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A community-based study for evaluation of Ayurvedic formulations in the management of Osteoarthritis Knee

Research Article

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Abstract

Background: Osteoarthritis (OA) of the knee is a major public health concern that leads to pain, disability and decreased quality of life. A similar condition has been described in Ayurveda under the name *Sandhigata Vata* which is caused by vitiation of *Vata* in the body. Objectives: Evaluation of the effectiveness and tolerability of *Yograj Guggulu*, *Ashwagandha Churna*, and *Narayana Taila* in OA knee. Materials and methods: The study was a prospective, multi-center, non-controlled interventional, community-based study conducted in 10 centres in India. 493 participants of any gender aged between 40 to 65 years & diagnosed with OA knee as per the diagnostic criteria American College of Rheumatology (2012), were enrolled in the study considering selection criteria. Ayurvedic formulations, *Yograj Guggulu* & *Ashwagandha Churna* were administered orally along with the local application of *Narayana Taila* twice daily for 12 weeks. The assessment was carried out on 28th, 56th, 84th and 112th day for any changes in the outcome measures. Results: The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total score, the WOMAC sub-scores for pain, stiffness and difficulty in physical activity, the Visual Analogue Scale (VAS) score for pain and the disease-specific symptoms were significantly decreased throughout treatment and during follow-up without intervention. Conclusion: The study demonstrates that the Ayurvedic interventions are well tolerable and beneficial in reducing the symptoms of OA knee.

Keywords: Osteoarthritis, *Sandhigata Vata, Yograj Guggulu, Ashwagandha Churna, Narayana Taila.*

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Introduction

Osteoarthritis (OA) is a very common musculoskeletal disorder that is characterised by a gradual deterioration of cartilage in the joints and subsequent synovial cavity inflammation. (1) It is one of the main causes of pain and disability around the world and raises healthcare expenses for both people

and society as a whole. India had a 2.66-fold increase in the number of cases of symptomatic OA over the past three decades, from 23.46 million in 1990 to 62.35 million in 2019. (2) The prevalence of OA is found to be increasing with age and body mass index (BMI). (3) According to the WHO, approximately 73% of patients with osteoarthritis are older than 55, and 60% of them are female. OA mostly affects the joints in the knee, hands, hip, and spine, but OA knee is the most common site with a prevalence of approximately 60.6%, followed by hand and hip. (4) The symptoms of OA include joint pain, swelling, and stiffness, which over time limit everyday activities and lower the quality of life.

Guidelines for the treatment and management of osteoarthritis in adults issued by the National Institute for Health and Clinical Excellence (NICE) suggest the use of analgesics along with NSAIDs topically or orally, non-pharmacological treatments such as exercise, weight loss, etc., and surgical intervention in cases of mechanical locking or evidence of loose bodies in x-ray. (5) NSAIDs can raise the risk of adverse drug reactions in patients, especially in the elderly. Chronic usage of these can result in a variety of impairments, including dyspepsia, gastrointestinal bleeding, renal impairments leading to acute renal failure & higher risk of cardiovascular disorders, etc. (6, 7)

Ayurvedic treatments for arthritis are gaining interest worldwide, and more studies are currently being carried out in search of a better alternative with fewer adverse effects than NSAIDs. According to a randomised controlled trial, in comparison to conventional care, Ayurveda resulted in significant improvements in the reduction of disease-specific symptoms of OA knee after 12 weeks of treatment, with the majority of effects lasting over 12 months. (8) The symptoms of OA are similar to *Sandhigata Vata* (9) mentioned in Ayurveda classics which is caused by the vitiated *Vata Dosha* localized in the knee joints. The *Vatakopa* is mainly caused by *Dhatukshaya* (Degeneration of tissue elements) or *Avarana* (Covering) with other vitiated *Doshas*. (10) In OA knee, degeneration of tissue elements occurs and the ayurvedic management of the condition is based on the alleviation of Doshas relieving the pain and stiffness, strengthening joints & muscles and improving quality of life. The drugs in the study were selected based on their activity in slowing down the *Dhatukshaya* and improving the body's strength to prevent the degenerative changes happening in the body along with *Sothahara* (Anti-inflammatory), *Vedanasamaka* (Analgesic) and *Snehana* (Lubrication) properties which help in the alleviation of symptoms. The effectiveness of drugs *Yograj Guggulu, Ashwagandha Churna,* and *Narayana Taila* has been demonstrated in a study conducted earlier in a smaller study setting. (11) The present study was designed for the evaluation of the selected Ayurvedic formulations in the OA knee.

Materials and methods

Study design

The study was designed as a prospective, single-arm, multicentre community-based, interventional study with endpoints as treatment and tolerability. The study was conducted by the Central Council for Research in Ayurvedic Sciences (CCRAS) under the Ayurveda Mobile Health Care Programme- Schedules Caste Sub-Plan (AMHCP-SCSP) program through 10 peripheral institutes.

Selection Criteria

Inclusion Criteria

The participants of any gender from the scheduled caste community in the age group 40–65 years were enrolled in the study after obtaining written informed consent. Participants of primary OA knee (Unilateral/ bilateral) as per any one of the following three American College of Rheumatology (ACR- 2012) diagnostic criteria were enrolled.

1. Using history and physical examination: Pain in the knee and 3 of the following
    a. Over 50 years of age
    b. <30 minutes of morning stiffness
    c. Crepitus on active motion
    d. Bony tenderness
    e. Bony enlargement
    f. No palpable warmth
2. Using history, physical examination and radiographic findings (if available): Pain in the knee and one of the following:
    a. Over 50 years of age.
    b. < 30 minutes of morning stiffness
    c. Crepitus on active motion and osteophytes
3. Using history, physical examination and laboratory findings (if available): Pain in the knee and 5 of the following:
    a. Over 50 years of age.
    b. < 30 minutes of morning stiffness
    c. Crepitus on active motion
    d. Bony tenderness
    e. Bony enlargement
    f. No palpable warmth of synovium
    g. ESR < 40mm/hour
    h. Rheumatoid Factor (RF) < 1:40
    i. Synovial fluid (SF) signs of osteoarthritis

Exclusion criteria

Individuals with a BMI≥32kg/m² at the screening visit or any co-morbid conditions such as cardiac arrhythmia, acute coronary syndrome, myocardial infarction, or stroke in the last 6 months were not enrolled in the study. People who had renal, hepatic, or pulmonary dysfunction (asthmatic and COPD patients), uncontrolled diabetes mellitus, and hypertension were excluded. Diagnosed cases of Rheumatoid Arthritis or other inflammatory arthritis and those who reported to have been under anti-arthritic medication were not enrolled. Those who had a history of trauma to the afflicted joint, or were using ambulatory aids such as a wheelchair, walker, etc. or those who had been

prescribed joint replacement surgery were excluded. Pregnant women or those who were planning for conception, lactating mothers, and participants in any other clinical trial were not enrolled. Any other condition that the principal investigator found that could jeopardize the study was also excluded.

Withdrawal criteria

The participants were free to leave at any time if they so desired, their condition worsened, or any of the other conditions listed in the exclusion criteria manifested during the trial period.

Study procedure

The screening of participants was carried out from the OPD and medical camps conducted in selected SC-dominated areas under the AMHCP-SCSP Programme. Permission from local administrative authorities was obtained before the onset of the study. The participants were screened for clinical symptoms and those fulfilling the defined selection criteria were enrolled after getting written informed consent. (Figure 1.) All the participants were thoroughly informed about the study, both verbally and in writing (in the local language). The trial was conducted in accordance with ethical principles as per the Declaration of Helsinki for biomedical research and ICMR ethical guidelines involving human participants (2006), which are consistent with ICH Good Clinical Practice (GCP) guidelines. Approval from the Institutional Ethical Committee (IEC) for each study centre was obtained and the study was registered in the Clinical Trial Registry of India (CTRI/2021/07/034925) before initiation. The study schedule is depicted in Figure 2.

Figure 1. Study procedure

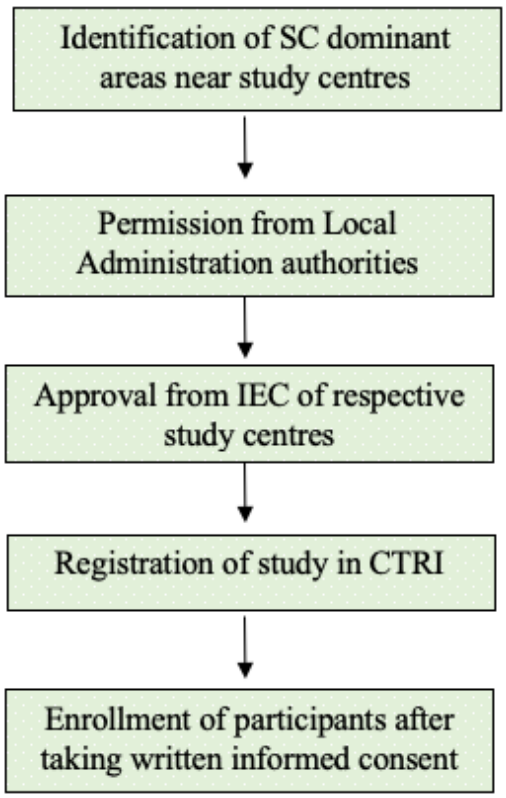
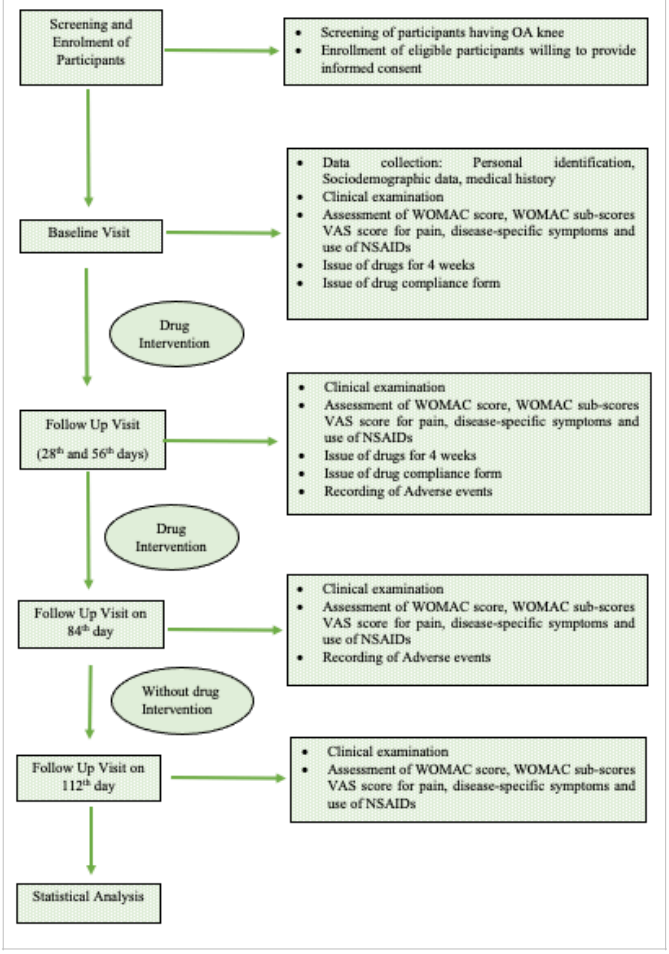


Figure 2. Flow chart depicting the study schedule



Intervention

The study drugs were procured from a Good Manufacturing Practice (GMP)-certified company, Indian Medicines Pharmaceutical Corporation Limited (IMPCL). *Yograj Guggulu* 500 mg and *Ashwagandha Churna* 3 g were administered internally with water after food twice daily along with local application of *Narayana Taila* for 12 weeks.

Assessment criteria

The primary outcome of the study was any change in the total score of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) modified CRD Pune Version. The secondary outcome measures were any change in WOMAC sub-scores (Pain, Stiffness, and Difficulty in physical activity), the Visual Analogue Scale (VAS) score for pain, frequency of use of NSAIDs or analgesic medication and change in Ayurvedic disease-specific symptoms of OA such as *Sandhishula* (Pain in joints), *Sandhishotha* (Joint swelling), *Akunchanaprasaranayoh Vedana* (Pain on movement), *Stambha* (Joint stiffness), and *Sandhisphutana* (Crepitus). The outcome measures were assessed on the 28th, 56th, 84th days and also on 112th day (without intervention). The drug's tolerability was assessed by the proportion of recruited participants completing the study.

Sample Size

The sample size was estimated based on the assumption of detecting a relevant change of 5 points in the WOMAC Score pre-and post-test and the standard deviation of 15 points with a 95% confidence level (α = 0.05) and 80% power. Expecting a dropout rate of 20% the sample size was calculated as below: -

$$\alpha = 0.05 \text{ Hence } Z_{1-\alpha/2} = 1.96$$
$$1-\beta = 80\% \text{ hence } Z_{1-\beta} = 0.8416$$
$$\sigma = 15 \text{ points}$$
$$\delta = 5 \text{ points}$$
$$= 41$$

Assuming a dropout rate of 20 % Sample size per centre = 41 + 8.2 = 49.2.

Thus, the total sample size calculated was 500 (50 participants from each study centre).

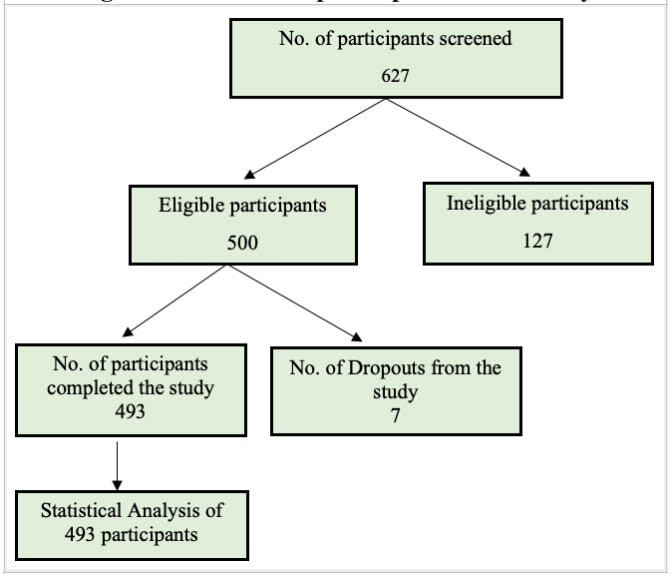
Statistical Analysis

All the descriptive and continuous data were summarized as number (%) and mean (SD) respectively. The outcome measures, changes in total WOMAC score, WOMAC sub-scores and VAS score for pain were analyzed using the Repeated Measures ANOVA test. The change in disease-specific symptoms and the frequency of use of NSAIDs during the study period were compared using the Cochrane Q-test. The data were analysed using Statistical Package for the Social Sciences (SPSS) software version 15.0.

Observation and Results

In this study, a total of 627 individuals were screened. 500 participants fulfilling the selection criteria were enrolled. Out of these, 7 participants dropped out from the study. The statistical analysis was carried out for the 493 participants who completed the study. The outflow of participants in the study is given in the Figure. 3.

Figure 3: Outflow of participants in the study



Sociodemographic and Baseline Data

Analysis of the data shows that the number of female participants was more in the study (66.2%) and most of the participants were of age greater than 50 years (66.4%). The maximum number of participants were involved in household work (67%). The majority of them were indulged in moderate to heavy labour (72.4%). The details of the demographic data are summarised in Table No.1. Data on disease-specific symptoms show that 86% of participants had bilateral knee joint involvement. The Body Mass Index (BMI) of the majority of participants (55.4%) was found to be in the normal range. 35.6% of them were in the overweight range and 6.4% had class I obesity.

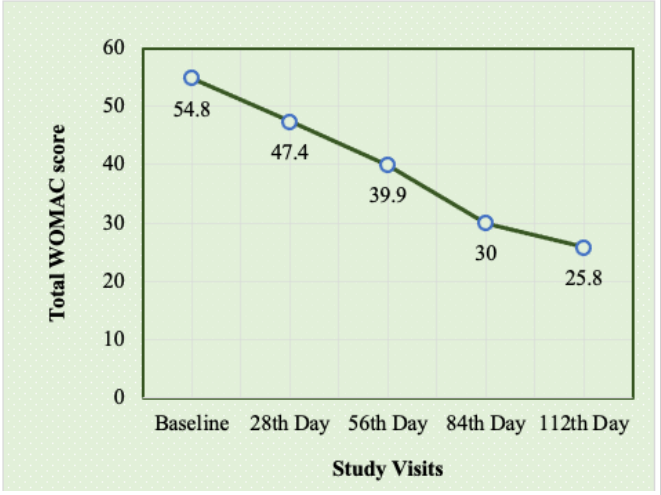
Table. 1. Sociodemographic & Baseline data

Sociodemographic and baseline characteristics		N (%)		
		Total	Male	Female
Age	≤50	168 (33.6)	45 (26.6)	123 (37.2)
	>50	332 (66.4)	124 (73.4)	208 (62.8)
Gender	Male	169(33.8)		
	Female	331(66.2)		
Socio -economic Status	Above poverty line	231(46.2)		
	Below poverty line	269(53.8)		
Present Occupation	Desk Work	23(4.6)		
	Fieldwork (Physical labour)	92(18.4)		
	Field Work	50(10.0)		
	Household Work	335(67.0)		
Habitat	Urban	107(21.4)		
	Semi-urban	20(4.0)		
	Rural	373(74.6)		
Dietary Habits	Vegetarian	153(30.6)		
	Non- Vegetarian	347(69.4)		
Addictions	Present	50(10.0)		
	Absent	450(90.0)		
Chronic Illness	Absent	485(97.0)		
	Present	15(3.0)		
Physical Exercise	Heavy Labour	75(15.0)		
	Moderate Labour	287(57.4)		
	Office Job	23(4.6)		
	Sedentary	115(23.0)		
Emotional stress	Average	331(66.2)		
	Moderate	152(30.4)		
	Too Much	17(3.4)		

Effect of intervention on outcome measures

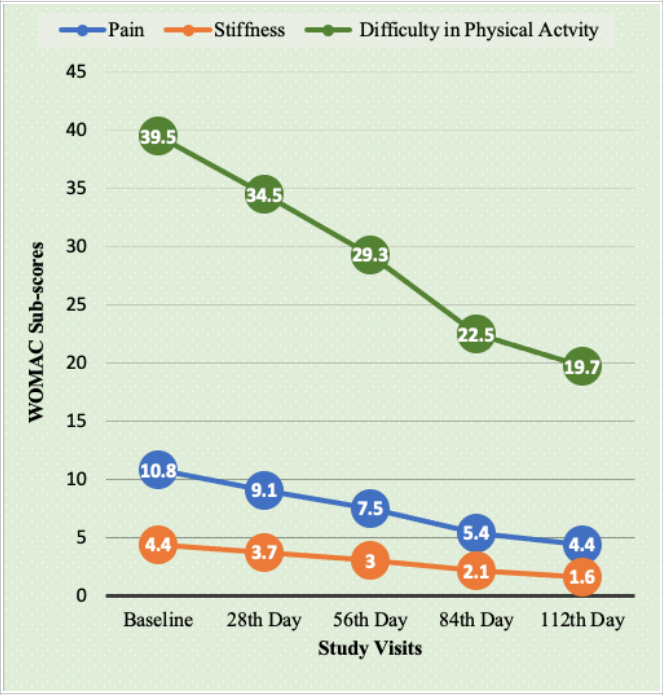
The WOMAC total score decreased during treatment from baseline (54.8±19.4) to 28th day (47.4±19.8), 56th day (39.9±18.4) and 84th day (30.0±15.7). On the 112th day, it further reduced (25.8±16). The reduction in the score was statistically significant ($p < 0.001$). (Graph.1)

Graph.1. Effect of intervention on Total WOMAC score



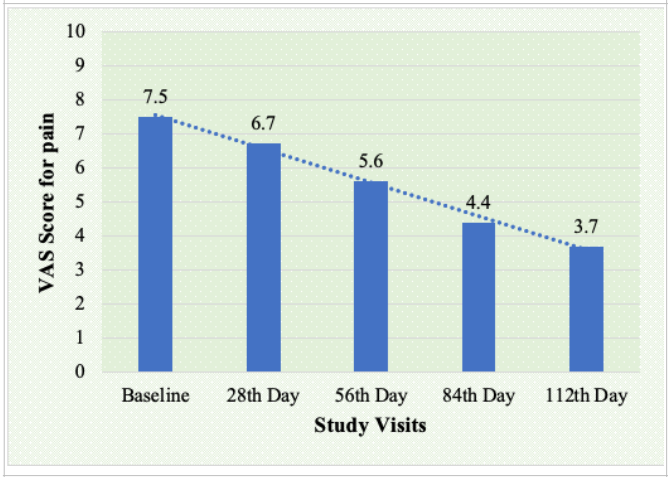
The WOMAC sub-score for 'pain' reduced significantly (p <0.001) from baseline (10.8±4.54) to 84th day (5.4±3.56) and 112th day (4.4±3.63). The 'stiffness' sub-score reduced significantly (p <0.001) from baseline (4.4±1.97) to 84th day (2.1±1.67) and 112th day (1.6±1.65). The analysis of the 'difficulty in physical activity' sub-score showed a significant reduction (p <0.001) from baseline (39.5±13.61) to 84th day (22.5±11.29) and 112th day (19.7± 11.29). (Graph 2.)

Graph 2. Effect of intervention on WOMAC sub-scores

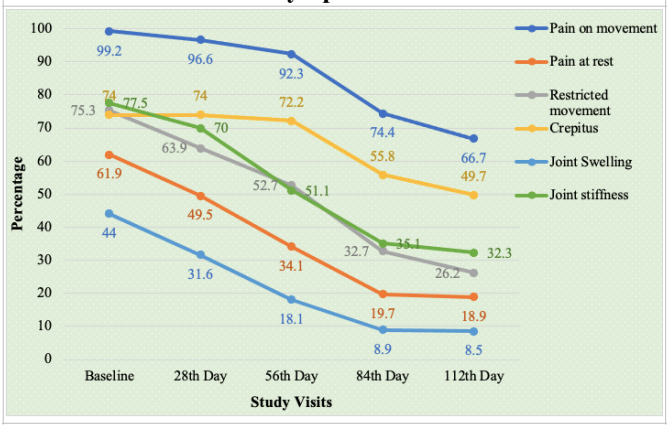


The VAS score for pain decreased significantly (p <0.001) from baseline (7.5±1.29) to 84th day (4.4±1.62) and 112th day (3.7±1.82). (Graph.3.) All the disease-specific symptoms such as joint pain at rest, swollen joints, joint pain on movement, joint stiffness, and crepitus significantly reduced (p<0.001) from baseline to 84th day and 112th day (Graph.4). The frequency of use of NSAIDs in participants reduced from baseline (2.8%) to 84th day (0.2%) at the end of treatment. However, the proportion of participants using NSAIDs/analgesics increased to 0.6% on 112th day (without intervention).

Graph 3. Effect of intervention on VAS score for pain



Graph 4. Effect of intervention on disease-specific symptoms



88.6% of participants reported sound sleep at baseline, which increased to 95.5% at the end of treatment and 97.7% had sound sleep at follow-up without intervention. Regular bowel habit was observed in 88.2%, 96.6% and 98% at baseline, 84th day and 112th day respectively. Good appetite was observed in 72.2% at baseline and 82.2% & 89.5% on the 84th day and 112th day respectively. No adverse events were observed during the study period. Out of 500 enrolled participants, the majority of participants (493) completed the study which shows the tolerability of the interventions.

Discussion

In this study, higher number of female participants was found which is in accordance with previous studies showing a higher prevalence in females. This could be linked to a variety of factors, including anatomical variations, genetics, and hormonal irregularities. (12) The majority of participants were of the age greater than 50 years. Ageing is one of the risk factors in the pathophysiology of OA, and studies show that older age contributes to the imbalance between catabolic and anabolic activity in the joint, leading to

OA. (13) The majority of the participants were involved in moderate to heavy physical activity. As per the study conducted to examine the risk of occupational physical activities in OA knee, prolonged kneeling, squatting and high physical workload can result in the disease's manifestation. (14) The majority of the participants were coming from lower socio-economic backgrounds and the studies conducted to assess socioeconomic level and the risk of OA also show that those who live in economically deprived regions are more likely to develop knee, hand, and hip OA. (15) As per Ayurveda, *Vata* is the major factor in the pathogenesis of *Sandhigata Vata*. With the increase in age, *Vata* gets aggravated in the body leading to degeneration. High physical activity contributes to further vitiation of *Vata dosha* and accelerates the process of degeneration and manifestation of OA.

The drug *Yograj Guggulu* is one of the traditional polyherbal formulations indicated in *Vatavyadhi* (diseases caused by aggravated *Vata dosha*) including *Sandhigata Vata*. Most of the ingredients of *Yograj Guggulu* alleviate all three doshas, especially *Vata*. It improves digestion and brings strength to the body. (16) *Yograj Guggulu* demonstrated a dose-dependent rise in the percentage inhibition of the 5-lipoxygenase enzyme that was significantly greater than aspirin. (17) *Guggulu* has also demonstrated anti-inflammatory and anti-arthritic pharmacological activities in albino rats with formaldehyde-induced arthritis. (18) The tolerability study of *Yograj Guggulu* also shows that the drug is tolerated by patients. (19) *Ashwagandha* has *Ushna Virya* (hot in potency) and *Madhura Vipaka* (sweet after digestion) properties, which help in pacifying *Vata Dosha.* (20) It contains a number of phytoconstituents, including withanolides and several sitoindosides, that bring about various pharmacological activities, including anti-inflammatory activity. The studies on *Ashwagandha* have documented the analgesic and anti-arthritic effects. (21, 22) It is proven to be a safe drug that can be used in chronic inflammatory conditions. (23) The anti-oxidant activity of Ashwagandha also contributes to the alleviation of symptoms as it helps in the prevention of cartilage damage caused by OA. (24, 25) The sleep quality and appetite of the participants have improved significantly. Many studies have demonstrated the effect of *Ashwagandha* on insomnia, which could be the reason behind the improvement in sleep in participants. (26) The improvement in appetite could be due to the *Deepana* (appetising) property of *Yograj Guggulu*. (27)

Narayana Taila is a polyherbal preparation used in Ayurveda both internally and externally for *Vatarogas*. (28) In this study, the drug was prescribed for external application for alleviating *Vatadosha* localized in knee joints. As per Ayurveda, *Snehana* (oleation) is one of the best managements described for *Vata Dosha*. The oils generally have *Snigdha* (unctuous), *Guru* (heavy), and *Mridu* (soft) properties, which act against the properties of Vata such as *Ruksha* (dry), *Laghu* (light), and *Khara* (rough). Apart from this, *Narayana Taila* is a medicated oil processed with drugs having *Vatahara* (Pacification of Vata) and *Sothahara* (Anti-inflammatory) properties. All these properties help in reducing pain, stiffness, and movement restrictions in OA. Even though the exact mechanism is unknown, studies have shown the effectiveness of oil application for various disease conditions, especially musculoskeletal disorders. The liposomal drug delivery system used in modern pharmacology incorporates hydrophilic and hydrophobic parts of drugs for enhanced absorption by accumulating at the site of administration in topical applications. Liposome molecules that encapsulate the drug molecules in a lipid bilayer can deliver active constituents by fusing with other bilayers, such as the cell membrane. The hypothesis, which discusses the similarities in structure and functions between liposomes and *Snehapaka* (preparations containing oils and ghee), attempts to give a possible mechanism for the mode of action of topical application of Taila. (29) As in this oil, the anti-inflammatory drugs are dissolved in both hydrophilic (in the form of decoction and paste) and hydrophobic (sesame oil) solvents the active phytoconstituents cross the lipid bilayer membrane of cells and bring about the desired effect at the site of application.

The use of NSAIDs in participants decreased significantly during treatment. but in the follow-up assessment without intervention, the percentage slightly increased. In OA knee, individuals show different clinical manifestations and different rates of progression. (30) The dropout rate during the entire study was very low (1.4%), and there were no adverse events during the intervention. This suggests that the study drugs were accepted and well tolerated by the participants.

Conclusion

The study demonstrates that Ayurvedic formulations- *Yograj Guggulu, Ashwagandha Churna*, and *Narayana Taila* are well tolerable and beneficial in reducing the symptoms of OA knee.

Limitation of study

The study was conducted as a single-arm, open-label study. As it was not a controlled study, the comparable results could not be studied.

Future Scope

A randomised control study with a longer follow-up period without intervention can be designed to validate the results.

Acknowledgement

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Conflicts of interest

There are no conflicts of interest in this study.

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