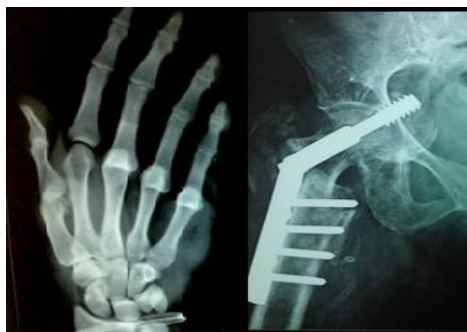




International Journal of Orthopaedics Sciences

E-ISSN: 2395-1958

P-ISSN: 2706-6630

Impact Factor (RJIF): 6.72

IJOS 2025; 11(3): 282-288

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www.orthopaper.com

Received: 03-07-2025

Accepted: 05-08-2025

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Real-world clinical experience with a combination of undenatured type II collagen (UC-II®), Mobilee®, and curcumin in osteoarthritis: Insights from a cross- sectional survey of orthopedic specialists

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DOI: <https://www.doi.org/10.22271/ortho.2025.v11.i3d.3816>

Abstract

Background: Osteoarthritis (OA) is one of the most prevalent degenerative joint disorders globally, characterized by progressive cartilage breakdown, subchondral bone remodelling, and chronic inflammation, leading to pain, stiffness, and impaired mobility. Despite its high burden, there are currently no approved disease-modifying therapies for OA. Conventional pharmacological options, such as NSAIDs and analgesics, offer symptomatic relief but are often associated with long-term safety concerns. This has prompted growing interest in evidence-based nutraceuticals that offer anti-inflammatory, antioxidant, and chondroprotective benefits with better tolerability. CollaFlex® PRO+, a combination of UC-II®, Mobilee®, and curcumin, is designed to address the multifactorial pathophysiology of OA through immune modulation, joint lubrication, and oxidative stress reduction.

Objective: To evaluate real-world clinical experience and perceptions of orthopedic specialists regarding the effectiveness, safety, and patient outcomes associated with CollaFlex® PRO+, in OA management.

Methods: A cross-sectional survey was conducted among 355 orthopedicians across India. The survey collected data on prescribing patterns, OA severity grades treated, treatment duration, observed clinical outcomes, safety profile, and overall willingness to recommend CollaFlex PRO+.

Results: CollaFlex® PRO+, was primarily prescribed for Grade II (45.74%) and Grade III (36.52%) OA. Most orthopedicians (76.58%) recommended a 3-month treatment duration. Regarding efficacy, 85.07% of orthopedicians rated CollaFlex® PRO+, as effective to highly effective for pain relief, and 85.11% for mobility improvement. Nearly all orthopedicians (95.99%) reported noticeable patient improvements, particularly in mobility, flexibility, and stiffness reduction. The product was well tolerated, with 95.71% of orthopedicians reporting no adverse events, only mild gastrointestinal disturbances were noted in a few cases. The key driver for adoption was the “Right Dose, Right Combination” (68.46%), and 97.71% expressed willingness to recommend the product to peer

Conclusion: The survey highlights strong clinical confidence in CollaFlex® PRO+, as a safe and effective nutraceutical for managing mild to moderate OA. Its favorable tolerability, patient-reported benefits, and evidence-backed formulation make it a valuable adjunct in long-term OA care.

Keywords: Osteoarthritis, undenatured type II collagen (UC-II®), curcumin, Mobilee® (hyaluronic acid), right dose, right combination, pain relief

Introduction

Osteoarthritis (OA) is among the most common chronic musculoskeletal disorders worldwide, affecting an estimated 500 million people. It is a heterogeneous disease of the whole joint and is a major cause of pain, disability, and early work loss. OA involves the progressive loss of articular cartilage, which disrupts the smooth movement of bones within the joint. This process is accompanied by subchondral bone remodelling, including sclerosis and osteophyte formation, and damage to other joint tissues, such as the meniscus, ligaments, synovium, and infrapatellar fat pad. Cartilage damage can result from overuse, abnormal mechanical stress, injury, or other pathological factors. As a chronic, progressive, and degenerative condition with no clearly defined cause, OA leads to structural changes not only in cartilage but also in the subchondral bone and synovial membrane, contributing to overall joint degeneration [1-4].

Currently, no disease-modifying drugs are available for OA management [5]. Pharmacological management primarily focuses on symptomatic relief with non-opioid analgesics such as acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors. Although these agents are effective for reducing pain and inflammation, prolonged NSAID use is associated with adverse effects, including gastrointestinal problems, congestive heart failure, and renal insufficiency [6]. Thus, concerns about the long-term safety of conventional treatments have increased interest in nutraceuticals as potentially safer alternatives for managing OA. Nutraceuticals are being increasingly investigated for their ability to provide symptom relief with a favorable safety profile. Several studies have demonstrated their potential benefits in clinical practice, owing to their antioxidant, anti-inflammatory, and anticatabolic properties when used as supplements in OA management [7].

Among the most commonly used nutraceuticals for OA, undenatured collagen, particularly type II (UC-II®), and Mobilee® have shown significant effects in reducing inflammatory markers, improving clinical symptoms, and providing disease modifying action in OA patients [8, 9]. Curcumin is another potent anti-inflammatory and antioxidant compound with strong supporting evidence for its role in OA management [10].

It contains active epitopes that interact with Peyer's patches in the gut, thereby inducing oral tolerance. This interaction activates immune cells, converting naïve T cells into regulatory T cells (Tregs) that specifically interacts with type II collagen. When these Tregs recognize type II collagen in joint cartilage, they secrete anti-inflammatory cytokines, including transforming growth factor-beta (TGF-β), interleukin-4 (IL-4), and interleukin-10 (IL-10). This activity helps reduce joint inflammation and supports cartilage repair [11].

Mobilee® (hyaluronic acid (60-75%) other polysaccharides (>10%) and collagen (>5%)) is a key component of synovial fluid and the cartilage extracellular matrix, providing the viscoelastic and lubricating properties essential for joint function. When administered orally, it has been shown to exert anti-inflammatory effects and improve symptoms of knee OA in a manner similar to glucosamine [12, 13].

Curcumin exhibits anti-inflammatory activity by inhibiting key enzymes such as cyclooxygenase-2, lipoxygenase, and inducible nitric oxide synthase (iNOS), which are central to the inflammatory process. It also plays a protective role in preventing cartilage damage caused by inflammation [14]. Acting as an NF-κB pathway suppressor, clinical studies have demonstrated that curcumin helps reduce pain and enhance physical function and overall quality of life in OA patients. Its therapeutic effects are largely attributed to its ability to protect chondrocytes from inflammation-induced apoptosis and oxidative stress. Additionally, curcumin promotes chondrocyte proliferation and stimulates collagen synthesis, while inhibiting matrix metalloproteinase activity. Together, these mechanisms contribute to its efficacy in alleviating pain and improving joint function in individuals with OA [15].

Thus, the combination of UC-II®, Mobilee®, and curcumin represents a promising therapeutic approach for OA, addressing both mechanical and immunological pathways, with a favorable safety profile and no reported adverse effects. While clinical trials have demonstrated significant benefits, there is a lack of real-world data capturing the clinical experiences and perceptions of orthopedic specialists regarding its effectiveness, safety, and patient outcomes. Therefore, this study aims to evaluate these real-

world insights specifically in the context of CollaFlex® PRO+ use in OA management.

Materials and Method

The Flexpro Survey, a structured paper-based questionnaire by Universal NutriScience (UNS), was designed to assess the clinical experience of orthopedicians with CollaFlex® PRO+ Approved by the Institutional Ethics Committee (ECR/644/Inst/MH/2014/RR-20) on 20th April 2024, the survey included nine multiple-choice questions (Table 1) evaluating the effectiveness, patient satisfaction, and safety of FreeFlex™ Emulgel in OA management. Responses were collected between May and October 2024, with written informed consent obtained from all participants. A total of 355 orthopedicians from hospitals and private practices across the country participated.

Questions

1. How many patients have you prescribed CollaFlex® PRO+?

- 10
- 20
- 30
- 40

2. Which grade of osteoarthritis patients were treated with CollaFlex® PRO+?

- Grade-I
- Grade-II
- Grade-III
- Grade-IV

3. What was the recommended duration of CollaFlex® PRO+ (OD) for the given indication?

- 1 Month
- 2 Months
- 3 Months
- 6 Months

4. One aspect about CollaFlex® PRO+ that convinced you to extend the benefit to patients?

- Indian patient Data
- Cost vs Value proposition
- Right Dose Right Combination
- Other (Please Specify)

5. How would you rate the effectiveness of CollaFlex® PRO+ in managing osteoarthritic pain on a scale of 1-5 (5 being highly effective and 1 being no effect)?

- 1: No Effect
- 2: Slightly Effective
- 3: Moderately Effective
- 4: Very Effective
- 5: Highly Effective

6. How would you rate the effectiveness of CollaFlex® PRO+ in managing mobility on a scale of 1-5 (5 being highly effective and 1 being no effect)?

- 1: No Effect
- 2: Slightly Effective
- 3: Moderately Effective
- 4: Very Effective
- 5: Highly Effective

7. In your experience, have patients reported improvements after using CollaFlex® PRO+?

- Yes, please specify
- No

8. Have you encountered any adverse effects or side effects reported by patients using CollaFlex® PRO+?

- No
- If yes, please specify

9. Would you recommend CollaFlex® PRO+ to your peers?

- Yes
- No
- Maybe

Results

A total of 355 healthcare professionals across India

participated in the survey. These participants varied in clinical experience, with the survey specifically capturing data on the number of patients each doctor had prescribed CollaFlex® PRO+ (UC-II 40 mg, Mobilee 80 mg, and Curcumin 200 mg) to. This information was critical for analysing their responses to the subsequent questions regarding prescription patterns, treatment outcomes, and physician perceptions of the product in OA management.

Number of Patients Prescribed with CollaFlex® PRO+

In terms of clinical usage, 32.0% of orthopedicians reported prescribing CollaFlex® PRO+ to approximately 30 patients, while 27.1% had used it in more than 40 patients. Additionally, 26.0% prescribed it to around 20 patients, and 14.9% had used it in fewer than 20 patients. These responses reflect a variable yet consistent pattern of product use in clinical practice.

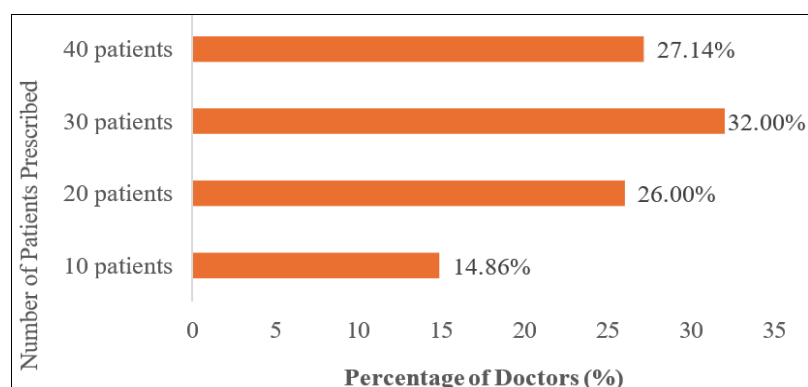


Fig 1: Distribution of Doctors According to the Number of Patients Prescribed CollaFlex® PRO+

Clinical Use of CollaFlex® PRO+ in Varying Grades of OA

Based on this classification, CollaFlex® PRO+ was most commonly prescribed by orthopedicians for patients with Grade II (mild to moderate) OA, accounting for 45.74% of cases, followed by Grade III cases at 36.52%. A smaller

proportion of orthopedicians reported prescribing it for Grade I patients (13.48%), while only 4.26% indicated its use in Grade IV (severe) OA.

These findings highlight that CollaFlex® PRO+ is primarily utilized in patients with mild to moderate OA, as per the K&L (Kellgren-Lawrence Grading). grading system.

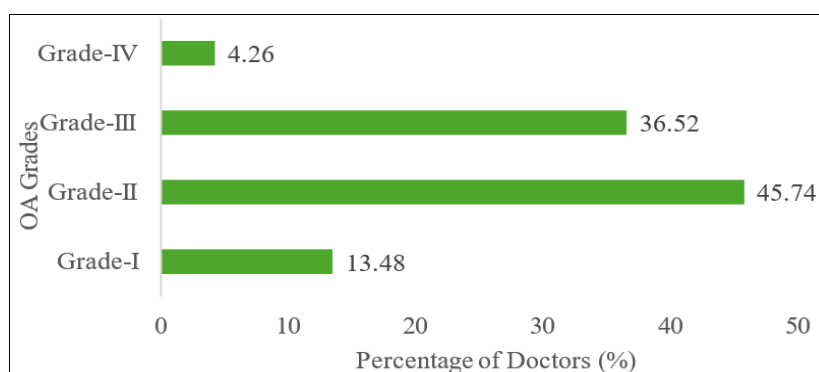


Fig 2: Distribution of Doctors' Responses by OA Grade"

Recommended Duration of CollaFlex® PRO+ (OD) for OA

The majority of orthopedicians 76.58%, recommended a duration of 3 months for the use of CollaFlex® PRO+ (OD)

for OA. A smaller proportion suggested a duration of 6 months (12.67%), 2 months (8.54%), or 1 month (2.20%), indicating a clear preference for the 3-month regimen surveyed patients.

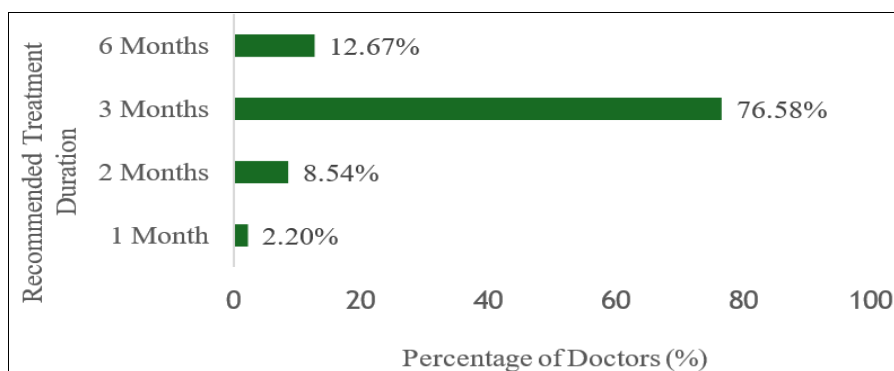


Fig 3: Distribution of Doctors According to Recommended Duration of CollaFlex® PRO+

Primary Rationale for Recommending CollaFlex® PRO+

Many orthopedicians 68.46% identified the “Right Dose, Right Combination” as the most compelling factor for extending the benefit of CollaFlex® PRO+ to their patients.

Other contributing factors included Indian patient data 19.80%, cost vs value proposition 8.56%, and other reasons 3.18%, highlighting that product composition was the most influential driver in clinical decision-making.

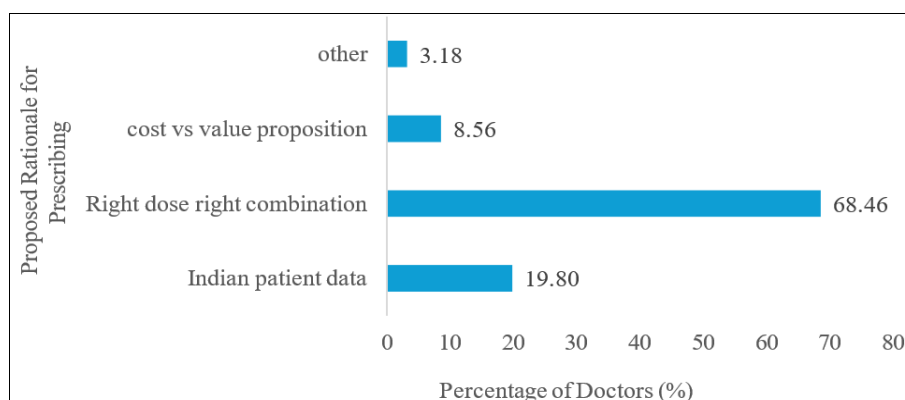


Fig 4: Rationale for Prescribing CollaFlex® PRO+ According to Doctors

Orthopedicians Rated Effectiveness of CollaFlex® PRO+ in Managing Osteoarthritic Pain

A significant majority of orthopedicians 55.49% rated CollaFlex® PRO+ as “4,” indicating it is very effective in managing osteoarthritic pain. Additionally, 29.58% rated it as “5,” reflecting high effectiveness. Moderate effectiveness

(“3”) was reported by 14.37% of orthopedicians, while only 0.56% rated it slightly effective (“2”), and none selected “1” (no effect). These findings highlight a strong positive clinical perception of the product’s efficacy in relieving osteoarthritic pain.

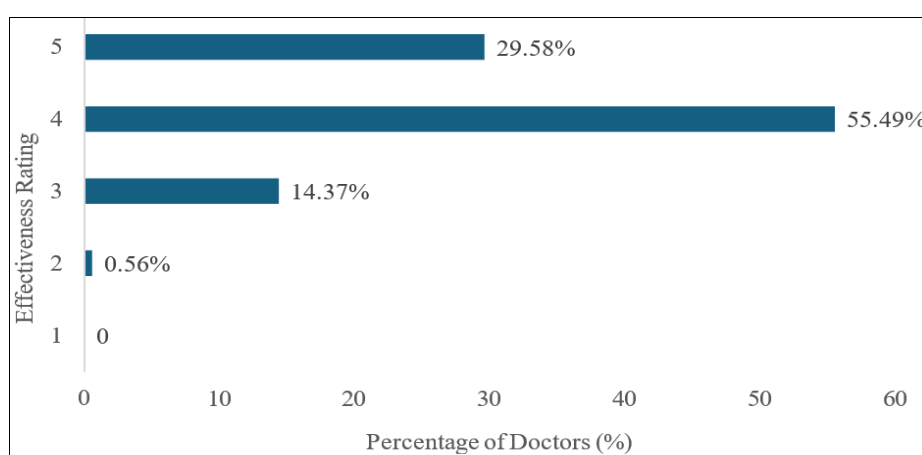


Fig 5: Orthopedicians Rated Effectiveness of CollaFlex® PRO+ for Osteoarthritic Pain

Orthopedician Perception of CollaFlex® PRO+ in Enhancing Mobility

More than half of the Orthopedician 53.93% rated CollaFlex® PRO+ as “4,” indicating it was perceived as very effective in improving mobility among OA patients. An additional 31.18% assigned the highest rating of “5,”

reflecting a strong impression of its effectiveness. A moderate effectiveness of “3” was given by 13.48%, while only 1.12% and 0.28% of orthopedicians selected ratings of “2” and “1,” respectively. These findings demonstrate an overall positive clinical perception of the product’s role in enhancing mobility in patients with OA.

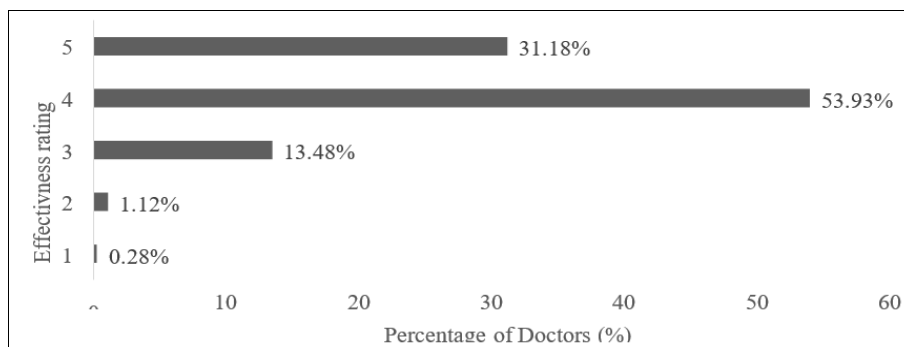


Fig 6: Orthopedicians Rated Effectiveness of CollaFlex® PRO+ for Osteoarthritic Mobility

Improvements Observed with CollaFlex® PRO+

A vast majority of orthopedician 95.99% reported that patients experienced noticeable improvements following the use of CollaFlex® PRO+, while only 4.01% indicated no such feedback.

Among those observing benefits, orthopedicians identified three primary areas of improvement. The most frequently

cited was enhanced mobility, reduced stiffness, and improved flexibility 40.90%, followed by increased patient satisfaction and adherence to therapy 33.73%. Additionally, 25.37% of orthopedician reported a reduction in pain and swelling. These findings highlight the broad therapeutic impact of CollaFlex® PRO+ across multiple aspects of patient well-being in the management of OA.

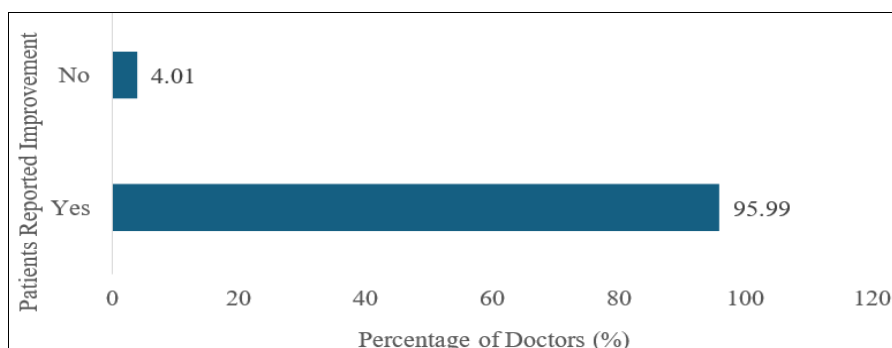


Fig 7: Doctors' Observations of Patient-Reported Improvement with CollaFlex® PRO+

Clinical Experience with Safety and Tolerability of CollaFlex® PRO+

A strong majority of orthopedician 95.71% reported that they had not encountered any adverse effects in patients using CollaFlex® PRO+, indicating a favorable safety profile. Only 4.29% of orthopedician noted any side effects. Among the

few reported cases, gastrointestinal disturbances were the most observed 73.33%, followed by a single instance of nausea. These findings suggest that CollaFlex® PRO+ is generally well-tolerated, with minimal adverse effects reported in clinical practice.

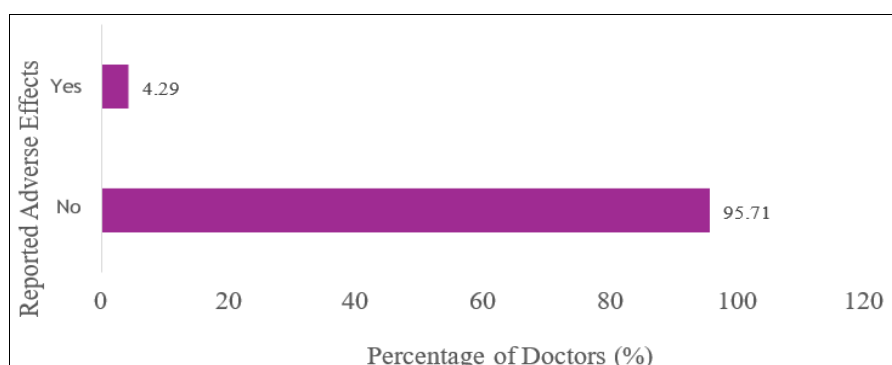


Fig 8: Clinicians' Responses on Patient-Reported Adverse Effects with CollaFlex® PRO+

Clinician Willingness to Recommend CollaFlex® PRO+

In response to whether they would recommend CollaFlex® PRO+ to their peers, 97.71% of orthopedicians responded "yes," while 2.29% selected "maybe." No orthopedicians

indicated a firm "no." This distribution suggests a positive clinical experience with the product, accompanied by a high degree of confidence among users in its potential value for peer practice.

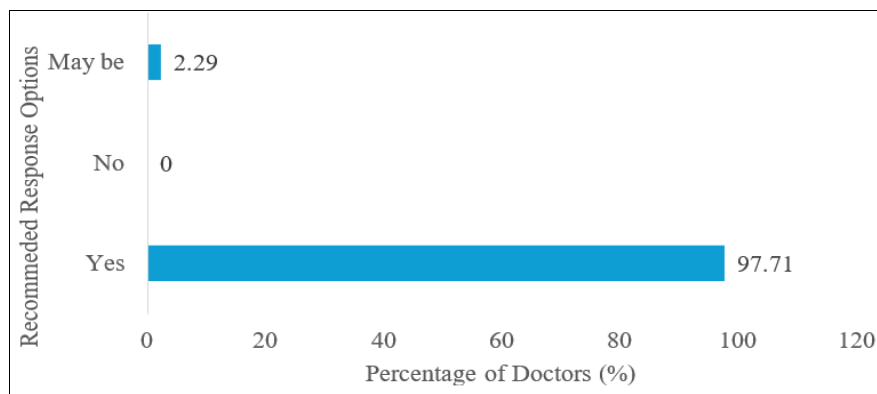


Fig 9: Recommendation Response for CollaFlex® PRO+

Discussion

The survey gathered insights from 355 orthopedician, offering a diverse and representative overview of the clinical use of CollaFlex® PRO+ (containing 40 mg UC-II®, 80 mg Mobilee® and 200 mg curcumin). A significant majority of orthopedician reported very good to excellent outcomes for pain relief (85.07%) and mobility improvement (85.11%), reflecting indicating high satisfaction and trust in the product's effectiveness. The WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) is a validated tool for assessing the severity of OA symptoms, where higher scores indicate greater impairment. A study conducted by Lugo et al. demonstrated a significant reduction in overall WOMAC scores ($P = 0.002$) after 6 months of supplementation with 40 mg UC-II®. Improvements were observed across all three WOMAC subscales: pain ($P = 0.0003$), stiffness ($P = 0.004$), and physical function ($P = 0.007$), along with a significant decrease in pain scores evaluated using the Visual Analogue Scale (VAS) ($P = 0.002$)^[16]. Similarly, Crowley et al. reported a 33% reduction in WOMAC scores and a 40% reduction in VAS scores after 3 months of treatment with 40 mg UC-II®^[17].

Orthopedician most commonly prescribed CollaFlex® PRO+ for patients with Grade II (45.74%) and Grade III (36.52%) OA, reflecting its strong preference for early to moderate disease stages where UC-II® is known to be most effective. Clinical studies in patients with Grade II and III OA have consistently shown that UC-II® supplementation leads to significant improvements in pain, stiffness, and joint function when cartilage damage is progressing but not yet irreversible. Majority (76.58%) of CollaFlex® PRO+ recommended a minimum treatment duration of three months, as clear benefits in pain reduction and mobility are typically observed after this period. While some patients may notice improvement within 2-4 weeks, a sustained course of at least 3-6 months is advised for optimal, long-term relief. Clinicians with more than a year of experience using this combination in the appropriate patient population typically those with Grade I to III OA report 60-80% symptom reduction within three months and meaningful long-term relief when the recommended duration is followed^[18].

Most orthopedicians cited the formulation's composition as the key driver for prescribing CollaFlex® PRO+ emphasizing the importance of delivering the right combination and dosage. Robust clinical evidence supports the synergistic action of 40 mg UC-II®, 80 mg Mobilee® (sodium hyaluronate), and 200 mg curcumin, which together address both the mechanical and inflammatory pathways in OA. Thus, as cited by majority of orthopedician (68.46%) the concept of the "Right Dose, Right Combination" would be a key factor

for prescribing CollaFlex® PRO+ in OA patients.

Orthopedicians also noted CollaFlex® PRO+'s excellent safety profile, with 95.71% of orthopedicians reporting no adverse events. Among the few reported side effects, mild gastrointestinal disturbances were the most common, reaffirming its suitability for long-term use in chronic OA management. Notably, 97.71% of orthopedicians expressed willingness to recommend CollaFlex® PRO+ to peers, highlighting strong satisfaction and confidence in its clinical utility.

Overall, the survey underscores the emerging role of CollaFlex® PRO+ as a clinically valuable nutraceutical in the management of OA, especially in cases where conventional therapies are inadequate or contraindicated.

Conclusion

Thus, CollaFlex® PRO+ emerges as a promising and well-tolerated nutraceutical option in the real-world management of mild to moderate osteoarthritis. Its unique combination of (UC-II®), Mobilee®, and curcumin demonstrated meaningful clinical benefits in reducing pain, improving mobility, and enhancing patient satisfaction. With minimal adverse effects and strong orthopedicians endorsement, CollaFlex® PRO+ can serve as a valuable adjunct to conventional OA therapies.

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Conflict of Interest

Not available

Financial Support

Not available

How to Cite This Article

Gandhi N, Teja R, Kumar SS, Gaonkar B, Katkar S, Garg M et al. Real-world clinical experience with a combination of undenatured type II collagen (UC-II®), Mobilee®, and curcumin in osteoarthritis: Insights from a cross-sectional survey of orthopedic specialists. *International Journal of Orthopaedics Sciences.* 2025; 11(3): 282-288.

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