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Original Research Article

# Management of Osteoarthritis: Clinical Efficacy of Nutraceuticals

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**Abstract**

**Aim:** The aim of the present study was to evaluate the marketed product TriNyros (combination of Rosehip, IridoForceTM, Aflapin) (Nutragenix Healthcare Pvt. Ltd.) as an additive treatment in OA patients and its effect in patients with & without comorbidity.

**Methods:** A phase IV post marketing surveillance study of Cap. TriNyros (Nutragenix Healthcare Pvt. Ltd.) was conducted at Department of Orthopaedics, Shree Narayan Medical Institute & Hospital, Saharsa, Bihar, India for 1.5 years. During the study total 80 patients were selected based on inclusion and exclusion criteria in which comprise 30 (37.5%) males and 50 (62.5%) females. The mean age of the subject was 58.60 years, and 70% patients belong to the age group above 50 years. Out of 80 patients, 75% patients had comorbidities such as hypertension, anxiety, diabetes mellitus, thyroid disorders etc. All the subjects selected during the study received TriNyros capsule two times daily for three months.

**Results:** During analysis of clinical symptoms parameters such as joint line tendinitis on palpations, limitation of mobility, joint crepitus, swelling and redness were included in the study. The treatment with TriNyros for 3 months leads to 60.64% reduction in pain on palpations of OA patient. Movement of a joint affected by OA may cause a crackling or grating sensation called "crepitus". The reduction rate for joint crepitus is similar in OA patient with comorbidity (72.65%) & without comorbidity (66.70%).

**Conclusion:** OA as it has an important effect on the treatment. Finally, only one fixed dose of TriNyros was used during the study to evaluate its efficacy; hence we could not validate effect of different doses on safety and efficacy in OA patient. The findings of the current phase IV post marketing surveillance suggest that TriNyros (Nutragenix Healthcare Pvt. Ltd) act synergistically to exert anti-inflammatory/anti-arthritic activity. Cap TriNyros efficaciously reduces joint pain and improves the physical functional ability of OA patient.

**Keywords:** Osteoarthritis, aflapin, devils claw, anti-inflammatory, nutraceuticals; pain relief



## Introduction

Osteoarthritis (OA) is one of the most prevalent and disabling chronic diseases affecting older people. A high prevalence of OA among older people and women and the moderate to severe impact on daily life pose a significant public health problem. [1,2] Estimates of the prevalence and incidence of OA vary widely as a result of heterogeneous definitions and the methods used to gather this information. Conservative estimates of prevalence derived from the presence of symptoms alone may be as low as 2–3 % of the

population, while including symptoms in combination with radiographic findings, radiographic findings alone or self-reporting of diagnosis can raise estimates of prevalence to over 30 % in patients over 60 years old. [3-5]

A comprehensive understanding of the risk factors and the long-term advantages of the management of OA, while abolishing social disparities that may inhibit proper access to health services, is of paramount importance. OA affects the whole joint and is strongly mediated by age-related cellular senescence6, genetics, and injury/ malalignment [7] and is possibly exacerbated and/orinduced by obesity and metabolic syndrome. [8,9] A stress stimulus can trigger innate immunity [10] and is partly due to the unique physiology of the articular cartilage inflammation that is sustained [11] in a catabolic, oxidative environment. [12] The activation of detrimental molecular cascades creates feedback loops that further contribute to the degradation and ossification of the cartilage, the inflammation of the synovium, and the formation of osteophytes.

The occurrence of OA is usually associated with synovial inflammation which is generally influenced by 5-lipoxygenase (5-LOX) pathway, proinflammatory cytokines and matrix metalloproteinases (MMP). These factors contribute to the enzymatic degeneration of cartilaginous matrix and leads to worsening the OA condition. Different treatment options such as use of drugs like NSAIDs and surgery can be considered for relieving pain from OA. However different study findings suggest that NSAIDs which are used to reduce the pain ultimately inhibit collagen matrix synthesis and thereby may cause more damage in OA. Literature review for OA treatment suggest that nutraceuticals has become a viable option for treatment of OA due to its low side effects. [13-15]

In recent years, interest in nutraceuticals such as Boswellia, Curcumin, Rose hip, aflapin, collagen peptide, ginger, glucosamine etc. is increasing owing to their strong ethnobotanical indication. [16]

Nutraceutical formulations which include rose hip, devils claw and aflapin are popular due to their synergistic action in OA. Rose hip (berry fruits of Rosa canina L) contains different active ingredient such as GOPO (1,2-di-O-α-linolenoyl-3-O-β-d-galactopyranosyl-sn-glycerol), gallic acid, astragalin, turmeric acid etc. which plays important role in the treatment of rheumatoid arthritis. It shows causes reduction in pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), inhibit COX 1 & 2, reduces levels of C-reactive protein (CRP). [17] Devils claw also known as Harpagophytum procumbens is a traditional African plant & it has been used as an anti-inflammatory agent in OA. It contains different acetylated phenolic glycosides, terpenoids and iridoid glycosides and primarily marketed as pain killer and anti-inflammatory agent in rheumatism and other joint disorders. IridoForceTM is the standardized extract of devils claw used in OA. [18] Aflapin is selective inhibitor of 5-LOX enzyme obtained from Boswellia serrata gum resin. It exerts its anti-inflammatory action by inhibition of 5-LOX & suppression of leukotrienes. [19]

The aim of the present study was to evaluate the marketed product TriNyros (combination of Rosehip, IridoForceTM, Aflapin) (Nutragenix Healthcare Pvt. Ltd.) as an additive treatment in OA patients and its effect in patients with & without comorbidity.

## Methods

The present observational study was conducted at Department of Orthopaedics, Shree Narayan Medical Institute & Hospital, Saharsa, Bihar, India for 1.5 years. The study protocol of Cap. TriNyros was duly approved by Ethics committee.

Methodology

All subjects who had signed written informed consent form before screening were enrolled and followed up-to three months. During the study total 80 patients were selected based on inclusion and exclusion criteria in which comprised 30 (37.5%) males and 50 (62.5%) females. The mean age of the subject was 58.60 years, and 70% patients belong to the age group above 50 years. Out of 80 patients, 75% patients had comorbidities such as hypertension, anxiety, diabetes mellitus, thyroid disorders etc. All the subjects selected during the study received TriNyros capsule two times daily for three months.

**Settings and participants**

Patients were recruited from Department of Orthopaedics, Lord Buddha Koshi Medical College & Hospital, Saharsa, Bihar, India aged between 18 to 70 years with the clinical diagnosis of osteoarthritis of the knee based on the American College of Rheumatology (ACR) criteria and at least moderate pain in the knee (rated at 5 or greater by the subject on a visual analog scale) during the most painful knee movement during the last month. Patients who had uncontrolled diabetes, hypertension, hepatic disorder, pregnant & lactating women, acute joint trauma of knee were excluded from the study.

**Study intervention**

During the study, the enrolled subjects were treated with TriNyros capsule [Rosehip 275 mg, Irido Force TM (Devil`s claw extract) 100 mg and Aflapin® 50 mg] twice daily for 3 months. All patients were advised not to consume other ayurvedic, herbal and homeopathic treatment during study period. The record of concomitant medication was maintained during study.

**Outcome and follow up**

At screening, baseline, day 15, 30, and 60 data was obtained using standard case report forms. The primary objective was to evaluate the OA symptoms, WOMAC score, and Pain during the study. Pain on palpation, limited mobility, joint crepitus, edema, and redness were all graded on a 4-point scale (0 = not at all, 1 = mild, 2 = moderate, 3 = severe). The Western Ontario and McMaster Universities (WOMAC) osteoarthritis index was used to quantify the severity of osteoarthritis symptoms, with a higher WOMAC score indicating more severe symptoms. The subjects rated their discomfort on a 10-mm visual analogue scale (VAS). At days 0, 15, 30 and 60, the WOMAC, pain, and OA symptoms were evaluated. On day 60, the patient's global assessment and the physician's global assessment were to be evaluated.

**Statistical analysis**

Demographic data were analyzed using descriptive statistics. The Difference in clinical response before and after the treatment was assessed for normal distribution using the Kolmogorov Smirnov test. The paired Student’s t-test was also used. For distribution free data, the Mann Whitney U test was used. All tests were carried out at 5% significance.

**Results**

**Table 1: Demographics, anthropometrics and clinical characteristics of OA patients that participated in the study**

| | TREATMENT | | |
|---|---|---|---|
| | **BT** | **AT** | **P** |
| | **N=40** | **N=40** | |
| **Sex** | | | |
| Men | 15 | 15 | |
| Women | 25 | 25 | 1.000 |

| | | | |
|---|---|---|---|
| **Age** | 58.60 | 60.4 | 0.890 |
| Fat %, mean (SD) | 38.6 (9.5) | 32.5 (10.6) | 0.086 |
| BMI (kg/m2), mean (SD) | 32.8 (6.2) | 28.4 (4.8) | 0.225 |
| WHR, mean (SD) | 0.92 (0.08) | 0.96 (0.07) | 0.720 |
| K&L (disease severity) | | | |
| 2 | 5 | 12 | 0.125 |
| 3 | 15 | 20 | |
| 4 | 20 | 8 | |

80 patients were randomized to receive the allocated intervention, either BT (N = 40) or AT (N = 40). Sample characteristics of the 80 participants with a mean age of 58.60 years (SD = 11.7) are presented in Table 1.

**Table 2: Clinical symptoms score at baseline and 60 days treatment with TriNyros**

| **Parameters** | **Before TriNyros at baseline (Mean + SD)** | **After TriNyros at Day 60 (Mean + SD)** | **% Change after 60 days of treatment** |
|---|---|---|---|
| Pain on Palpations | 1.90 + 0.70 | 0.75 + 00.44 | 60.64% |
| Limitation of Mobility | 2.10 + 0.65 | 0.72 + 0.45 | 62.70% |
| Joint Crepitus | 1.36 + 0.62 | 0.43 + 0.55 | 66.50% |
| Swelling | 1.40 + 0.65 | 0.26 + 0.44 | 82.50% |
| Redness | 0.65 + 0.55 | 0. 07 + 0.24 | 86.80% |

During analysis of clinical symptoms parameters such as joint line tendinitis on palpations, limitation of mobility, joint crepitus, swelling and redness were included in the study. The treatment with TriNyros for 3 months leads to 60.64% reduction in pain on palpations of OA patient. (Table 2)

**Table 3: Clinical symptoms score changes in OA patient with comorbidity and without comorbidity after treatment with TriNyros**

| Parameters | At baseline | After 60 days | % Change after 60 days of treatment | Significance |
|---|---|---|---|---|
| **Pain on Palpation** | | | | |
| With comorbidity | 1.94 + 0.70 | 0.75 + 0.48 | 64.40% | P< 0.05 |
| Without comorbidity | 1.90 + 0.65 | 0.70 + 0.43 | 60.20% | |
| **Limitation of mobility** | | | | |
| With comorbidity | 2.10 + 0.60 | 0.78 + 0.45 | 62.80% | P< 0.05 |
| Without comorbidity | 1.95 + 0.55 | 0.68 + 0.50 | 65.55% | |
| **Joint crepitus** | | | | |
| With comorbidity | 1.37 + 0.65 | 0.43 + 0.55 | 66.70% | P< 0.05 |
| Without comorbidity | 1.39 + 0.68 | 0.45 + 0.56 | 72.65% | |
| **Swelling** | | | | |
| With comorbidity | 1.46 + 0.67 | 0.25 + 0.45 | 82.20% | P< 0.05 |

| | | | | |
|---|---|---|---|---|
| Without comorbidity | 1.42 + 0.68 | 0.27 + 0.49 | 80.45% | |
| **Redness** | | | | |
| With comorbidity | 0.75 + 0.55 | 0.07 + 0.26 | 87.70% | P< 0.05 |
| Without comorbidity | 0.65 + 0.66 | 0.09 + 0.32 | 83.40% | |

Movement of a joint affected by OA may cause a crackling or grating sensation called "crepitus". The reduction rate for joint crepitus is similar in OA patient with comorbidity (72.65%) & without comorbidity (66.70%). (Table 3)

## Discussion

Osteoarthritis (OA) as a degenerative chronic joint cartilage disorder is the most prevalent and principal reason for joint pain and functional impairment in the world. [20] OA is more prevalent in older adults and it will inflict incredible economic and societal charges and disturb life quality in different aspects subsequently in the future. [21] On the other hand, discomfort, pain and decreases in functional ability because of OA can consequence a greater risk of overweight/obesity, diabetes mellitus and falls and fractures. [22]

The improvement in OA was observed in early 1st week after initiation of treatment with TriNyros. Patient and physician global assessment revealed that TriNyros is highly accepted and shows no non-compliance during the study. The results obtained in the current study are in line with the previously published study performed by Anand et al. (2020). [23]

Osteoarthritis treatment possesses a huge cost with the restrictions in physical performance and discomfort. Despite this burden and the high prevalence of osteoarthritis, little has been done to alter the disease's course and ameliorate symptoms. The current conventional treatment is nonsteroidal anti-inflammatory drugs (NSAIDs), which relieve symptoms such as pain but do not change the course of cartilage loss and joint degeneration. Furthermore, NSAIDs are linked to a high prevalence of gastrointestinal, cardiovascular, and renal adverse effects, all of which are potentially lethal. [24,25]

Innovations that provide symptomatic relief as well as changethe course of the disease are desperately needed, and nutraceutical techniques have piqued interest as an alternative to pharmacological approaches. TriNyros is the mixture of Rosa canina L. (Rosehip), Boswellia serrata and Harpagophytum procumbens (Devil`s claw) extract, which are most commonly referred in traditional herbal system. Oral administration of Rosa canina L. for three months significantly reduced WOMAC score & stiffness in OA patients. It also reduced the consumption of rescue medication required during OA treatment. [26] Bosewelliaserrata extract consist of 3-O-Acetyl-11-keto-beta-boswellic acid (AKBA) which contribute to its anti-inflammatory action by inhibiting 5-lipoxygenase. Aflapin is a novel composition derived from Bosewellia serrata and Vishal AA et al. 2011 shows that it is more effective in alleviating pain, joint stiffness and improves physical functioning of patients with OA. [27,28]

## Conclusion

OA as it has an important effect on the treatment. Finally, only one fixed dose of TriNyros was used during the study to evaluate its efficacy; hence we could not validate effect of different doses on safety and efficacy in OA patient. The findings of the current phase IV post marketing

surveillance suggest that TriNyros (Nutragenix Healthcare Pvt. Ltd) act synergistically to exert anti-inflammatory/anti-arthritic activity. Cap TriNyros efficaciously reduces joint pain and improves the physical functional ability of OA patient. Further clinical trials with larger sample numbers and varied dosages are needed to establish safety and efficacy.

## References


1. Malemud CJ, Islam N, Haqqi TM. Pathophysiological mechanisms in osteoarthritis lead to novel therapeutic strategies. Cells Tissues Organs. 2003; 174(1-2):34-48.
2. Yelin E. The economics of Osteoarthritis In Brandt KH, Doherty M and Lohmander LS (eds) Osteoarthritis.
3. Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. Bull World Health Organ. 2003;81(9):646–56.
4. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: part II. Arthritis Rheum. 2008;58(1):26–35.
5. Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: part I. Arthritis Rheum. 2008;58(1):15–25.
6. Hou A, Chen P, Tang H, Meng H, Cheng X, Wang Y, Zhang Y, Peng J. Cellular senescence in osteoarthritis and anti-aging strategies. Mechanisms of ageing and development. 2018 Oct 1; 175:83-7.
7. Palazzo C, Nguyen C, Lefevre-Colau MM, Rannou F, Poiraudeau S. Risk factors and burden of osteoarthritis. Annals of physical and rehabilitation medicine. 2016 Jun 1;59(3):134-8.
8. Berenbaum F, Eymard F, Houard X. Osteoarthritis, inflammation and obesity. Current opinion in rheumatology. 2013 Jan 1;25(1):114-8.
9. Courties A, Sellam J, Berenbaum F. Metabolic syndrome-associated osteoarthritis. Current opinion in rheumatology. 2017 Mar 1;29(2):214-22.
10. Woodell-May JE, Sommerfeld SD. Role of inflammation and the immune system in the progression of osteoarthritis. Journal of Orthopaedic Research®. 2020 Feb;38(2):253-7.
11. Robinson WH, Lepus CM, Wang Q, Raghu H, Mao R, Lindstrom TM, Sokolove J. Low-grade inflammation as a key mediator of the pathogenesis of osteoarthritis. Nature Reviews Rheumatology. 2016 Oct;12(10):580-92.
12. Lepetsos P, Papavassiliou AG. ROS/oxidative stress signaling in osteoarthritis. Biochimicaet Biophysica Acta (BBA)-Molecular Basis of Disease. 2016 Apr 1;1862(4):576-91.
13. Heidari-Beni M, Moravejolahkami AR, Gorgian P, Askari G, Tarrahi MJ, Bahreini-Esfahani N. Herbal formulation turmeric extract, black pepper, and ginger versus Naproxen for chronic knee osteoarthritis: A randomized, double-blind, controlled clinical trial. Phytother Res. 2020 Aug; 34(8):2067-2073.
14. da Costa BR, Reichenbach S, Keller N, Nartey L, Wandel S, Jüni P, Trelle S. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis. The Lancet. 2017 Jul 8;390(10090):e21-33.
15. Izzo AA, Hoon-Kim S, Radhakrishnan R, Williamson EM. A critical approach to evaluating clinical efficacy, adverse events and drug interactions of herbal remedies. Phytotherapy Research. 2016;30(5):691-700.
16. Panahi Y, Rahimnia AR, Sharafi M, Alishiri G, Saburi A, Sahebkar A. Curcuminoid Treatment for Knee Osteoarthritis: A Randomized Double-Blind Placebo-Controlled Trial.

Phytotherapy Research. 2014; 28 (11): 1625-1631.
17. Mármol I, Sánchez-de-Diego C, Jiménez-Moreno N, Ancín-Azpilicueta C, Rodríguez-Yoldi MJ. Therapeutic Applications of Rose Hips from Different Rosa Species. Int J Mol Sci. 2017;18(6):1137.
18. Williams CA. Specialized dietary supplements. Equine applied and clinical nutrition. Elsevier Ltd., Edinburgh, United Kingdom. 2013 Jan 1:351-66.
19. Suva MA, Kheni DB, Sureja VP. Aflapin®: A novel and selective 5-lipoxygenase inhibitor for arthritis management. Indian Journal of Pain. 2018 Jan 1;32(1):16.
20. Szychlinska MA, Trovato FM, Di Rosa M, Malaguarnera L, Puzzo L, Leonardi R, Castrogiovanni P, Musumeci G. Co-expression and co-localization of cartilage glycoproteins CHI3L1 and lubricin in osteoarthritic cartilage: morphological, immunohistochemical and gene expression profiles. International journal of molecular sciences. 2016 Mar 11;17(3):359.
21. Ameye LG, Chee WS. Osteoarthritis and nutrition. From nutraceuticals to functional foods: a systematic review of the scientific evidence. Arthritis research & therapy. 2006 Aug;8(4):1-22.
22. Concetta Aiello F, Maria Trovato F, Anna Szychlinska M, Imbesi R, Castrogiovanni P, Loreto C, Musumeci G. Molecular links between diabetes and osteoarthritis: The role of physical activity. Current diabetes reviews. 2017 Feb 1;13(1):50-8.
23. Chakraverty G, Gupta A, Desai A, Anand SS. Clinical benefits and risk assessment of TriNyros in osteoarthritis of the knee: BRATO evidence generation program. International Journal of Orthopaedics. 2020;6(4):954-60.
24. Bjarnason I, Thjodleifsson B. Gastrointestinal toxicity of non-steroidal anti-inflammatory drugs: the effect of nimesulide compared with naproxen on the human gastrointestinal tract. Rheumatology (Oxford, England). 1999 May 1;38(suppl_1):24-32.
25. Lindler BN, Long KE, Taylor NA, Lei W. Use of Herbal Medications for Treatment of Osteoarthritis and Rheumatoid Arthritis. Medicines (Basel). 2020 Oct 28;7(11):67.
26. Winther K, Apel K, Thamsborg G. A powder made from seeds and shells of a rose-hip subspecies (Rosa canina) reduces symptoms of knee and hip osteoarthritis: a randomized, double-blind, placebo-controlled clinical trial. Scand J Rheumatol. 2005 Jul-Aug; 34(4):302-8.
27. Vishal AA, Mishra A, Raychaudhuri SP. A Double Blind, Randomized, Placebo Controlled Clinical Study Evaluates the Early Efficacy of Aflapin® in Subjects with Osteoarthritis of Knee. Int J Med Sci. 2011;8(7):615-622.
28. Batool D. R., Jamal D. K., Sheroze D. M. W., Bhatti D. I. A., Jaffar D. N., Haider D. G., & Faridi D. M. A. Clinical features of colorectal carcinoma at the Jinnah Postgraduate Medical Centre, Karachi, Pakistan: a cross-sectional study. Journal of Medical Research and Health Sciences, 2022;5(9): 2203–2209.