

Treatment of Rheumatoid Arthritis Using Undenatured Type II Collagen

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Introduction

Arthritis is a general term used to describe more than 100 chronic diseases of the joints, bones, and muscles. Nearly 43 million Americans — one out of six people or 15% of the population — have some kind of arthritis. The two most common and best known types are osteoarthritis, a wearing away of the cushioning cartilage in the joints, and rheumatoid arthritis, an autoimmune disease that attacks the type II collagen in joint cartilage, causing painful and often debilitating inflammation.¹

The symptoms and seriousness of arthritis vary widely. It can be a mild condition, controllable with over-the-counter pain relievers, or it can cause severe pain and inflammation that drastically change the quality of life. Left untreated, some forms of arthritis can be life-threatening.

Arthritis strikes almost twice as many women as men but can attack people of either gender and any age or race. Nearly 300,000 children have arthritis, called “juvenile rheumatoid arthritis,” and almost everyone

over the age of 60 eventually gets some kind of wear-and-tear osteoarthritis. Altogether, rheumatic diseases, such as arthritis, are the leading cause of disability in the United States.

According to the Center for Disease Control and Prevention, arthritis is the reason for 44 million outpatient visits and more than three-quarters of a million hospitalizations every year, and is second only to heart disease as a cause of work disability, costing the nation \$65 billion each year.²

As baby boomers age, the number of people with arthritis could surge to nearly 60 million, or almost 20% of the population. By the year 2020, one in five people will likely have some form of arthritis.

Overview of Rheumatoid Arthritis

Rheumatoid arthritis is a chronic inflammatory disease that is characterized by pain, swelling, and stiffness of multiple joints. Chronic joint inflammation usually results in progressive joint destruction, deformity, and loss of function. Current therapies for rheumatoid arthritis are often disappointing, both because of inadequate efficacy and unacceptable toxic effects.^{3,4}

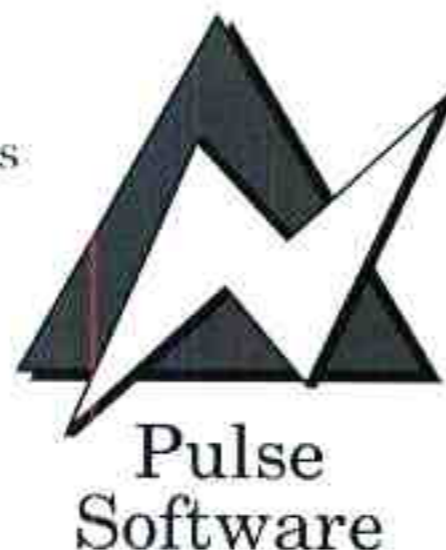
Direction to the search for therapeutic strategies based on specific immunosuppressive actions that would be both highly effective and minimally toxic has been provided by evidence that auto-reactive, sensitized T-cells participate in sustaining the inflammation of rheumatoid arthritis.⁵ It is presumed that the physiologic interaction of proteins with the gut immune system has evolved to prevent systemic immune responses to ingested proteins, and the ability to induce antigen-

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specific peripheral immune tolerance by oral administration of antigens has been recognized for some time. Investigations are currently underway regarding the possibility that autoimmune disease may be ameliorated by the induction of oral tolerance to disease-relevant auto-antigens.⁵ Oral administration of auto-antigens suppresses a variety of experimental autoimmune diseases, including experimental allergic encephalomyelitis (EAE), as well as collagen-, adjuvant-, and antigen-induced arthritis.⁶

Current Treatments for Rheumatoid Arthritis

Unfortunately, there is no cure for most types of arthritis. However, many types respond favorably to a wide range of conventional treatments, self-care techniques, and alternative therapies, including:

- 1) Over-the-counter pain relievers, such as aspirin, acetaminophen, and ibuprofen, which treat the symptoms but not the cause. They can also cause side effects, such as liver disease and stomach problems.⁷
- 2) Prescription drugs, such as Vioxx and Celebrex, which produce side effects such as stomach pain, vomiting, nausea, and serious cardiovascular disorders.⁸
- 3) Surgery, such as hip and knee replacements, which is costly and involves a prolonged recovery time.³
- 4) Dietary supplements, such as glucosamine and chondroitin, which provide substrate for rebuilding joint cartilage, but do not address the underlying cause of arthritis.⁹
- 5) Various other treatments, such as physical therapy and acupuncture, which offer varying degrees of success.³

However, not one of these therapies has been demonstrated to provide long-term benefits to rheumatoid arthritis patients.

Mechanism of Oral Tolerization

Undenatured type II collagen administered orally works with the immune system to promote healthy joints by a process called *oral tolerization*.⁵ This process helps the body to differentiate between foreign invaders, such as bacteria, and elements that are good for the body, such as nutrients.

The process of oral tolerization takes place in the small intestine where food is absorbed.¹⁰ Through a complex series of immunological events, patches of lymphoid

tissue surrounding the small intestine screen incoming compounds and serve as a “switch” to turn the body’s immune response to foreign substances on or off, depending on the nature of the substance.^{5,10}

In the case of undenatured type II collagen, small amounts (typically 10 mg or less) taken orally have been shown to turn off the immune response targeted at the undenatured type II collagen present in bone joint cartilage.⁶

Undenatured Type II Collagen

Cartilage is one of the primary connective tissues of the body, providing flexibility and support to bone joints. Undenatured type II collagen is the principal structural protein in the cartilage that is responsible for its tensile strength and toughness. When cartilage wears away, such as with advancing age and environmental stress, or is destroyed by disease, such as rheumatism, arthritis can result.¹¹ In the case of rheumatoid arthritis, the body’s immune system mistakes undenatured type II collagen as a foreign substance and sends antibodies to attack and destroy the collagen. When the body attacks itself in this manner, it is called an autoimmune disease.

Recent studies at Harvard Medical School, and elsewhere, have shown that small doses of undenatured type II collagen derived from chicken cartilage work with the human immune system to prevent the body from attacking its joints.¹²

Undenatured versus Denatured

Undenatured type II collagen can be manufactured from chicken sternum cartilage using a low-temperature process that ensures the biological activity of the undenatured type II collagen; this activity has been validated by a very specific and highly sensitive antibody analysis called an “ELISA” test. Other forms of type II collagen sold as dietary supplements are denatured, or hydrolyzed.¹³ In other words, their molecular configuration has been changed, either through chemical or high-temperature processing, rendering them inactive. Another benefit of undenatured type II collagen is that it contains small amounts of glucosamine and chondroitin, which are also good for joint health.

Human Clinical Studies

Numerous animal models of arthritis have demonstrated significant benefit from orally administered, undenatured type II collagen. Its administration has been

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able to suppress almost all experimentally inducible forms of rheumatoid arthritis in animals, including antigen-induced arthritis, adjuvant arthritis, undenatured type II collagen-induced arthritis, streptococcal cell-wall arthritis, and silicone-induced arthritis. These impressive results led to the investigation of undenatured type II collagen supplementation in humans with rheumatoid arthritis.⁶

Several studies were conducted at Harvard University Medical School under the direction of Dr. David E. Trentham, MD. In the first study, 10 patients diagnosed with rheumatoid arthritis had their immunosuppressive and disease-modifying drugs discontinued and were given 0.1 mg of undenatured type II collagen daily for one month, followed by 0.5 mg of undenatured type II collagen for the next two months. Six of the 10 patients experienced significant improvement, while one patient experienced complete remission. In addition, there were no side effects.⁶ In the second study, 60 patients with severe, active rheumatoid arthritis were split into two groups. One group was given a daily dose of 0.1 mg undenatured type II collagen for a month and was then switched to 0.5 mg undenatured type II collagen for the next two months. The second group was given a placebo. In this 90-day, double-blind, placebo-controlled study, 28 patients taking undenatured type II collagen showed considerable improvement compared to the placebo group, while four patients recovered completely. Again, no side effects were noted.⁶ In a third study, 10 patients between the ages of 8 and 14 years, who had active rheumatoid arthritis, were treated orally with undenatured type II collagen for three months. Eight out of the 10 patients with juvenile rheumatoid arthritis had a reduction in both swollen and tender joints, while one patient experienced complete remission.¹⁴ A fourth study consisted of 111 patients who met the cumulative Paulus criteria (morning stiffness, joint tenderness, joint swelling, and erythrocyte sedimentation rate). These patients were split into two groups. After 24 weeks, 21 out of 54 patients demonstrated significant improvement following treatment with undenatured type II collagen, while only 11 of the 57 patients taking a placebo showed improvement.¹²

Two other independent clinical studies were conducted in Germany. The first study consisted of 90 patients with early rheumatoid arthritis. The patients were divided into three groups. The first group was given a daily dose of 1 mg of undenatured type II collagen, the second group was given 10 mg of undenatured type II collagen, and the third group was given a placebo. At the end of the study, one patient in the 1 mg group, three patients in the 10 mg group, and no patients in the placebo group had experienced a marked improvement. In the second study, 1 mg and 10 mg daily doses of undenatured type II collagen resulted in reduced collagen type II antibody titres in patients showing a clinical response. This study also showed that the 10 mg dose level was more effective than the 1 mg dose level. These studies provide the basis and rationale for the use of undenatured type II collagen as a safe and effective modality of treatment for those suffering with rheumatoid arthritis.¹⁵ The above human studies demonstrate that small doses of undenatured type II collagen work with the human immune system to promote healthy joints and improve mobility and flexibility, as well as attenuate the symptoms of rheumatoid arthritis. It is also recommended to take undenatured type II collagen on an empty stomach.

Use of Undenatured Type II Collagen in Osteoarthritis Patients

Osteoarthritis is characterized by an inflammatory synovial response that leads to joint wear and tear. As it has been demonstrated, rheumatoid arthritis can cause gradual deterioration and inflammation of certain joints due to immune disorders, similar to the way osteoarthritis can cause a wear and tear from advancing age. Furthermore, the biochemical markers associated with osteoarthritis inflammation, including IL-4, IL-10, and TNF- α , are also associated with rheumatoid arthritis inflammation.¹⁶ Thus, undenatured type II collagen may also provide significant benefit to osteoarthritis patients.

Conclusion

Undenatured type II collagen may serve as a novel therapeutic tool in rheumatoid arthritis with no adverse side effects. Currently a number of products are available, which may provide temporary relief, but no long-term benefits. Such products include NSAIDs, anti-inflammatory drugs, monoclonal antibody and COX-II inhibitors, which exhibit major adverse side effects, including liver disease, gastritis, nausea, vomiting, cardiovascular diseases, and tuberculosis. Some of these drugs are also very expensive. Another expensive al-

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ternative is surgery, which has a long recovery time and may cause serious infections. Human clinical trials conducted in the United States and in Germany, demonstrated the novel therapeutic benefits of undenatured type II collagen in reducing the painful symptoms of debilitating rheumatoid arthritis with no significant side effects.

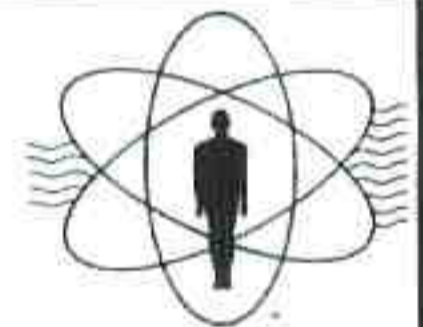
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