International Journal of Research in Orthopaedics
Deb B et al. Int J Res Orthop. 2024 Sep;10(5):954-959
http://www.ijoro.org

Original Research Article

DOI: https://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20241962

Evaluation of efficacy and safety of Collashot C2 plus capsule in osteoarthritis patients

Bijoy Deb[1], Bhuvanesh Gobaloussamy[2], Sakthibalan Murugesan[3]*, Gayathri Sivakumar[1]

[1]Ki3 Private Limited, Chennai, Tamil Nadu, India
[2]Sri Ortho Care Clinic, Pondicherry, India
[3]Thirumalai Medical Centre, Pondicherry, India

Received: 21 June 2024
Accepted: 08 July 2024

***Correspondence:**
Dr. Sakthibalan Murugesan,
E-mail: sakthibalanki3@gmail.com

ABSTRACT

Background: Osteoarthritis (OA), the most prevalent joint disease, is marked by chronic joint pain and debilitating symptoms. Many drugs are available in the market for treating osteo arthritis symptoms but there is still need for drugs with least adverse effects. So, in this study, an attempt has been done with Collashot C2 plus capsule, a nutraceutical for treating OA symptoms.
Methods: This is an outcome, quasi-experimental study where patients with OA were included. Patients were given capsule Collashot C2 plus daily for 3 months. A total of 30 male and female patients were included in the study. Changes from baseline to 12 weeks in knee pain intensity measured by pain visual analogue scale (VAS) and in Western Ontario and McMaster universities OA index (WOMAC) pain subscale, laboratory parameters, participant's global assessment of improvement of OA were assessed. Adverse drug reactions were also observed during the study period.
Results: There was a statistically significant improvement in the VAS pain scale, WOMAC pain score and in participant's global assessment of improvement of OA at week 4, week 8, and week 12 compared to baseline ($p<0.001$) was observed.
Conclusions: Collashot C2 plus capsule has proved to be very safe and effective in the management of OA Participants by reducing inflammation, providing adequate pain relief without causing any major side effects.

Keywords: OA, Collashot C2 plus capsule, ESR, C-telopeptide, Pain VAS

INTRODUCTION

Osteoarthritis (OA) is a joint disorder that leads to pain, stiffness, restricted movement and disability mostly in the elderly. The prevalence of OA in India is about 22-39% and is more common in women.[1] The disease typically affects the knee but can also impact the hips, hands, shoulders, and spine.[2] OA, particularly in the hip and knee, leads to significant locomotor disability.[3] Medical management of OA includes weight reduction, physiotherapy, and pharmacotherapy (mainly non-steroidal anti-inflammatory drugs), which provide modest benefits, primarily aiming to reduce pain and improve joint mobility and quality of life.[4,5] Collashot C2 plus capsule is a nutraceutical, which contains *Commiphora myrrha* extract 4% (MyrLiq)-100 mg, choline -60 mg, *Curcuma longa* extract-50 mg, *Boswellia serrata* extract-50 mg, native (Undenatured) collagen type-II-40 mg, sodium hyaluronate-40 mg.

Commiphora myrrha extract contains phytochemicals like terpenoids, triterpenoids, and steroids which has anti-inflammatory activity.[6] Choline-stabilized ortho-silicic acid promotes the activity of osteoblasts, their differentiation and the production of osteo-pontin, osteocalcin, alkaline phosphatase.[7] *Curcumin longa* extract-pharmacological use is by its ability to inhibit nuclear factor-Kappa B (NF-κB) pathway and by acting as

a scavenger of reactive oxygen and nitrogen species.[8] *Boswellia serrata* also known as Salai guggul, has potent anti-inflammatory effect that can effectively relieve pain and help prevent cartilage loss.[9] Type II collagen has positive effects on inflammation and in degradative joint diseases.

It is a nutritional supplement indicated for joint pain, swelling, stiffness and other symptoms of arthritis. The capsule increases bone strength and mineral content and reduces the chance of falls and fractures.[10] Many drugs are available in the market for treating Osteo arthritis symptoms but there is still need for drugs with least adverse effects. So, in this study, an attempt has been done with Collashot C2 plus capsule for treating OA symptoms.

METHODS

The present study is an outcome, quasi-experimental study where patients with OA according to inclusion criteria were included and assessed after treatment. Patients were given capsule Collashot C2 plus daily for 3 months. Collashot C2 plus capsule sponsored by Innovcare lifesciences pvt ltd, Mumbai. The study was done in Thirumalai medical centre and in Sri ortho care clinic in Pondicherry during September 2023-April 2024.The study was registered in clinical trial registry of India CTRI/2023/09/057515. Independent ethics committee approval obtained for this study from Ethique De La nature association in 19th August 2023.

Inclusion criteria

Participants with OA of knee joint based on American college of rheumatology (ACR) criteria and confirmed with X-rays and ACR functional class of III and with grade 3 or 4 as per Kellgren and Lawrence classification system. Participants who were on stable doses of nonsteroidal anti-inflammatory drugs (NSAIDS) of at least 2000 mg per day for at least 20 days in the past month. Participants with OA pain defined by a level greater than or equal to 30 mm on a 100 mm VAS. The participant who had not participated in any other clinical trial during the past 3 months. Participants, who were willing to give written, signed, and dated informed consent to participate in the study were included in study.

Exclusion criteria

Arthritis of knee from other systemic causes, uncontrolled hypertension or diabetes, patients having OA pain that requires treatment with potent opioids, systemic corticosteroids, intra-articular injections, duloxetine or venlafaxine, moderate to severe renal impairment, pregnant or lactating women, patients who received any other investigational medicine within 7 days prior to screening which can interfere with investigational product activity, participants who suffered from any illness which will interfere with the present study as decided by the clinical investigator and history of hypersensitivity to any of the test product composition were excluded.

Investigational drug

Collashot C2 plus-One capsule daily orally after food in the morning for 12 weeks. Collashot capsule composition is shown in Table 1.

Table 1: Collashot C2 plus capsule composition.

Ingredient	Strength (mg)
***Commiphora myrrha* extract 4% (MyrLiq)**	100
Choline*	60
***Curcuma longa* extract (CurQlife)**	50
***Boswellia serrata* extract (60%)**	50
Native (Undenatured) collagen type II (Collavant n2)	40
Sodium hyaluronate	40

*Choline-stabilized orthosilicic acid.

Duration of study drug given was 12 weeks.

Primary outcome

Change from baseline to 12 weeks in knee pain intensity measured by pain VAS scale (0-100 nm). Change from baseline to 12 weeks in the WOMAC pain subscale. [Maximum score=96 (Worst condition), minimum score=0 (Best condition)]. Changes from baseline to 12 weeks in the following laboratory parameter(s): Hs-C reactive Protein (high sensitivity C-reactive protein), ESR and C-telopeptide. Change in baseline to 12 weeks in participant's global assessment of improvement of OA. (0-to-10-point scale: 0-less disease activity and 10-more disease activity). Number of participants with a response rate measured by the outcome measures for rheumatology committee and OA research society international standing committee for clinical trials response criteria initiative (OMERACT-OARSI). Changes from baseline to 12 weeks in quality of life-questionnaires (Short form health-12).

Secondary outcome

Adverse drug reactions observed during the study period (for safety assessment).

Statistical analysis

Changes in score of pain intensity, improvement scores between baseline and at 4th, 8th and at 12th week of treatment in Collashot capsule group is measured by repeated measures of ANOVA. Statistical significance is measured by $p<0.05$.

RESULTS

Age and gender wise distribution of patients with Osteoarthritis included in the study is depicted in Table 2.

Table 2: Age and gender wise inclusion of patients in Collashot C2 plus group.

Variables	Collashot C2 plus capsule
Age (in years), mean	62
Female	24
Male	6

Knee pain intensity by pain VAS scale was assessed between baseline and 4th, 8th and 12 weeks of treatment in Collashot C2 plus group OA patients shown in Table 3.

Table 3: Change from baseline vs 4th, 8th, 12th week in knee pain intensity measured by pain VAS scale.

GROUP	Pain VAS scale (0-100 mm) (Mean±SD)			
	Day 0	Week 4	Week 8	Week 12
Collashot C2 plus, (n=30)	6.5± 2.3*	4.30± 2.10*	3.33± 1.72*	2.45± 1.23*
P value*		0.0003	<0.0001	<0.0001

*Statistically significant.

Table 4: Change from baseline versus 4th, 8th, 12th week in the WOMAC pain subscale.

Group	WOMAC-pain subscale (Mean±SD)			
	Day 0	Week 4	Week 8	Week 12
Collashot C2 plus, (n=30)	65.2± 18.18	43.1± 16.35*	31.56± 9.98*	12.45± 5.31*
P value*		<0.001	<0.0001	<0.0001

Maximum score=96 (Worst condition), minimum score=0 (Best condition).

There was a statistically significant improvement in the WOMAC pain score at week 4, week 8, and week 12 compared to the baseline after treatment with the Collashot C2 plus.

Reduction in ESR and Hs CRP levels when compared to baseline and after 12 weeks treatment showed in the Figure 1.

Table 5: Changes from baseline to 12 weeks in C-telopeptide levels (a marker of the bone degeneration).

Group	C- Telopeptide pg/ml (Mean±SD)	
	Day 0	Week 12
Collashot C2 plus, (n=30)	520.75±145.83	320.65±112.5
P value	<0.0001*	

*There was a statistically significant improvement (reduction) in the C telopeptide levels which is a marker of bone resorption/degeneration, from baseline to week 12 after treatment with Collashot C2 plus.

Table 6: Change from baseline versus 4th, 8th, 12th week in participant's global assessment of improvement of OA.

Group	Participant's global assessment (Mean±SD)			
	Day 0	Week 4	Week 8	Week 12
Collashot C2 plus, (n=30)	6.62± 1.49	4.20± 1.21	2.25± 0.84	1.20± 0.41
P value*		<0.0001	<0.0001	<0.0001

*0-to-10-point scale: 0-Less disease activity and 10-more disease activity.

There was a statistically significant improvement in the participant's global assessment score at week 4, week 8, and week 12 compared to baseline post-treatment with Collashot C2 plus as shown in Table 6.

There was a good response percentage of improvement after treatment with Collashot C 2 plus shown in Table 7, as evidenced by the response rate measured by the OMERACT-OARSI beginning from week 4 week to week 12.

Changes from baseline in quality of life-questionnaires (Short form health-12) from baseline to 12 weeks of study drug shown in Table 8.

Table 7: Number of participants with a response rate measured by the OMERACT-OARSI.

Group	OMERACT-OARSI response %			
	Day 0	Week 4	Week 8	Week 12
Collashot C2 plus (n=30)	No (100%)	Yes (43%), n=13	Yes (73%), n=22	Yes (93%), n=28
		No (57%), n=17	No (27%), n=8	No (7%), n=2

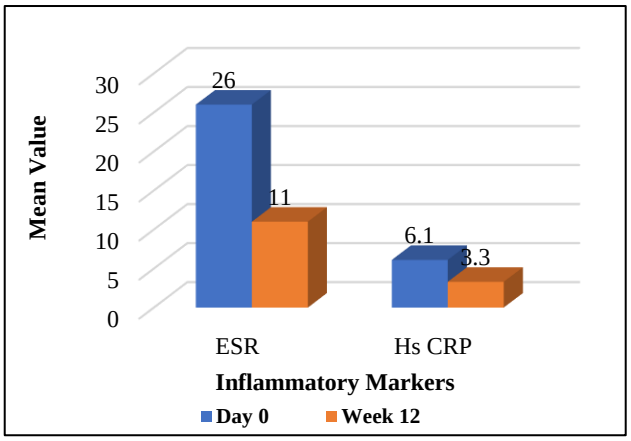

Figure 1: Improvement in ESR and Hs CRP levels after treatment with Collashot C2 plus.

Table 8: Quality of life-questionnaires-short form health-12 with Collashot C2 plus capsule in baseline and after 12 weeks treatment.

Questionnaire	Collashot C2 plus group (%), (n=30)	
	Day 0	Week 12
In general, would you say your health is:*		
Excellent	0	8
Very good	2	50
Good	24	40
Fair	65	2
Poor	8	0
Moderate activities such as moving a table, pushing a vacuum cleaner, or playing*		
YES, limited a lot	40	0
YES, limited a little	46	17
No, not limited at all	13	83
Climbing several flights of stairs*		
YES, limited a lot	54	4
YES, limited a little	33	23
No, not limited at all	13	73
Accomplished less than you would like (due to problems in physical health)*		
Yes	27	3
No	73	97
Were limited in the kind of work or other activities (due to problems in physical health)*		
Yes	14	3
No	86	97
Accomplished less than you would like (due to any emotional problems)*		
Yes	24	7
No	76	93
Did work activities less carefully than usual. (due to any emotional problems)*		
Yes	7	3
No	93	97
During past 4 weeks, how much did pain interfere with normal work (Including outside home and housework)?*		
Not at all	6	40
A little bit	30	40
Moderately	50	20
Quite a bit	4	0
Extremely	10	0
Have you felt calm and peaceful?*		
All of the time	0	24
Most of the time	24	36
A good bit of the time	24	17
Some of the time	36	10
A little of the time	16	13
None of the time	0	0
Did you have a lot of energy?*		
All of the time	0	10
Most of the time	3	20
A good bit of the time	24	34
Some of the time	16	14
A little of the time	40	16
None of the time	17	6
Have you felt downhearted and blue?		
All of the time	0	0
Most of the time	0	0
A good bit of the time	0	0
Some of the time	0	0
A little of the time	10	10
None of the time	90	90

Continued.

Questionnaire	Collashot C2 plus group (%), (n=30)	
	Day 0	Week 12
During the last 4 weeks, how much of the time have your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?*		
All of the time	0	0
Most of the time	4	0
Some of the time	40	10
A little of the time	54	70
None of the time	2	20

*There was a significant improvement in the mean percentage scores of quality of life-questionnaires on physical activity status after treatment for week 12 with Collashot C2 plus $p<0.05$.

Adverse effects during the study period shown in Table 9.

Table 9: Side effects observed during the study period in the treatment group.

Side effects observed	Collashot C 2 plus group, (n=30)
Nausea	2
Vomiting	1
Gastritis	3

DISCUSSION

OA, the most prevalent joint disease, is marked by chronic joint pain and debilitating symptoms. OA, particularly in the hip and knee, leads to significant locomotor disability. Collashot C2 plus capsule is a nutraceutical, which contains *Commiphora myrrha* extract 4% (MyrLiq)-100 mg, choline -60 mg, *Curcuma longa* extract-50 mg, *Boswellia serrata* extract-50 mg, native undenatured collagen type II-40 mg, sodium hyaluronate-40 mg. It is a nutraceutical indicated for joint pain, swelling, stiffness and other symptoms of arthritis.

Commiphora myrrha extract, also known as myrrh, is a resin that comes from the bark of *Commiphora myrrha* plant. It has analgesic, anti-inflammatory and antioxidant properties.[11] Choline-stabilized orthosilicic acid is a bioavailable and stable form of silicon. Supplementation promotes the mineralization of the bone matrix.[12]

Curcumin longa has immense pharmacological properties like anti-inflammatory, antioxidant and also has anticancer activity.[13] Hsiao et al in a meta-analysis with *Curcumin longa* extract with a total of 1258 participants in 11 randomised trials in patients with knee OA, showed more pain relief than non-steroidal anti-inflammatory drugs.[14]

The resinous component of *Boswellia serrata* contains monoterpenes, diterpenes, triterpenes, tetracyclic triterpenic acids and four major pentacyclic triterpenic acids. It has potent anti-inflammatory that can effectively relieve pain and help prevent cartilage loss.[15] Collagen type-II is the main structural component of the cartilage tissue. It is a nutraceutical derived from chicken sternum cartilage. In Bakilan et al study native undenatured type II collagen with acetaminophen is more effective than using acetaminophen alone for alleviating symptoms in patients with knee OA.[16] Cicero et al in a study found that Oral supplementation with sodium hyaluronate has been linked to short-term improvement in symptoms and functionality in patients with OA.[17]

Each ingredient in Collashot C2 plus capsule has shown anti-inflammatory activity and improvement in patients with OA in clinical trials. In this study all ingredients together in a capsule is evaluated for its efficacy in osteo arthritis patients. Our study also showed a statistically significant improvement in the VAS pain scale, WOMAC pain score, significant reduction in inflammatory parameters (ESR, C-telopeptide, Hs-CRP levels) and improvement in participant's global assessment of OA at week 4, week 8, and week 12 compared to baseline ($p<0.001$).

Limitations

This study was done without any comparator groups which may increase bias in outcome of study. Small sample size of study group in this study.

CONCLUSION

The test product Collashot C2 plus has proved to be very safe and effective in the management of OA participants by reducing inflammation, providing adequate pain relief and by improving the participant's functional capacity without causing any major side effects.

Funding: Funding sources by Innovcare Lifesciences Pvt Ltd, Mumbai)
Conflict of interest: Yes - study drug sponsored by Innovcare Lifesciences Pvt Ltd, Mumbai
Ethical approval: The study was approved by the Institutional Ethics Committee, CTRI/2023/09/057515.

REFERENCES

1. Abhishek J, Kiran G, Partha H, Ramesh H. Prevalence of knee osteoarthritis, its determinants, and impact on the quality of life in elderly persons in rural Ballabgarh, Haryana. J Prim Care Spec. 2021;10(1):354-60.

2. Primorac D, Molnar V, Matisic V, Hudetz D, Jelec Z, Rod E, et al. Comprehensive Review of Knee Osteoarthritis Pharmacological Treatment and the Latest Professional Societies' Guidelines. Pharmaceuticals (Basel). 2021;14(3):205.
3. Altman R, Brandt K, Hochberg M, Moskowitz R, Bellamy N, Bloch DA, et al. Design and conduct of clinical trials in patients with osteoarthritis: recommendations from a task force of the Osteoarthritis Research Society. Results from a workshop. Osteoarthritis Cartilage. 1996;4(4):217-43.
4. Rosemann T, Wensing M, Joest K, Backenstrass M, Mahler C, Szecsenyi J. Problems and needs for improving primary care of osteoarthritis patients: the views of patients, general practitioners and practice nurses. BMC Musculoskelet Disord. 2006;7(1):48.
5. DaCosta BR, Pereira TV, Saadat P, Rudnicki M, Iska nder SM, Bodmer NS, et al. Effectiveness and safety of non-steroidal anti-inflammatory drugs and opioid treatment for knee and hip osteoarthritis: network meta-analysis. BMJ. 2021;375:n2321.
6. Ammon HP. Boswellic acids in chronic inflammatory diseases. Planta Med. 2006;72(12):100-16.
7. Geusens P, Pavelka K, Rovensky J, Vanhoof J, Demeester N, Calomme M, et al. A 12-week randomized, double-blind, placebo-controlled multicenter study of choline-stabilized orthosilicic acid in patients with symptomatic knee osteoarthritis. Musculoskelet Disord. 2017;18(1):2.
8. Wang Z, Jones G, Winzenberg T, Cai G, Laslett LL, Aitken D, et al. Effectiveness of *Curcuma longa* Extract for the Treatment of Symptoms and Effusion-Synovitis of Knee Osteoarthritis: A Randomized Trial. Ann Intern Med. 2020;173(11):861-9.
9. Siddiqui MZ. *Boswellia serrata*, a potential anti-inflammatory agent: an overview. Indian J Pharm Sci. 2011;73(3):255-61.
10. Luo C, Su W, Song Y, Srivastava S. Efficacy and safety of native type II collagen in modulating knee osteoarthritis symptoms: a randomised, double-blind, placebo-controlled trial. J Exp Orthop. 2022;9(1):123.
11. Batiha GE, Wasef L, Teibo JO, Shaheen HM, Zakariya AM, Akinfe OA, et al. Commiphora myrrh: a phytochemical and pharmacological update. Naunyn Schmiedebergs Arch Pharmacol. 2023;396(3):405-20.
12. Prabhoo R. Choline-Stabilized Orthosilicic Acid and Bone Health. Curr Med Issues. 2020;18(4):312-6.
13. Wang Z, Jones G, Winzenberg T, Guoqi C, Laura LL, Dawn A, et al. Effectiveness of *Curcuma longa* extract for the treatment of symptoms and effusion–synovitis of knee osteoarthritis: a randomized trial. Ann Intern Med. 2020;173(11):861-9.
14. Hsiao AF, Lien Y, Tzeng IF, Lieu CT, Chou SH, Horng YS. The efficacy of high- and low-dose curcumin in knee osteoarthritis: A systematic review and meta-analysis. Complementary Therapies in Med. 2021;63:102775.
15. Yu G, Xiang W, Zhang T, Zeng L, Yang K, Li J. Effectiveness of *Boswellia* and *Boswellia extract* for osteoarthritis patients: a systematic review and meta-analysis. BMC Complement Med Ther. 2020;20(1):225.
16. Bakilan F, Armagan O, Ozgen M, Tascioglu F, Bolluk O, Alatas O. Effects of Native Type II Collagen Treatment on Knee Osteoarthritis: A Randomized Controlled Trial. Eurasian J Med. 2016;48(2):95-101.
17. Cicero AF, Girolimetto N, Bentivenga C, Grandi E, Fogacci F, Borghi C. Short-Term Effect of a New Oral Sodium Hyaluronate Formulation on Knee Osteoarthritis,A Double-Blind, Randomized, Placebo-Controlled Clinical Trial. Diseases. 2020;8(3):26.

Cite this article as: Deb B, Gobaloussamy B, Murugesan S, Sivakumar G. Evaluation of efficacy and safety of Collashot C2 plus capsule in osteoarthritis patients. Int J Res Orthop 2024;10:954-9.