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Original Research Article

Assessing the effectiveness and NSAIDs sparing effect of celery seeds and *Boswellia serrata* in osteoarthritis management

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ABSTRACT

Aim and Objective: This study examines the anti-inflammatory and analgesic properties of Celery seed and *Boswellia serrata* extracts as potential alternatives for OA treatment, focusing on their effectiveness in reducing pain and improving joint functionality.

Background: Osteoarthritis (OA), a prevalent joint disorder, particularly affects the knees and hips. Current management primarily involves NSAIDs, which can lead to severe side effects, especially in older adults with comorbidities.

Materials and Methods: A multicentre observational study enrolled 394 participants clinically diagnosed with knee osteoarthritis. They continued their usual treatment while taking Celery seeds and *Boswellia serrata* extract tablet twice daily for three months. Primary outcomes included Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores and changes in painkiller and NSAID usage. Secondary outcomes included visual analogue scale (VAS) pain scores.

Results: The study demonstrated significant improvements in primary outcome measures: WOMAC score improved by 17.07% ($p<0.001$), WOMAC pain score by 75.00% ($p<0.001$), WOMAC stiffness score by 72.05% ($p<0.001$) and WOMAC physical function score by 78.93% ($p<0.001$). Secondary outcomes showed VAS score reductions at rest by 67.17% ($p<0.001$) and during movement by 64.28% ($p<0.001$). There was a notable decrease in NSAID usage from baseline 70.09% to 31.89% ($p<0.001$).

Conclusion: Celery seeds and *Boswellia serrata* extract demonstrate promising efficacy as a safer and effective adjunctive therapy for knee osteoarthritis, offering pain relief, enhanced joint functionality and potential reduction in NSAID usage.

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1. Introduction

Osteoarthritis (OA) is a chronic condition marked by the progressive deterioration of joints, which is caused by various factors.[1] It is characterized by the gradual loss of articular cartilage, the growth of bone at joint margins, subchondral sclerosis (hardening of the bone beneath the cartilage) and various biochemical and structural changes in the synovial membrane and joint capsule.[2] OA can impact various joints, with the knee and hip joints being among the most frequently affected.[3] OA stands as the second most prevalent rheumatologic issue and ranks as the most common joint ailment in India, with a prevalence ranging from 22% to 39%. (2) Globally, it's estimated that around 10% to 15% of adults over the age of 60 experience some level of OA, with a higher prevalence observed in women compared to men. Research conducted in Asian nations such as India, Pakistan and Bangladesh revealed that OA of the knee is more prevalent in rural areas, with a rate of 13.7%, compared to 6.9% in urban areas.[3] The pain associated with OA results from a combination of nociceptive and neuropathic mechanisms,

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as well as abnormalities in pain pathways within both the peripheral and central nervous systems (CNS).[4] Inflammatory processes within the joint trigger a series of responses that lead to increased sensitivity of nociceptive primary afferent neurons, peripheral sensitization and increased excitability of nociceptive neurons within the CNS.[5]

In OA, the primary objective of treatment is to alleviate pain intensity and enhance functionality and overall quality of life by employing a blend of non-pharmacological and pharmacological interventions.[6] Guidelines recommend non-steroidal anti-inflammatory drugs (NSAIDs) as first-line therapy for OA.[7] NSAIDs work by inhibiting the production of prostaglandins (PG) and thromboxane A through the blockade of cyclooxygenase (COX). Traditional NSAIDs (tNSAIDs) target both the COX-1 and COX-2 isozymes to varying degrees and are commonly used for symptomatic pain relief in musculoskeletal disorders. However, their long-term use is restricted due to associated toxicities, notably cardiovascular (CV), gastrointestinal (GI) and renal toxicities. While COX-2-selective NSAIDs (coxibs) were initially thought to be safer alternatives, their use has been linked to a heightened risk of cardiovascular events.[8,9]

Elderly patients face a heightened risk of experiencing adverse events (AEs) associated with NSAIDs due to factors such as increased likelihood of polypharmacy and age-related declines in renal function. This population also tends to have a higher prevalence of CV disease, which further elevates the risk of CV, hematologic and renal AEs. Guidelines for the non-surgical management of knee OA by the Osteoarthritis Research Society International suggest that oral non-selective NSAIDs (nsNSAIDs) may be suitable for individual OA patients without comorbidities. However, their appropriateness becomes uncertain for individuals with moderate comorbidity risks and is not recommended for those with high comorbidity risks.[10]

Celery seed extract exerts its anti-inflammatory effects with mechanisms similar to those of NSAIDs, it doesn't cause the unwanted side effects (in particular lesions of the gastrointestinal mucosa) that are determined by prolonged treatments with NSAID.[11] Celery seeds extract, in addition to acting as an analgesic and inflammatory agent, has been shown to protect against and/or reduce gastric irritation caused by NSAIDs, as well as act synergistically with them to reduce inflammation.[12] As per Ayurveda, celery possesses a diverse range of applications, functioning as an aphrodisiac, anthelmintic, antispasmodic, carminative, diuretic, emmenagogue, laxative, sedative, stimulant and toxic agent. Celery is recognized for its mild diuretic properties and urinary antiseptic qualities, traditionally used to alleviate flatulence and gripping pains.[13,14]

Boswellic acid is the active ingredient in *Boswellia serrata*; it has shown significant pharmacological activity in the treatment of inflammatory diseases such as rheumatoid arthritis, chronic bronchitis, asthma and chronic inflammatory bowel diseases.[15] Clinical studies indicates that *Boswellia serrata* extract exhibits anti-inflammatory and anti-arthritis effects, along with enhancing pain relief and physical functionality.

The current study was conducted to evaluate the effectiveness and NSAID sparing effect of Celery seeds and *Boswellia serrata* in osteoarthritis.

2. Materials and Methods

2.1. Study design

The study was a multicentre, prospective, observational study involving patients clinically diagnosed with knee OA according to the criteria set by the American College of Rheumatology (ACR). It was conducted as an observational trial where patients were instructed to continue their usual anti-osteoarthritis treatment, with Celery seeds and *Boswellia serrata* extract tablet serving as an adjunct therapy. The patients were instructed to consume Celery seeds and *Boswellia serrata* extract tablet twice a day for a period of three months.

2.2. Study Participants

The study enrolled 394 participants of both genders aged 18 years and above.

2.3. Inclusion criteria

In this study participants with comprised individuals clinically diagnosed with knee OA according to the criteria outlined by the American College of Rheumatology (ACR), experiencing at least moderate knee pain (rated at 5 or higher on a visual analog scale) during the most painful knee movement within the preceding month and subjects who have not participated in a similar investigation in the past four weeks are included.

2.4. Exclusion criteria

In this study exclusion of participants with pregnancy or breastfeeding women, acute knee joint trauma, uncontrolled diabetes, hypertension, severe cardiac, renal, or hepatic conditions, end-organ damage and individuals unable to comprehend the study procedures and protocols are done.

2.5. Study Outcome

The primary outcome measures included the Western Ontario McMaster Osteoarthritis Index (WOMAC) for pain, stiffness and physical function, the percentage of patients experiencing a reduction in painkiller usage, the percentage of patients needing a decrease in oral NSAID dosage, the percentage of patients shifting from oral NSAIDs to oral

paracetamol.

The secondary outcome measures comprised the Visual Analog Scale (VAS) scores for pain at rest (rated on a scale of 0-10 mm) and pain during movement (rated on a scale of 0-10 mm).

2.6. Statistical analysis

Data collection was conducted using paper case report forms (CRFs) and MS Excel was used for data management. The analysis was performed on predefined parameters corresponding to the efficacy and safety endpoints. Since the observations were on an ordinal scale, the Wilcoxon Signed Rank Test was used to assess the significance between baseline and end-of-treatment values.

3. Result

The present study comprised of 394 patients, out of which 201 (51.02%) were females and 193 (48.98%) were males. (Table 1) The mean age of the patients was 51.35 years. (Table 2) Among all the patients, 145 (42.03%) were on concomitant medications including NSAIDs and paracetamol while 249 (72.17%) were not on any medications for pain relief. (Table 3)

Table 1: Gender wise distribution in percentage

Gender	No of Patients	Percentage
Male	193	48.98%
Female	201	51.02%
Total	394	100.00%

Table 2: Age distribution of participants

	N	Mean	Minimum	Maximum
Age (Years)	394	51.35	21	85

Table 3: Distribution of patients receiving concomitant medication

Concomitant medications	No of Patients	Percentage
No	249	72.17%
Yes	145	42.03%
Total	394	114.20%

3.1. Primary outcome measures

The overall WOMAC score improved by 17.07% (69.98 to 58.03, p<0.001). The change in WOMAC score at day 0, 30, 60 and 90 (Figure 1). The treatment resulted in a 17.07 % improvement in WOMAC score.

The WOMAC pain score significantly reduced from 16.16 at baseline to 4.04 (p<0.001) at the end of the treatment. The change in WOMAC score at day 0, 30, 60 and 90 (Figure 2). The treatment resulted in an overall 75.00% improvement in WOMAC pain score.

The WOMAC stiffness score significantly reduced from 7.82 at baseline to 2.19 (p<0.001) at the end of the treatment. The change in WOMAC score at day 0, 30, 60 and 90 (Figure 3). The treatment resulted in a 72.05% improvement in WOMAC stiffness score.

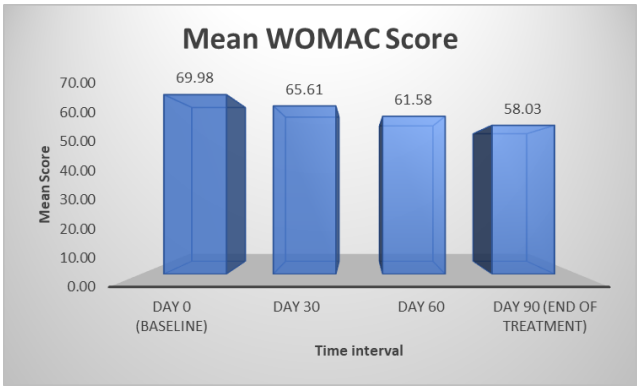

Figure 1: Improvement in overall WOMAC score

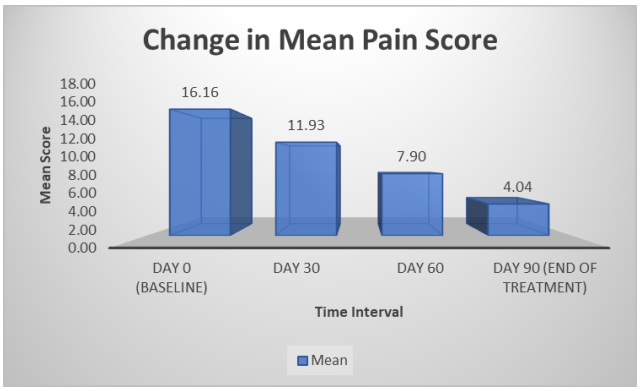

Figure 2: Improvement in WOMAC pain score

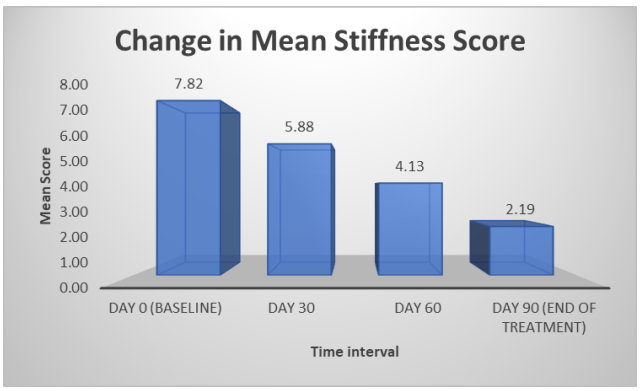

Figure 3: Improvement in WOMAC stiffness score

The WOMAC physical function score significantly reduced from 48.69 at baseline to 10.26 (p<0.001) at the end of the treatment. The change in WOMAC score at day 0, 30, 60 and 90 (Figure 4). The treatment resulted in 78.93% improvement in physical function score.

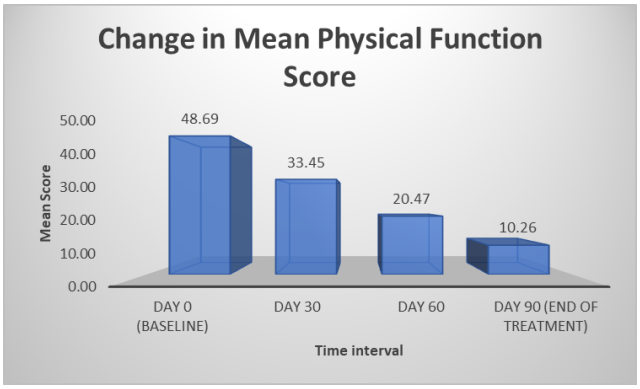

Figure 4: Improvement in WOMAC Physical Function Score

At baseline, the utilization of NSAIDs was recorded at 70.09%, which decreased to 31.89% at the end of the treatment. The usage of paracetamol at the baseline was 8.46%, increasing to 31.89% at the end of treatment. This indicates that certain patients were switched from NSAIDs to paracetamol. Concurrent usage of NSAIDs and paracetamol was observed to be 10.88%, at baseline which dropped to 4.29% at day 90. The change in usage at day 0, 30, 60 and 90 (Figure 5). NSAID dosage reduction was required in 3.55% of patients on day 30 and in 10.65% by the end of the treatment.

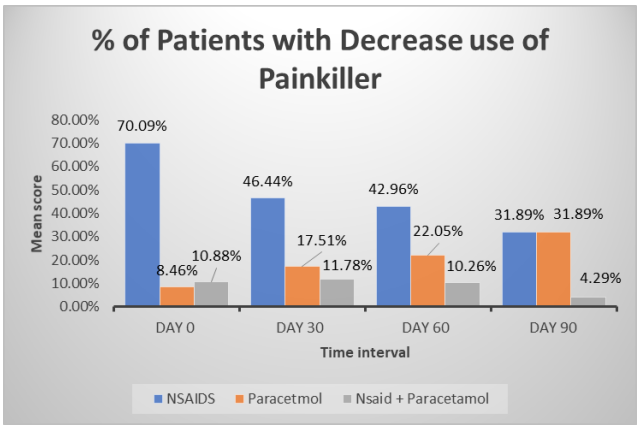

Figure 5: Graphical representation of decreased use of painkillers

3.2. *Secondary outcome measures*

The VAS Score at rest significantly reduced from 7.81 at baseline to 2.57 at the end of the treatment (p<0.001). The change in VAS score at day 0, 30, 60 and 90 (Figure 6). The treatment resulted in a 67.17% improvement in VAS score.

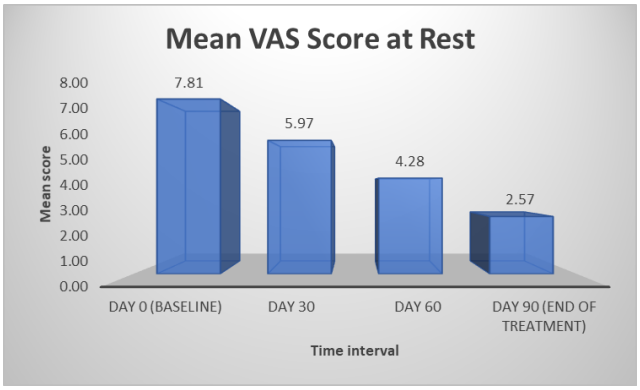

Figure 6: Change in VAS Score at rest

The VAS Score at movement significantly reduced from 8.47 at baseline to 3.02 (p<0.001) at the end of the treatment. The change in VAS score at day 0, 30, 60 and 90 (Figure 7). The treatment resulted in a 64.28% improvement in VAS score.

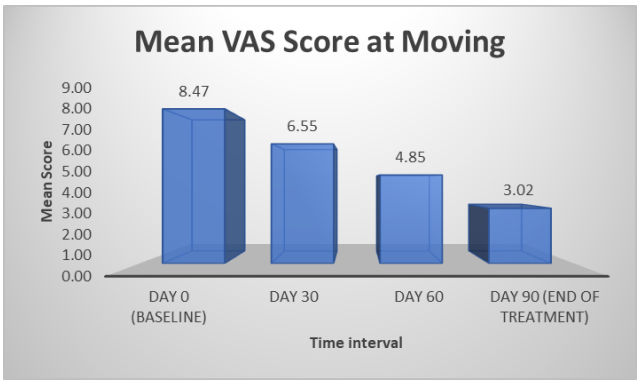

Figure 7: Change in VAS score at movement

4. Discussion

The effectiveness and potential of Celery seeds and *Boswellia serrata* in managing osteoarthritis and reducing the need for NSAIDs were assessed in the recent study. The study product demonstrated significant improvements in pain intensity, stiffness and overall functionality, as measured by the WOMAC index. Primary outcomes indicated reductions in both pain and stiffness scores, with pain scores decreasing. Secondary outcomes, assessed through VAS scores, further supported the positive impact on pain relief.

The study also evaluated the potential sparing effect of the study product on NSAID usage, addressing concerns regarding adverse effects associated with long-term NSAID use. Results indicate a noticeable decrease in painkiller consumption, an increase in patients who needed to lower their NSAID dosage and an increase in those transitioning

from NSAIDs to paracetamol. The reduction in NSAID usage and the decline in the number of patients who no longer required NSAIDs demonstrate the NSAID-sparing effect of the study product. By reducing pain intensity and improving functional outcomes, study product may offer an alternative or adjunctive therapy to NSAIDs, potentially minimizing risks of gastrointestinal, cardiovascular and renal complications commonly associated with NSAID use.

A systematic review and meta-analysis encompassing seven randomized controlled trials with 545 OA patients found that *Boswellia* or its extracts were more effective to placebo, ibuprofen, or glucosamine sulfate (control group) in alleviating pain and stiffness and enhancing joint function.[16] 3-O-Acetyl-11-keto-beta-boswellic acid (AKBA) found in *Boswellia serrata* extract contributes to its anti-inflammatory effects by inhibiting 5-lipoxygenase. A meta-analysis of 28 studies concluded that *Boswellia serrata* extract is safe and effective for patients with osteoarthritis.[17]

Celery preparations are widely utilized for managing both acute and chronic inflammatory conditions. Celery Seed Extract (CSE) demonstrates comparable efficacy to aspirin, ibuprofen and naproxen in suppressing arthritis in a polyarthritis model. Moreover, it has been validated as an analgesic in two experimental models. CSE also offers protection against gastric irritation caused by NSAIDs and exhibits synergistic effects with them in reducing inflammation.[12] Celery seed inhibits COX 1 and 2 and prostaglandin synthesis. A 12-week clinical trial was conducted involving OA patients who received a celery extract tablet twice daily. Results indicated a substantial 68% reduction in pain scores after 3 weeks of treatment, with some patients experiencing complete pain relief. Those who continued treatment for 6 weeks demonstrated further benefits. Additionally another study investigated higher doses of the extract (75 mg) and reported statistically significant improvements in pain scores, mobility and overall quality of life.[13]

5. Limitation

This is the first study to focus on NSAID sparing effect of a nutraceutical product in the management of OA. Being an observational study, there are certain limitations including randomization and sample size.

6. Further direction

In the future, a larger sample size and active control group study design would help in strengthening the efficacy of Celery seeds and *Boswellia serrata* in OA.

7. Conclusion

In conclusion, Celery seeds and *Boswellia serrata* has shown significant potential as an effective and safer alternative or adjunctive therapy to NSAIDs in the management of knee OA. Its ability to reduce pain, improve joint functionality and spare the use of NSAIDs addresses the critical need for sustainable, long-term management strategies for OA.

8. Acknowledgments

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9. Conflict of Interest

None.

10. Source of Funding

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