

**Original Article**  
**Orthopaedics**

# THE STUDY OF UNDENATURED TYPE II COLLAGEN IN THE KNEE OSTEOARTHRITIS

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**Abstract**

**Introduction:** Medical management of osteoarthritis has evolved considerably over last two decades. The purpose of the present study was to assess the outcome of collagen type II in osteoarthritis of knee joint.

**Methods:** one hundred randomly selected patients who received a daily dose of UC-II (40 mg) for 120 days. Results were confirmed using the Lequesne functional index (LFI), visual analogue scale (VAS) for pain and WOMAC after 120 days of observation.

**Results:** In 120 days of observation, UC-II showed a significant reduction in the overall WOMAC score, LFI, VAS. The UC-II led to significant changes in the three WOMAC subscales: pain  $p = 0.0005$ ; stiffness  $p = 0.004$ ; Physical function  $p = 0.004$ .

**Conclusion:** UC-II improved knee joint function in knee OA

**Keywords:** undenatured type II collagen, osteoarthritis of the knee joint.

## Introduction

Osteoarthritis, which involves the destruction of articular cartilage and remodeling of the adjacent bone, is the most common form of arthritis. Current treatments for OA include several analgesics, several non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular injections of corticosteroids or hyaluronic acid, as well as tramadol and other opioid analgesics to relieve severe pain<sup>1,2</sup>. Although these treatments can alleviate symptoms in the short term, their final effect on the pathophysiological progression of OA is limited<sup>3</sup>.

In previous studies, it has been reported that UC-II is effective in treating arthritis<sup>4,5,6</sup>. More recently, a statistically significant improvement in knee function compared with placebo was also reported in a clinical study that included a group of healthy people with UC-II supplements who had temporary joint pain after intense exercise. These same people took longer to experience pain after 120 days of supplementation. Based on these observations, a current study was developed to evaluate the effectiveness of UC-II in knee OA, which is a widely available supplement that is used to reduce joint pain.

## Materials and Methods

The UC-II product studied was obtained from chicken sternum. Patients randomly selected and a daily dose in the form of a capsule of 40g OD of collagen (UCII), administered on an empty stomach for 120 days, and subsequent visits were conducted on days 10, 30, 60, 90 and 120.

Results were evaluated in all visits and included WOMAC, VAS and LFI indices. A knee flexion range (ROM) test was performed at each visit.

A total of 100 randomly selected

patients, including 57 (female) and 43 men. The criteria for inclusion in the study were 45-65 years old with a body mass index (BMI) of 24-30 kg / m<sup>2</sup>, OA with a physical assessment of moderate to severe (cracks, bone growth, joint swelling, etc.) In one or both knees with knee pain for at least 3 months before the beginning of the investigation, a LFI score somewhere in the range of 6 and 10 and a VAS score of 40-70 mm 7 days after the end of the dressings and a radiograph of the knee, classified as X-ray, Kellgren and Lawrence (CL) 2 or 3<sup>8</sup>. In the case of bilateral lesion of the knee joint, the most severe symptoms of OA joint included.

WOMAC scores were determined: pain, stiffness and physical function. Each average WOMAC score was determined by dividing the score of the subscale by the number of questions - Pain, stiffness, physical function that it contained. The average VAS score was determined using the VAS questionnaire, containing 7 questions related to pain, and then dividing the total score by seven. The LFI score was determined using the LFI questionnaire, which assessed pain, distance travelled and daily life activity,

## Inclusion

- Physically active, 45-65 years old, with a BMI of 23 to 30 kg / m<sup>2</sup>
- Unilateral or bilateral OA of the knee for more than 3 months plus Kellgren and Lawrence radiographic grade 2 or 3 and more affected joint is included.
- VAS score during knee movement between 40-70 mm after 7 days of elimination excluded drugs
- LFI score between 6-10 points

after 7 days of withdrawal of excluded drugs

- Clinical laboratory results that are within the normal range.

## Total WOMAC score

WOMAC mean subscores—pain, stiffness and physical function

At day 120, we observed significant reductions in all three WOMAC subscales for UC-II Patient : Pain P= 0.0005, stiffness p = 0.004, and physical function p = 0.004.

## Mean VAS score

The UC-II supplemented group had a significant decrease in mean VAS score at day 120 p = 0.002

## LFI score

A significant reduction was observed in the LFI score for the UC-II group at day 120 supplementation also has a greater improvement in p = 0.008

## Knee flexion

No significant differences were observed between the study groups (data not shown).

## Reduction in WOMAC in UC II over 120 days

Parameter Reduction	Day	UC – II
WOMAC Pain	30	0.011
	60	0.0059
	90	0.0030
	120	0.0005
WOMAC stiffness	30	0.010
	60	0.0039
	90	0.0020
	120	0.004
WOMAC Physical function	30	0.020
	60	0.0149
	90	0.0080
	20	0.004

## Discussion

We evaluated the ability of UC-II to improve joint symptoms in moderate to severe OA of the knee joint. The results presented here demonstrate that in people taking UC-II, the clinical results are better. Analysis of WOMAC scores, VAS or LFI scores showed that the reduction and improvement in the patient ended with UC-II. These results support previous findings by Crowley et al.<sup>4</sup>, which reported a greater reduction in the symptoms of knee OA after 90 days of integration with UC-II.

The importance of these results remains to be understood; we find this preliminary observation interesting for further research and confirmation.

The etiology of the effect of UC-II on OA symptoms is unknown. However, it was shown that undenatured type II collagen protects animals from the occurrence of joint damage in models of arthritis experimentally induced by OA and RA<sup>6-9</sup>. It is assumed that this protection occurs through the induction and migration of regulatory T-cells (Tregs) into the zone of inflammation and damage<sup>10-11</sup>.

The proposed role of Treg may also be relevant to alleviate the symptoms of OA, since in vitro studies have shown that Treg produces anti-inflammatory cytokines that stimulate chondrocytes to synthesize the components of cartilage matrix<sup>12-14</sup>. More research is needed to find out the exact mechanism by which UC-II reduces the symptoms of knee OA.

The above effects in natural conditions can only be initiated by taking type II undenatured collagen, since denatured (for example, hydrolyzed) type II collagen cannot protect animals from the onset of arthritis<sup>6</sup>.

We did not observe any changes in the ROM of the knee and the distance travelled. It is likely that the improvement of these clinical outcomes is based not only on the symptomatic reduction of pain, but also on the physical improvement of the overall functionality of the knee joint. Until we conduct longer tests, it remains an open question whether a slow-acting additive, such as UC-II, can affect the biomechanical condition of the knee with OA sufficient to improve the knee's ROM.

## Conclusion

This study showed that UC-II, a food ingredient containing type II undenatured collagen, significantly improved knee function in a patient with OA knee joint after 120 days of observation.

## References

1. Hochberg MK, Altman RD, April KT, Benkhalti M., Guyatt G., McGowan J., et al. Recommendations of the American College of Rheumatology in 2012 on the use of non-pharmacological and pharmacological therapy for hand osteoarthritis, hips and knees. *Res treatment of arthritis (Hoboken)*. 2012; 64 (4): 465-74.
2. National Institute of Excellence in Health and Health Care; Clinical guide NICE 177. <https://www.nice.org.uk/guidance/cg177>. Access October 19, 2015
3. Hunter DJ. Pharmacological therapy of osteoarthritis: the era of disease modification. *Nat Rev Rheumatol*. 2011; 7 (1): 13-22. Doi: 10.1038 / nrrheum.2010.178.
4. Crowley DC, Lau FC, Sharma P, Evans M, Guthrie N, Bagchi M, et al. Safety and efficacy of undenatured type II collagen in the treatment of osteoarthritis of the knee: a clinical trial. *Int J Med Sci*. 2009; 6 (6): 312-21.
5. Bagchi D, Misner B, Bagchi M, Kothari SC, Downs BW, Fafard RD, et al. Effects of non-denatured type II collagen administered orally against inflammatory diseases in arthritis: a mechanistic study of *Int J ClinPharmacol Res*. 2002; 22 (3-4): 101-10.
6. Nagler-Anderson S, Bober LA, Robinson ME, Siskind G.V., Torbecke G.J. Suppression of arthritis induced by type II collagen by intragastric administration of soluble type II collagen. *ProcNat-I AcadSci U S A*. 1986; 83 (19): 7443-6.
7. T, Zhao W, Wu YQ, Chang Y, Wang QT, Zhang LL, et al. Chicken type II collagen induced immune balance of main subtype of helper T cells in mesenteric lymph node lymphocytes in rats with collagen-induced arthritis. *Inflamm Res*. 2010;59(5):369-77. doi:10.1007/s00011-009-0109-4.
8. Di Cesare ML, Micheli L, Zanardelli M, Ghelardini C. Low dose native type II collagen prevents pain in a rat osteoarthritis model. *BMC MusculoskeletDisord*. 2013;14:228. doi:10.1186/1471-2474-14-228.
9. Asnagli H, Martire D, Belmonte N, Quentin J, Bastian H, Boucard-Jourdin M, et al. Type 1 regulatory T cells specific for collagen type II as an efficient cell-based therapy in arthritis. *Arthritis Res Ther*. 2014;16(3):R115. doi:10.1186/ar4567.
10. Broere F, Wieten L, Klein Koerkamp EI, van Roon JA, Guichelaar T, Lafeber FP, et al. Oral or nasal antigen induces

- regulatory T cells that suppress arthritis and proliferation of arthritogenic T cells in joint draining lymph nodes. *J Immunol.* 2008;181(2):899–906.
11. Weiner HL, da Cunha AP, Quintana F, Wu H. Oral tolerance. *Immunol Rev.* 2011;241(1):241–59. doi: 10.1111 / j. 1600- 065 X. 2011. 01017.x.
  12. Muller RD, John T, Kohl B, Oberholzer A, Gust T, Hostmann A, et al. IL-10 overexpression differentially affects cartilage matrix gene expression in response to TNF- $\alpha$  in human articular chondrocytes in vitro. *Cytokine.* 2008; 44(3): 377– 85. doi: 10.1016/j.cyto. 2008.10.012.
  13. Roman-Blas, Yu.A., D.G. Stokes, Jimenez SA Modulation of TGF- $\beta$  signaling by pro-inflammatory cytokines in articular chondrocytes. *Cartilage osteoarthritis.* 2007; 15 (12): 1367-77. doi: 10.1016 / j.joca. 2007.04.011.
  14. Van Meegeren, ME, Roosendaal, J., Jansen, N.V., Wenting, M.J., Van Wesel, AS, Van Roon, J.A. and others. IL-4 alone and in combination with IL-10 protects against damage to cartilage caused by blood. *Cartilage osteoarthritis.* 2012; 20 (7): 764-72. Doi: 10.1016 / j.joca.2012.04.002.
  15. Van Viiven, Yu.P., Luijsterburg, PA, Verhagen, AP, Van Osh, GJ, Kloppenburg, M., Burma-Zeinstra, S.M. Symptomatic and chondroprotective treatment of collagen derivatives in osteoarthritis: a systematic review. *Cartilage osteoarthritis.* 2012; 20 (8): 809-21. Doi: 10.1016 / j.joca.2012.04.008.