[Downloaded free from http://www.jcrsmed.org on Wednesday, July 13, 2022, IP: 157.49.221.19]

Original Article

A randomized, open-label, multicentered parallel-group clinical study to evaluate the efficacy and safety of Joint Core™ compared to Jointace DN™ in osteoarthritis patients

Ramesh Kannan[1], Sriram Bakthavatchalam[2], Sakthibalan Murugesan[3], B. Aravinda Kumar[4], Bijoy Deb[5], Chandramohan Marimuthu[6], Priya Rajendran[7]

Departments of [1]Pharmacology and [2]Orthopedics, Government Medical College, Vellore, Tamil Nadu, [3]Department of Pharmacology, Sri Venkateswaraa Medical College Hospital and Research Centre, Puducherry, [4]Department of Pharmacology, Pondicherry Institute of Medical Sciences, Puducherry, [5]Medical Advisor, Ki3, Clinical Research Organisation, Chrompet, Chennai, Tamil Nadu, [6]Managing Director and [7]Executive Director, Microcore Research Lab India Pvt. Ltd., Erode, Tamil Nadu, India

Abstract

Background: Osteoarthritis (OA) is one of the most common musculoskeletal diseases worldwide, with pain, joint stiffness, fatigue associated with disability, and loss of physical activity. There is a need for an effective and safer alternative medication for the management of OA knee in elderly patients as the current medications possess severe risks to the patient compromising the quality of life.

Methodology: The study design and setting were phase 3, randomized, open-label, multicentered, active-controlled parallel-group interventional trial conducted at secondary care centers in Puducherry. Fifty patients (50) patients with OA knee were enrolled as per study criteria and randomized to receive Joint Core™ and Jointace DN™ for 12 weeks. The outcomes were assessed using various pain scales and subscales, Short-Form Health-12 (SF-12) questionnaire, and inflammatory markers. The data obtained at baseline and weeks 4, 8, and 12 were compared and statistically analyzed.

Results: Joint Core™ showed continuous reduction in the Visual Analog Scale pain scores at 4, 8, and 12 weeks and improvement in Western Ontario and McMaster Universities OA Index subscale and pain global assessment scales and good response rate in the Outcome Measures for Rheumatology Committee and OA Research Society International Standing Committee for Clinical Trials Response Criteria Initiative scores proving it to be efficacious in the treatment of OA knee compared to Jointace DN™. The safety assessed showed that Joint Core™ produces minimal gastrointestinal side effects and does not affect any organs as assessed by the laboratory parameters.

Conclusion: Joint Core™ is effective and safe in the treatment of OA knee when compared to its comparator Jointace DN™. Joint Core™ can be an alternative treatment option in the patients with OA knee who are intolerant to diacerein-based combinations available to treat OA.

Keywords: Anti-inflammatory agents, curcumin, eggshell membrane *Boswellia serrata*, osteoarthritis knee

Address for correspondence: Dr. B. Aravinda Kumar, Department of Pharmacology, Pondicherry Institute of Medical Sciences, Puducherry - 605 014, India.
E-mail: aravindkumar007@gmail.com

Submitted: 24-Mar-2022 **Revised:** 29-Apr-2022 **Accepted:** 29-Apr-2022 **Published:** 08-Jul-2022

Access this article online	
Quick Response Code:	Website: http://www.jcrsmed.org
	DOI: 10.4103/jcrsm.jcrsm_21_22

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Kannan R, Bakthavatchalam S, Murugesan S, Kumar BA, Deb B, Marimuthu C, *et al*. A randomized, open-label, multicentered parallel-group clinical study to evaluate the efficacy and safety of Joint Core™ compared to Jointace DN™ in osteoarthritis patients. J Curr Res Sci Med 2022;8:44-51.

[Downloaded free from http://www.jcrsmed.org on Wednesday, July 13, 2022, IP: 157.49.221.19]

INTRODUCTION

Osteoarthritis (OA) of the knee is a highly prevalent condition among older adults and it is the fourth leading cause of disability.[1] Functional limitations and restriction of activities gradually reduce the physical, psychological, and social well-being of the elderly population with OA knee leading to poor quality of life.[2] Studies have shown that patients with OA knee experienced worst quality of life, especially for items related to poor general health, pain, and activity limitation.[3] The financial burden on patients, their families, and health-care systems while managing OA knee is very high.

At present, recommendations for the management of OA knee comprise exercise, weight management, and pain medications with the goals to improve physical function and slow the progression of the disease.[4] The first-line pharmacological therapy for OA knee consists of topical or oral nonsteroidal anti-inflammatory drugs (NSAIDs) which only provide symptomatic pain relief and it is associated with serious risk after prolonged use. The elderly population with OA knee on chronic use of NSAIDs are at enhanced risk of gastrointestinal bleeding, hypertension, congestive heart failure, and renal insufficiency. Hence, there is a need for an effective and safer alternative medication for the management of OA knee in elderly patients.

Glucosamine, chondroitin sulfate, methylsulfonylmethane (MSM), and diacerein, available alone or in various combinations, are some of the widely marketed dietary supplements to treat joint pains due to OA. They are considered supplementary to analgesics and NSAIDs. Clinical studies, namely (Glucosamine/Chondroitin Arthritis Intervention) trial and GUIDE trial, have shown promise that these supplements had shown improvement in patients with OA knee.[5,6]

Joint Core™ is one such novel product containing Natural Eggshell Membrane (NEM) (Muttai Jow Complex™) 400 mg + Akbacore™ *Boswellia serrata* (30% Akba) 90 mg + Cumincore™ (curcumin extract 96%) 10 mg. NEM is a naturally rich source of combined proteins, elastin, collagen type 1, glucosamine, chondroitin, dermatan sulfate, and hyaluronic acid. It is a novel dietary supplement that contains naturally occurring glycosaminoglycans and proteins essential for maintaining healthy joint and connective tissues.[7] NEM's high content of bioactive components, as well as properties of moisture retention and biodegradability, suggests that it has potential use for clinical applications. *Boswellia serrata* extract has gained much attention as a potent anti-inflammatory, anti-arthritic, and analgesic agent. 3-O-acetyl-11-keto-beta-boswellic acid (AKBA) is the most active component of *Boswellia* extract and has been demonstrated to be a potent inhibitor of 5-lipoxygenase, which is a key enzyme in the biosynthesis of leukotrienes from arachidonic acid in the cellular inflammatory cascade.[8] Curcumin is a spice that comes from the root *Curcuma longa* with diverse pharmacological and biological properties. The efficacy of curcumin is shown to be similar as ibuprofen for the treatment of OA knee.[9]

Taking into consideration of all the above beneficial effects of individual components of Joint Core™, this study has been planned with the objectives to evaluate the efficacy, safety, and tolerability of Joint Core™ in OA patients.

METHODOLOGY

This trial was designed as a phase 3, randomized, open-label, multicentered, active-controlled parallel-group interventional trial conducted at two secondary care centers in India.

All patients diagnosed to have OA of the knee joint for at least 3 months with no joint deformities and requiring treatment with anti-inflammatory drugs were screened for eligibility after providing written informed consent. Patients meeting the American College of Rheumatology (ACR) criteria for OA knee (confirmed by X-ray), satisfying ACR functional class of III, with Grade 3 or 4 as per Kellgren and Lawrence classification system, and having pain defined by a level of ≥30 mm on a 100-mm in the Visual Analog Scale (VAS) at baseline were included in the study. Patients who have been on stable dose of prescription of paracetamol at least 2000 mg/day, on and off for at least 3 months in the past, were allowed to participate in the study.

The following patients were excluded from the study: those with arthritis of the knee from other causes, having OA pain that requires treatment with potent opioids, systemic corticosteroids, intra-articular injections, duloxetine, or venlafaxine; those with a history of uncontrolled hypertension, diabetes, and moderate-to-severe renal impairment; those who received any other investigational medicine within 7 days before screening which can interfere with study drug activity; those who were suffering from any illness on treatment which can interfere with study drugs; those with history of hypersensitivity to any of the test products and any other condition; and pregnant or lactating women, decided as unfit for study by the clinical

[Downloaded free from http://www.jcrsmed.org on Wednesday, July 13, 2022, IP: 157.49.221.19]

investigator. The patients were advised not to change their routine dietary habits and physical activity which can lead to weight gain or loss.

The sample size was calculated based on a previous study's mean difference value between the test group and the placebo group in the improvement of stiffness in OA patients.[7] Assuming a pooled standard deviation (SD) of 25 units, the study would require a minimum sample size of 22 for each group (i.e., a total sample size of 44, assuming equal group sizes), to achieve a power of 80% and a level of significance of 5% (two-sided), for detecting a true difference in means between the test group and the reference group of 21.5 (i.e., 35–56.5) units. Hence, a total sample size of 50 participants were calculated considering the dropouts and randomized into 2 groups with 25 in each group. The test group comprised patients diagnosed with OA knee and was advised to take one tablet of Joint Core thrice daily orally for 12 weeks. The comparator group comprised patients diagnosed with OA knee and was advised to take one tablet of Jointace DN twice daily orally for 12 weeks. Paracetamol and other NSAIDs were used as rescue medications at the discretion of the investigator.

The study drug Joint Core, available as tablet formulation, was sponsored by Microcore Research Laboratories Pvt. Ltd., Erode, Tamil Nadu, India. Active ingredients of one Joint Core tablet contained NEM 96% (Muttai Jow Complex) –400 mg, Akbacore™ *Boswellia serrata* (30% AKBA) –90 mg, and CUMIN CORE™ curcumin extract 96% –10 mg.

The drug was given orally in a dose of 1 tablet thrice daily after food for 12 weeks.

The comparator or reference drug Jointace DN, available as tablet formulation, was sponsored by Meyer Organics Pvt. Ltd., India. Active ingredients of one Jointace DN tablet contained glucosamine 750 mg + diacerein 50 mg + MSM 250 mg. The drug was given orally in a dose of 1 tablet twice daily after food for 12 weeks.

The study was approved by the Independent Ethics Committees of the study centers, namely PM Ethics Committee and Ki3 Ethics Committee for AYUSH (PM/ECR/JOINTCORE/031/21), and registered prospectively at CTRI [CTRI/2021/08/035335]. Recruitment of participants was done as per the inclusion and exclusion criteria after taking informed written consent from the eligible participants.

Evaluation of the study participants was done at baseline (visit 1) and the end of the study at 12 weeks (visit 2). The initial visit comprised screening for baseline investigations, study recruitment, assessment of baseline outcome parameters, and administration of test/comparator drugs. Demographic data (height, weight, body mass index [BMI], and age), personal history, medical history, vital signs, systemic examination, and clinical laboratory examination (complete hemogram, absolute eosinophil count, biochemistry-blood sugar levels, high-sensitivity-C-reactive protein (hs-CRP), and erythrocyte sedimentation rate [ESR]) were done at screening. Study participants who required additional intervention at any time of the study were withdrawn from the study.

The primary outcome measure was to assess the efficacy of the Joint Core™. The outcome parameters included change from baseline at 12 weeks in Pain visual analog scale (VAS) scale, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale, Patient's Global Assessment of Osteoarthritis scale, response rate measured by the Outcome Measures for Rheumatology Committee and Osteoarthritis Research Society International Standing Committee for Clinical Trials Response Criteria Initiative (OMERACT-OARSI), laboratory parameters like Hs-CRP, ESR and fibrinogen and quality of life assessed by Short form health -12 (SF-12) questionnaire. The secondary outcome measures included safety and tolerability parameters by assessment of clinical adverse events and abnormality in clinical and laboratory (hematological and biochemical) parameters.

The data on discrete variables and survey results were represented as *n* (%) and the data on continuous variables were represented as mean (SD). All the results were evaluated and compared between the test and comparator groups. Pain scale scores between the groups were analyzed using independent *t*-test. $P < 0.05$ was considered statistically significant. The data were analyzed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, N.Y., USA).

RESULTS

In this study, 50 study participants were enrolled who satisfied the study criteria. The study participants were allotted equally to the test and reference groups as per randomization. There was one patient who was lost to follow-up in the test (Joint Core) group. Hence, 49 subjects' data were only used for data analysis. Figure 1 the baseline demographic characteristics of the study participants are depicted in [Table 1]. There is no significant difference between the test and reference

[Downloaded free from http://www.jcrsmed.org on Wednesday, July 13, 2022, IP: 157.49.221.19]

groups with respect to mean age, BMI, and laboratory parameters. The mean age group of the study participants involved in the study was 55.7 years. Out of the 49 study participants enrolled, 39 (80%) were female and 10 (20%) were male participants. Thus, the baseline demographics were comparable between the two groups.

Both the treatment groups showed a significant reduction in the VAS pain score trend lines on weeks 4, 8, and 12 from their baselines. However, there was no significant difference in reduction in pain intensity between the groups [Figure 2]. With respect to WOMAC pain score and Patient's Global Assessment of improvement of OA, there was a statistically significant improvement at weeks 4, 8, and 12 compared to baseline in both the Joint Core™ and Jointace DN™ groups. However, there is no significant difference between the groups except on week 12 ($P < 0.0006$) [Figures 3 and 4]. The OMERACT-OARSI set of response criteria by both the groups showed good response percentage of improvement beginning from week 4 to week 12 [Table 2]. Inflammatory biomarkers such as ESR, hs-CRP, and fibrinogen improved significantly over 12 weeks in both the groups but did not show any significant difference between the test and comparator groups [Table 3].

The quality of life assessed by SF-12 questionnaire showed improvement in the mean percentage scores on physical activity status in both groups [Table 4].

The adverse effects during the study period comprised mainly gastrointestinal side effects such as nausea, vomiting, diarrhea, and gastritis which were evenly distributed in both the groups [Table 5]. The hematological and biochemical parameters did not show any derangements at the end of the study of period in both the groups [Table 3].

Table 1: Baseline demographic details of the study participants

Parameters	Joint Core™ (mean±SD)	Jointace DN™ (mean±SD)
Age (years)	55.08±8.75	56.33±8.94
Gender (*n*)		
Male	4	6
Female	21	18
BMI (kg/m^2)	25.80±2.38	26.73±1.54
Blood glucose (g/dL)	108.6±30.7	116.3±44. 3
Liver function tests		
SGOT	20.27±9.25	17.6±5.91
SGPT	19.08±8.08	15.12±7.26
Renal function test		
Urea	24.85±5.14	26.36±4.97
Creatinine	1.1±1.0	0.84±0.21

SD: Standard deviation, BMI: Body mass index, SGPT: Serum glutamic pyruvic transaminase, SGOT: Serum glutamic-oxaloacetic transaminase

Table 2: Number of participants with a response rate measured by the Outcome Measures for Rheumatology Committee and Osteoarthritis Research Society International Standing Committee for Clinical Trials Response Criteria Initiative

Group	OMERACT-OARSI response (%)			
	Day 0	Week 4	Week 8	Week 12
Joint Core™	No (100%)	Yes (42%) No (58%)	Yes (83%) No (17%)	Yes (100%)
Jointace DN™	No (100%)	Yes (40%) No (60%)	Yes (80%) No (20%)	Yes (100%)

OMERACT-OARSI: Outcome Measures for Rheumatology Committee and Osteoarthritis Research Society International Standing Committee for Clinical Trials Response Criteria Initiative

DISCUSSION

This study demonstrated that Joint Core™ has similar pain-relieving effect on patients with OA knee compared with Jointace DN™. There was a female preponderance of study participants with OA as proposed in previous literatures.[10] Overall, both the treatment groups showed similar continuous reduction in VAS pain scores and improvement in other scales, namely WOMAC, Global Pain Assessment Scale, good response rate in OMERACT-OARSI scale, and improvement in quality of life. The need for rescue medication (paracetamol) was numerically similar in both the groups, and none of the patients required anti-ulcer medications.

The Pain VAS is the most reliable, valid, sensitive to change, and easy to measure severity of pain in OA knee. The effectiveness of specific treatment can be accurately measured as pain relief considering all data points between "no treatment" and "treatment effect."[11] In this study, Joint Core™ and Jointace DN™ clearly demonstrated the reduction in pain score over the study period denoting pain relief. However, there was no significant difference in pain relief between the two groups ($P = 0.05$).

The WOMAC scale is a disease-specific instrument that measures the domains of pain, stiffness, and physical function of any joint with a range of 0–10 as the highest level.[12] In our study, the trend for improving in the Joint Core™ group was seen similar to other studies, and the difference between was significant at 12 weeks alone.[13]

The OMERACT-OARSI had developed two sets of responder criteria to represent the results of changes after treatment in three symptomatic domains (pain, function, and patient's global assessment) as a single variable for clinical trials. For each domain, a response was defined by both a relative and an absolute change, with different cutoffs with regard to the drug, the route of administration,

[Downloaded free from http://www.jcrsmed.org on Wednesday, July 13, 2022, IP: 157.49.221.19]

Table 3: Hematological, inflammatory, and biochemical parameters of study participants at baseline compared to end of study

Parameter	Joint Core™ (mean±SD)		Jointace DN™ (mean±SD)	
	Day 0	Week 12	Day 0	Week 12
Hemoglobin	12.49±2.57	12.77±2.07	12.63±1.11	12.16±1.57
Total leukocyte count	9400.00±2714.11	9185.7±2112.5	9280.0±2535.19	9107.0±2133.72
Total RBC count	4.75±0.54	4.71±0.56	4.69±0.43	4.52±0.48
Platelet count	313714.3±81536.5	324571.1±95335.61	337733.7±76529.6	325285.5±65866.5
ESR	45.75±32.83	9.0±4.5*	45.2±40.16	11.24±5.55*
hs-CRP (0–6 mg/L)	7.15±4.6	3.86±2.91#	6.47±6.13	3.54±3.13#
Fibrinogen	309.29±96.31	248.7±75.9#	283.36±85.53	246.12±62.92#
Blood urea	24.85±5.14	24.5±6.4	26.36±4.97	23.79±6.87
Serum creatinine	1.1±1.0	0.83±0.19	0.84±0.21	0.90±0.19
SGPT	19.08±8.08	18.75±8.05	15.12±7.26	17.37±7.13
SGOT	20.27±9.25	22.35±8.63	17.6±5.91	20.60±9.14
Blood glucose	108.6±30.7	103.7±24.4	116.3±44.3	114.5±45.6

*$P<0.0001$, #$P<0.05$. SD: Standard deviation, hs-CRP: High-sensitivity C reactive protein, RBC: Red blood cell, SGPT: Serum glutamic pyruvic transaminase, SGOT: Serum glutamic-oxaloacetic transaminase, ESR: Erythrocyte sedimentation rate

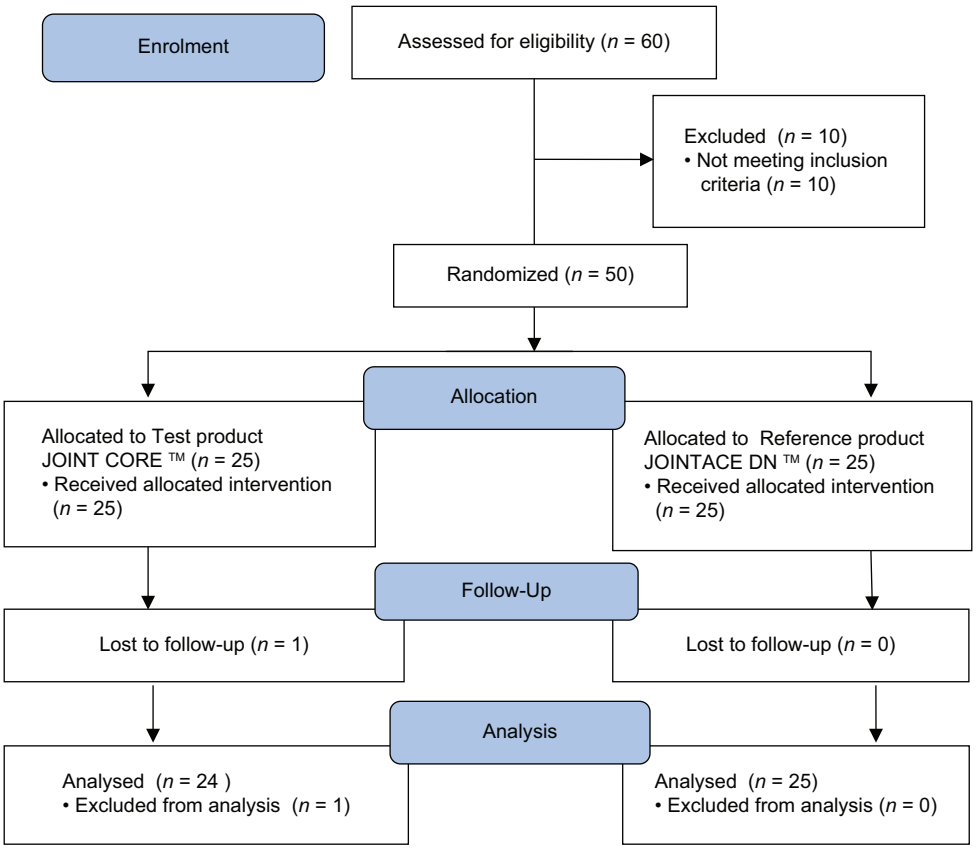

Figure 1: Consort 2010 flow diagram of the study

and the OA localization.[14] In this study, good response rate was shown by Joint Core™ and Jointace DN™ with respect to improvement in all the domains from the beginning till the end of the study. The 12-item Short-form Health Survey (SF-12) was used to assess the quality of life during the treatment period, which included mental and physical domains ranging from 0 to 100, with higher scores indicating a better quality of life.[15] The study participants of both the groups showed improvement in quality of life along with symptomatic relief.

NEM is reported to comprise combined proteins, elastin, collagen type 1, glucosamine, chondroitin, dermatan sulfate, and hyaluronic acid essential for joint and connective tissue disorders. *Boswellia serrata* has been reported to reduce pain and considerably improve knee joint functions due to the anti-inflammatory property of its active moiety, namely boswellic acid.[8] The anti-inflammatory effect of curcumin has been reported to be mediated by several mechanisms such as downregulation of cyclooxygenase-2 (COX-2) activity; inhibition of the production of cytokines such as interferons,

[Downloaded free from http://www.jcrsmed.org on Wednesday, July 13, 2022, IP: 157.49.221.19]

Table: 4: Changes from baseline in quality of life questionnaires (Short-Form Health-12)

Questionnaire	Joint Core™ (%) (*n*=24)		Jointace DN™ (%) (*n*=25)	
	Day 0	Week 12	Day 0	Week 12
In general, would you say your health is				
Excellent	0	8	0	15
Very good	2	50	0	37
Good	24	40	20	44
Fair	65	2	67	4
Poor	8	0	13	0
Moderate activities such as moving a table, pushing a vacuum cleaner, or playing				
Yes, limited a lot	40	0	37	0
Yes, limited a little	46	17	43	17
No, not limited at all	13	83	20	83
Climbing several flights of stairs				
Yes, limited a lot	54	4	44	0
Yes, limited a little	33	23	40	30
No, not limited at all	13	73	16	70
Accomplished less than you would like (due to problems in physical health)				
Yes	27	4	8	0
No	73	96	92	100
Were limited in the kind of work or other activities (due to problems in physical health)				
Yes	14	4	8	4
No	86	96	92	96
Accomplished less than you would like (due to any emotional problems)				
Yes	24	6	8	0
No	76	94	92	100
Did work activities less carefully than usual (due to any emotional problems)				
Yes	7	2	8	0
No	93	98	92	100
During the past 4 weeks, how much did pain interfere with your normal work (including work outside the home and housework)?				
Not at all	6	40	0	38
A little bit	30	40	40	45
Moderately	50	20	50	17
Quite a bit	4	0	4	0
Extremely	10	0	6	0
Have you felt calm and peaceful?				
All of the time	0	24	0	16
Most of the time	24	36	46	56
A good bit of the time	24	17	4	4
Some of the time	36	10	30	20
A little of the time	16	13	20	4
None of the time	0	0	0	0
Did you have a lot of energy?				
All of the time	0	10	4	10
Most of the time	3	20	16	20
A good bit of the time	24	34	46	44
Some of the time	16	14	16	26
A little of the time	40	16	16	0
None of the time	17	6	2	0
Have you felt down-hearted and blue?				
All of the time	0	0	0	0
Most of the time	0	0	0	0
A good bit of the time	0	0	0	0
Some of the time	0	0	0	0
A little of the time	10	10	14	10
None of the time	90	90	86	90
During the last 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (such as visiting friends and relatives)?				
All of the time	0	0	0	0
Most of the time	4	0	0	0
Some of the time	40	10	30	0
A little of the time	54	70	70	70
None of the time	2	20	0	30

interleukins (IL), tumor necrosis factor (TNF)-alpha, and inducible nitric oxide synthase; and suppression of activation of nuclear factor-kappa B.[16] Curcumin has been reported to inhibit COX-2, which results in prostaglandin

[Downloaded free from http://www.jcrsmed.org on Wednesday, July 13, 2022, IP: 157.49.221.19]

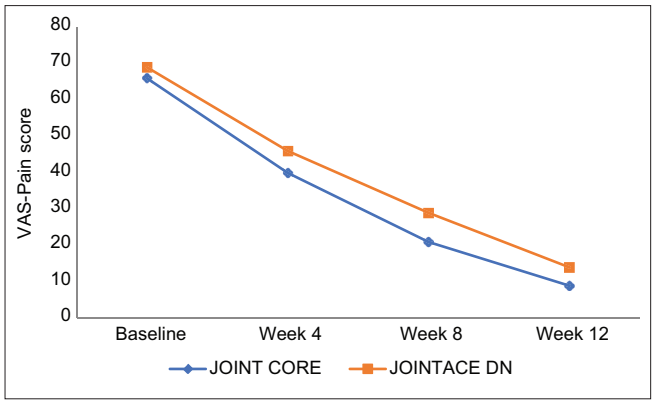

Figure 2: Change from baseline to 12 weeks in knee pain intensity measured by Pain VAS. VAS: Visual analog scale

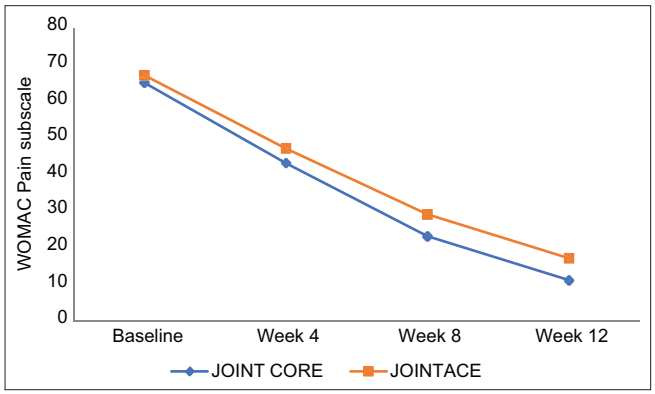

Figure 3: Change from baseline to 12 weeks in the WOMAC pain subscale. WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

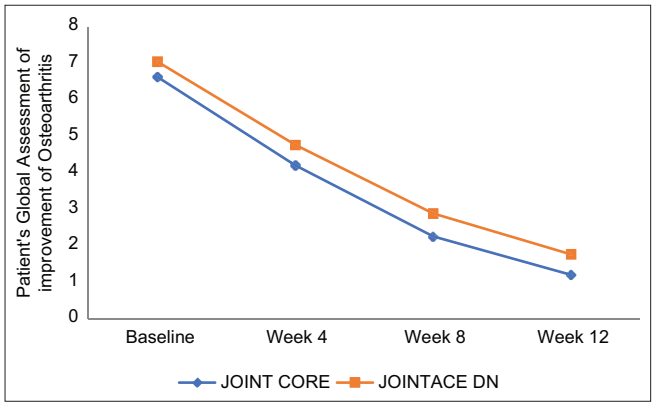

Figure 4: Change From Baseline to 12 Weeks in Patient's Global Assessment of improvement of Osteoarthritis. (0 to 10 point scale: 0 – Less disease activity and 10- more disease activity)

synthesis and thus anti-inflammatory action. In addition, it is reported to suppress pro-inflammatory cytokines such as TNF, IL-1, IL-8, and nitric oxide synthase.[17] In addition, curcumin is reported to have anti-obesity and antiulcer action, both of which can reduce the symptom of OA knee and prevent gastritis of NSAIDs, respectively. Hence, the combination of all these components in the form of Joint Core™ exhibits clinical efficacy and safety in the treatment of OA knee.

Table 5: Safety profile of Joint Core™ versus Jointace DN™ in study participants

Side effects observed	Joint Core™ (*n*=24)	Jointace DN™ (*n*=25)
Nausea	2	1
Vomiting	2	3
Gastritis	2	4
Diarrhea	1	1

There are some limitations in this study. Both the treatment groups did not show any statistically significant difference between the groups. This could have been overcome by inclusion of a placebo control, which would have provided greater clinical meaning. However, it would have required a significantly larger study population. However, the reference drug Jointace™ is a widely used product indicated in the treatment of OA knee and marketed. Its superiority over placebo has been reliably established and its safety is well documented. The participants and outcome parameters in the present study were also similar to those previously published studies. In addition, a broad spectrum of disease severity was included in both the groups which would have resulted in ambiguous results. Despite these potential pitfalls, the results from these open-label trials suggest that Joint Core™ may be an effective therapeutic option for OA knee patients.

CONCLUSION

Joint Core™ is effective and safe in the treatment of OA knee when compared to its comparator Jointace DN™. Joint Core™ can be an alternative treatment option in the patients with OA knee who are intolerant to diacerein-based combinations available to treat OA.

Acknowledgment

We acknowledge the CRO-Ki3 for supporting us right throughout this study.

Financial support and sponsorship

Nil.

Conflicts of interest

This study was sponsored by Microcore Research Lab India Pvt. Ltd, Erode, Tamilnadu , India.

REFERENCES

1. Fransen M, Bridgett L, March L, Hoy D, Penserga E, Brooks P. The epidemiology of osteoarthritis in Asia. Int J Rheum Dis 2011;14:113-21.
2. Cook C, Pietrobon R, Hegedus E. Osteoarthritis and the impact on quality of life health indicators. Rheumatol Int 2007;27:315-21.

[Downloaded free from http://www.jcrsmed.org on Wednesday, July 13, 2022, IP: 157.49.221.19]

3. Dominick KL, Ahern FM, Gold CH, Heller DA. Health-related quality of life among older adults with arthritis. Health Qual Life Outcomes 2004;2:5.
4. Sharma L. Osteoarthritis of the Knee. N Engl J Med. 2021;384:51-9.
5. Clegg DO, Reda DJ, Harris CL, Klein MA, O'Dell JR, Hooper MM, *et al*. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. N Engl J Med 2006;354:795-808.
6. Herrero-Beaumont G, Ivorra JA, Del Carmen Trabado M, Blanco FJ, Benito P, Martín-Mola E, *et al*. Glucosamine sulfate in the treatment of knee osteoarthritis symptoms: A randomized, double-blind, placebo-controlled study using acetaminophen as a side comparator. Arthritis Rheum 2007;56:555-67.
7. Ruff KJ, DeVore DP, Leu MD, Robinson MA. Eggshell membrane: A possible new natural therapeutic for joint and connective tissue disorders. Results from two open-label human clinical studies. Clin Interv Aging 2009;4:235-40.
8. Siddiqui MZ. *Boswellia serrata*, a potential antiinflammatory agent: An overview. Indian J Pharm Sci 2011;73:255-61.
9. Kuptniratsaikul V, Thanakhumtorn S, Chinswangwatanakul P, Wattanamongkonsil L, Thamlikitkul V. Efficacy and safety of *Curcuma domestica* extracts in patients with knee osteoarthritis. J Altern Complement Med 2009;15:891-7.
10. Hame SL, Alexander RA. Knee osteoarthritis in women. Curr Rev Musculoskelet Med 2013;6:182-7.
11. Wilderman I, Berkovich R. Integral of pain relief as an innovative method of pain measurement. J Pain Relief. 2017;6:277. Available from: https://www.omicsgroup.org/journals/integral-of-pain-relief-as-an-innovative-method-of-pain-measurement-2167-0846-1000277.php?aid=83586. [Last accessed on 2022 Jan 19].
12. White DK, Master H. Patient-reported measures of physical function in knee osteoarthritis. Rheum Dis Clin North Am 2016;42:239-52.
13. Bolten WW, Glade MJ, Raum S, Ritz BW. The safety and efficacy of an enzyme combination in managing knee osteoarthritis pain in adults: A randomized, double-blind, placebo-controlled trial. Arthritis 2015;2015:251521.
14. Smith TO, Hawker GA, Hunter DJ, March LM, Boers M, Shea BJ, *et al*. The OMERACT-OARSI core domain set for measurement in clinical trials of hip and/or knee osteoarthritis. J Rheumatol 2019;46:981-9.
15. Li SM, Li TL, Guo R, Chen P, Du WS, Kang SB, *et al*. Effectiveness and safety of acupotomy for knee osteoarthritis: Study protocol for a randomized controlled trial. Trials 2021;22:824.
16. Ross SM. Turmeric (*Curcuma longa*): Effects of *Curcuma longa* extracts compared with ibuprofen for reduction of pain and functional improvement in patients with knee osteoarthritis. Holist Nurs Pract 2016;30:183-6.
17. Shep D, Khanwelkar C, Gade P, Karad S. Safety and efficacy of curcumin versus diclofenac in knee osteoarthritis: A randomized open-label parallel-arm study. Trials 2019;20:214.