cell and Cytokine Activity in Joints*
- Improves Knee Function*

SynovX® AI provides a proprietary blend of ingredients that specifically target tissues, immune cells, and cytokines in joints. Type II collagen is the main structural protein in cartilage, and research suggests that low-dose, native-form type II collagen—as found in b-2Cool®—positively influences the immune response in joints via a mechanism called oral tolerization (a desensitization process). Xanthohumol, from hops, and hesperidin complement the activities of b-2Cool to deliver specialized joint support. Let SynovX AI help you stay active and moving!*
Serving Size: 2 Capsules

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount Per Serving</th>
<th>% Daily Value</th>
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<tbody>
<tr>
<td>Hesperidin (from Citrus sinensis)</td>
<td>469 mg</td>
<td>**</td>
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<tr>
<td>b-2Cool® native collagen type II</td>
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<td>and xanthohumol (from Humulus lupulus)</td>
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** Daily Value not established.

Other Ingredients: Dicalcium phosphate, HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, silica, and medium-chain triglyceride oil.

Directions: Take two capsules on an empty stomach, or as directed by your healthcare practitioner. For best results, take the capsules at bedtime.

Consult a healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

Storage: Keep closed in a cool, dry place out of reach of children.

Does Not Contain: Wheat, gluten, corn, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

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References