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Original Research Article

Native collagen type II and Aflapin® in the management of hip and knee osteoarthritis: a single-centre prospective observational study

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ABSTRACT

Background: Osteoarthritis (OA) affects over 595 million people worldwide, with cases rising by 132% from 1990. Standard NSAID therapy offers only symptomatic relief and has safety limits, driving interest in alternatives. Native type II collagen and Aflapin provide complementary immunomodulatory and anti-inflammatory effects. This study evaluates their combined efficacy and safety in hip or knee OA over 12 weeks.
Methods: Adults (≥40 years) with confirmed hip or knee OA receiving native collagen type II 40 mg + Aflapin 100 mg as routine treatment were enrolled after consent. Key exclusions were recent corticosteroid/NSAID or intra-articular therapy, major comorbidities, obesity, pregnancy, or any other investigational drug use. Efficacy and safety were assessed via 100 mm VAS for pain and stiffness and a 5-point Likert scale for global OA status at weeks 4 and 12.
Results: A total of 100 subjects (mean age 58.6 years; 57% female) were enrolled. Significant improvements in pain, stiffness, and overall OA status were observed by weeks 4 and week 12, with all subjects reporting pain relief and 99% showing reduced stiffness by week 12. No rescue medication was needed, and three minor adverse events (AEs) (headache, bloating, mild gastritis) resolved without treatment.
Conclusions: Native collagen type II 40 mg + Aflapin 100 mg significantly improved joint pain, stiffness, and overall OA status by Week 4, with further gains by Week 12. No rescue medication was needed, and only mild, self-limiting AEs occurred. The combination was well tolerated and effective for knee or hip OA symptom relief.

Keywords: Osteoarthritis, Native collagen type II, Aflapin, Pain, Stiffness, Global assessment

INTRODUCTION

Osteoarthritis (OA) is the most common degenerative joint disease and a leading cause of pain and disability worldwide. According to the global burden of disease study, over 595 million people were living with OA globally in 2020, marking a 132% increase since 1990.[1] Recent epidemiological modeling predicts that OA cases may exceed 800 million by 2050, primarily due to aging populations, obesity, and sedentary lifestyles.[2,3] The disease predominantly affects weight-bearing joints, such as the knees and hips, and disproportionately impacts women and older adults, ranking among the top causes of years lived with disability.[4,5]

Conventional OA management primarily aims at symptom relief through a combination of non-pharmacologic strategies (exercise, weight control, physiotherapy) and pharmacologic therapies such as acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs). However, these treatments often fail to modify the underlying pathophysiology of cartilage degeneration and are limited by potential systemic adverse effects during long-term use.[6,7] This gap has prompted exploration of

nutraceutical and biologically active interventions that may provide structural and immunologic benefits.[8]

Among these, undenatured (native) type II collagen (UC-II) has emerged as a promising bioactive compound for joint health. UC-II preserves its natural triple-helix structure, which allows interaction with the gut-associated lymphoid tissue, promoting oral tolerance and activation of regulatory T cells that suppress immune-mediated cartilage degradation.[9,10] Clinical and preclinical studies demonstrate that undenatured type II collagen (NC-II) is safe, effective, and supports cartilage regeneration in OA through oral tolerance mechanisms that reduce immune-mediated cartilage damage and improve joint health. NC-II aids cartilage repair, enhances joint mobility, and reduces pain by lowering inflammation and slowing collagen degradation. It activates regulatory T cells that release anti-inflammatory cytokines (IL-10, IL-4, TGF-β), promoting immune balance and cartilage protection. Aflapin, a selective 5-LOX inhibitor, complements NC-II by reducing leukotriene-mediated inflammation. Together, they act through distinct pathways to provide effective symptomatic relief and better control of OA progression.[11,12]

This study was conducted to evaluate the efficacy and safety of a nutraceutical combination of Native collagen type II (40 mg) and Aflapin (100 mg) in managing symptoms of OA of the hip or knee over a 12-week treatment period.

METHODS

Study population and design

We conducted a prospective, observational data collection study evaluating the efficacy and safety of commercially available native collagen type II 40 mg + Aflapin 100 mg capsules in 100 subjects with OA of the hip or knee attending Maheshwari Hospital, Bhopal Madhya Pradesh, India. This study was reviewed and approved by institutional ethics committee Charak Hospital, Bhopal, Madhya Pradesh, India (Registration number: ECR/1562 /Inst/MP/2021). The study was conducted from November 22, 2024, to May 17, 2025. Written informed consent was obtained from all subjects who were ready to comply with study-required visits. Male and female subjects of at least 40 years old and above with a confirmed diagnosis of hip or knee OA and have been prescribed native collagen type II 40 mg plus Aflapin 100 mg as part of their routine treatment were included in the study. Subjects receiving systemic or topical corticosteroids, NSAIDs, analgesics, or immunosuppressive agents within five half-lives prior to the study intervention, subjects receiving any intra-articular treatment within the past 12 months, or with a history of knee or hip surgery, inflammatory polyarthritis, or class II obesity (BMI ≥35) were excluded. Subjects with major medical conditions that could interfere with efficacy or safety assessments, or those with known allergies or intolerance to native collagen type II, Aflapin, or any product components, were also excluded. Subjects with a history of recreational drug use within the past 12 months, pregnant/lactating women, and those who have received an investigational product or used an invasive investigational device within 30 days prior to the first dose or are currently enrolled in another investigational study were not eligible for participation.

Study medication

All enrolled subjects were instructed to take commercially available native collagen type II 40 mg + Aflapin 100 mg capsules once daily for 12 weeks.

Study assessment

Subjects were monitored for efficacy and safety. Both pain and stiffness in joints were measured using a 100 mm VAS scale at week 4 and week 12. Additionally, subject's global assessment of OA status was captured using a 5-point Likert scale-very good, good, fair, poor and very poor at week 4 and week 12. Proportion of subjects requiring rescue medication was also evaluated. Any untoward event satisfying the definition of adverse event was reported as AE and was analyzed.

Statistical analysis

Descriptive statistics were used to summarize subject characteristics and baseline scores. The primary analysis compared pre- and post-treatment (weeks 4 and 12) pain and stiffness scores using paired *t*-tests. Subgroup analyses were conducted based on age, gender, and baseline severity of OA. Adverse events were reported using descriptive statistics.

Ethical approval

The study was reviewed and approved by Institutional Ethics Committee Charak Hospital, Bhopal, Madhya Pradesh, India (Registration number: ECR/1562/Inst/MP/ 2021).

RESULTS

Demographics

A total of 100 subjects were enrolled in the study, comprising 57 females and 43 males. The mean age of the participants was 58.6 years (SD 6.65; range 45-72 years). Among the enrolled subjects, 70% had knee OA and 30% had hip OA. All 100 subjects completed the 12-week study period, and their data were included in the analysis. Demographic and baseline characteristics of the study population are summarized in Table 1.

Efficacy

Degree of pain and stiffness: Out of 100 enrolled subjects, the mean pain score (VAS, 0-100 mm) decreased from

74.9±10.3 at baseline to 62.1±10.85 at week 4 and further to 52.1±10.85 at week 12, demonstrating a progressive and clinically meaningful improvement over time. Similarly, the mean stiffness score reduced from 74.5±10.29 at baseline to 65.0±10.59 at week 4 and 55.1±10.68 at week 12. The reductions in both pain and stiffness from baseline were statistically significant at Week 4 and Week 12 (p<0.0001 for both time points) (Table 2, Figure 1 and 2).

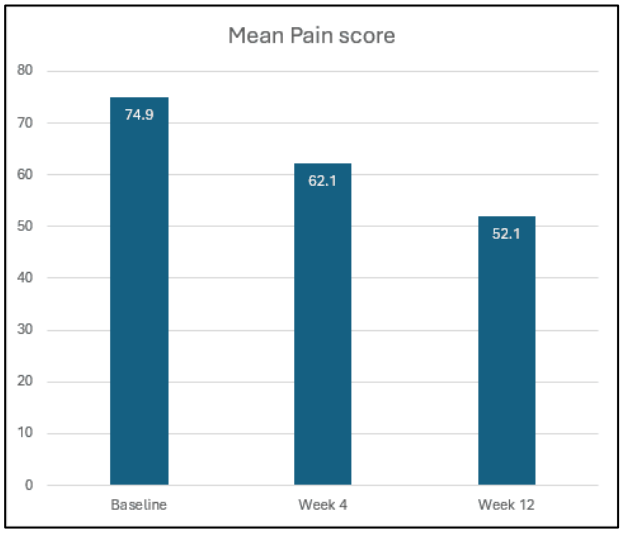

Figure 1: Mean pain score.

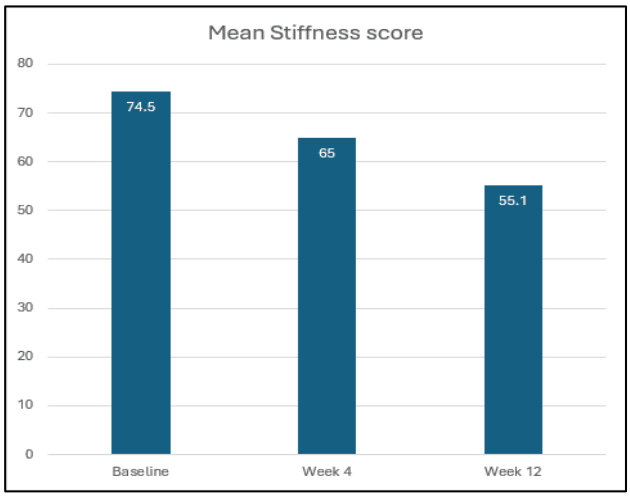

Figure 2: Mean stiffness score.

At an individual level, 91% of subjects reported a reduction in pain at week 4, increasing to 100% by week 12. Likewise, 95% of subjects experienced a reduction in stiffness at week 4, and 99% showed improvement by week 12.

Subjects' global assessment of OA

The mean baseline assessment score was 3.16, which improved to 2.16 at Week 4 and then to 1.24 at week12. The change from baseline was statistically significant, with a p<0.0001 (Table 3).

Rescue medication

None of the subjects required rescue medication during the study period.

Safety

A total of three AEs were reported during the study, headache, bloating, and mild gastritis. All events were mild in intensity, required no medical intervention, and resolved spontaneously.

Table 1: Demographic and baseline characteristics of study participants, (n=100).

Parameters	Category/statistic	Value
Total subjects enrolled		100
Sex distribution	Male	43 (43.0 %)
	Female	57 (57.0 %)
Age (in years)	Mean±SD	58.6±6.65
	Median (Range)	59.5 (45-72)
Type of OA	Knee OA	70 (70%)
	Hip OA	30 (30%)
Study completion	Completed 12-week study	100 (100%)
Data analyzed		All subjects included

OA=Osteoarthritis; SD=Standard deviation.

Table 2: Pain and stiffness.

	Baseline	Week 4	Week 12
Pain score			
Mean±SD	74.9±10.3	62.1±10.85	52.1±10.85
P value		<0.0001	<0.0001
Stiffness score			
Mean±SD	74.5±10.29	65±10.59	55.1±10.68
P value		<0.0001	<0.0001

*SD=Standard deviation; p=Probability value.

Table 3: Subjects' global assessment status of OA.

Global assessment score	Baseline	Week 4	Week 12
Mean±SD	3.16±0.39	2.16±0.39	1.24±0.43
Min, max	2, 4	1, 3	1, 2
P value		<0.0001	<0.0001

*SD=Standard deviation; P=Probability value.

DISCUSSION

OA is a chronic, progressive joint disorder characterized by cartilage degradation, synovial inflammation, and subchondral bone remodeling. The condition is commonly associated with pain, stiffness, and impaired joint function, which significantly affect quality of life. Conventional therapies such as NSAIDs and acetaminophen primarily

offer symptomatic relief but are often limited by gastrointestinal, renal, and cardiovascular adverse effects and do not address the underlying pathophysiology of OA. These limitations have prompted exploration of nutraceutical and biologically active compounds with potential structural and immunomodulatory benefits, such as undenatured type II collagen (NC-II) and Aflapin, a standardized *Boswellia serrata* extract.

In the present prospective observational study, oral supplementation with native collagen type II (40 mg) +Aflapin (100 mg) once daily for 12 weeks led to statistically significant reductions in joint pain and stiffness, as assessed by VAS scores, with progressive improvement over time. By week 12, nearly all participants reported symptomatic relief, and patient-reported global assessments indicated marked improvement in overall OA status. These findings suggest a clinically meaningful improvement in joint function and quality of life with the combined formulation.

The observed outcomes are consistent with earlier clinical trials evaluating the individual components. Undenatured type II collagen (UC-II) has been shown to reduce WOMAC and VAS scores significantly over 12-24 weeks compared with placebo, with additional benefits versus glucosamine-chondroitin in some studies.[9,10] Its mechanism involves inducing oral tolerance through interaction with the gut-associated lymphoid tissue, promoting T-regulatory cell activation and subsequent release of anti-inflammatory cytokines (IL-10, IL-4, TGF-β), which help prevent immune-mediated cartilage degradation. In a multicenter, double-blind, placebo-controlled trial, Lugo et al reported that supplementation with undenatured type II collagen led to significant improvement in knee joint flexibility and pain reduction, confirming its efficacy and tolerability in knee OA.[13]

Similarly, Aflapin has demonstrated rapid-onset anti-inflammatory effects by selectively inhibiting 5-lipoxygenase (5-LOX) and reducing leukotriene-mediated inflammation. Clinical studies have shown significant reductions in joint pain and improvements in physical function within 2-4 weeks of administration.[14] A recent 30-day randomized, double-blind, placebo-controlled study by Karlapudi et al further confirmed that Aflapin® significantly improved pain, stiffness, and physical function, with early symptomatic benefits evident by day 5 and maintained through day 30.[15] When used together, NC-II and Aflapin act via complementary pathways, immune modulation and enzymatic inhibition, providing enhanced symptomatic control, improved mobility, and better joint function.

The results of the current study are also in line with emerging real-world evidence. Stabile et al demonstrated that supplementation with a UC-II and *Boswellia serrata* combination improved mobility impairment within 4-8 weeks.[16] Similarly, Zapata and Fernández-Parra reported additive benefits of UC-II and *Boswellia serrata* in reducing pain and improving activity levels in OA.[17] The degree of improvement observed in our study, particularly the near-universal reduction in pain and stiffness by week 12, suggests potentially greater clinical benefit compared to previously reported findings, which may reflect the synergistic anti-inflammatory and immunomodulatory effects of this specific formulation.

The safety profile in this study was favorable and consistent with published data. Only three mild adverse events, headache, bloating, and mild gastritis, were reported, all resolving spontaneously without intervention. Previous randomized trials have similarly shown that NC-II and Aflapin are generally well tolerated, with no serious or treatment-related toxicities, supporting their use as safe adjunctive options in the management of OA, especially for patients unsuitable for long-term NSAID therapy.[7,10]

However, several limitations must be acknowledged. The study was observational and lacked a control arm, which limits causal inference. The use of patient-reported outcomes may introduce subjective bias related to daily activity, mood, or lifestyle factors. The sample size was modest, and the 12-week duration may not capture long-term effects on disease progression. Moreover, radiographic/MRI evaluations not included, preventing assessment of structural changes/cartilage regeneration. Despite these limitations, the findings provide valuable real-world insights supporting the clinical utility of NC-II and Aflapin in symptomatic OA management.

The study results demonstrate that, Native collagen type II (40 mg)+Aflapin (100 mg) significantly reduced pain and stiffness and improved joint function with excellent tolerability, supporting its role as a safe and effective adjunct in managing hip and knee OA

CONCLUSION

Treatment with native collagen type II 40 mg+Aflapin 100 mg capsules resulted in statistically significant improvement in joint pain and stiffness as early as week 4, with further reduction observed by week 12. Improvement in subjects' global assessment scores corroborated these findings, reflecting enhanced overall joint function and comfort. None of the subjects required rescue medication during the study period, highlighting the effectiveness of the therapy in managing symptoms. The combination was well tolerated, with only three mild, self-limiting adverse events (headache, bloating, and mild gastritis) reported. These results suggest that daily supplementation with native collagen type II and Aflapin provides a safe and effective therapeutic option for patients with knee or hip OA, improving functional outcomes and potentially reducing need for additional analgesic/anti-inflammatory medications.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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