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Assessment of Pain Relief and Mobility Improvement: A Randomized Clinical Trial Comparing *Commiphora myrrha* and Etoricoxib in Osteoarthritis Patients

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Abstract

Osteoarthritis pain refers to the discomfort and aching experienced in the joints, often accompanied by stiffness, swelling, and reduced range of motion. NSAIDs are the most commonly prescribed medicines for the management of arthritis-induced pain. Prolonged NSAID use can lead to several health issues, such as gastric ulcers, hypertension, and cardiovascular risks, and also significantly impact their quality of life. So, patients on chronic NSAID therapy require careful monitoring and alternative treatment options. The purpose of the present study was to compare the safety and efficacy of *Commiphora myrrha* versus Etoricoxib in patients with osteoarthritis pain. In this, a 30-day randomised, parallel-group trial was conducted among 102 osteoarthritis patients aged between 40 and 75 who were treated with either *Commiphora myrrha* (100 mg, twice daily) or Etoricoxib (90 mg, once daily). Outcomes were assessed using WOMAC scores (pain, stiffness, function), VAS pain scale, PGA for pain, and 6MWT to evaluate mobility. Adverse medication events were recorded for assessing the safety of both. When compared to the Etoricoxib group, the *Commiphora myrrha* was safer and exhibited a long-term improvement in mobility and pain reduction than Etoricoxib. In conclusion, *Commiphora myrrha* showed as an effective alternative to Etoricoxib for managing osteoarthritis pain and improving functional mobility.

Keywords: Osteoarthritis, Nutraceutical, *Commiphora myrrha*, Etoricoxib, Pain, Mobility

Introduction

Osteoarthritis is a chronic inflammatory disorder characterised by immobility, joint pain and stiffness, ligament abnormalities, and swelling in one or more joints. This condition can significantly impact a person's quality of life, making everyday activities challenging. Early diagnosis and appropriate management are essential to alleviate symptoms and improve mobility. Arthrits is classified into several types, such as rheumatoid arthritis (RA), gouty arthritis (GA), osteoarthritis (OA), psoriatic arthritis (PA), and ankylosing spondylitis, based on the mechanism and location of joints affected (hips, knees, toes, and hands) (1, 2). Among these, RA, OA, and GA are more prevalent and also an economical burden in many countries (3). Global arthritis prevalence rates surged in 2020, with osteoarthritis (OA) affecting 5,780.1 men and 8,058.9 women per 100,000 individuals, projected to rise

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132.2% by 2050 (4). As the burden of osteoarthritis continues to grow, it is crucial for healthcare systems to adapt and respond effectively to this escalating crisis. Preventative measures, early diagnosis, and innovative treatment options will be essential in managing the increasing prevalence and improving the quality of life for those affected. Addressing these conditions effectively could alleviate not only the personal suffering of millions but also the considerable economic strain on healthcare systems globally.

To minimize osteoarthritis pain symptoms, clinicians routinely prescribe NSAIDs for instant relief (6-8). However, long-term NSAID intake isn't advisable due to potential side effects like increased risk of heart attack, stroke, hypertension, congestive heart failure, gastric ulcers and bleeding, abdominal pain and digestive issues, altered kidney blood flow, sodium and water retention, mouth ulcers, and skin rashes (9-13). Therefore, NSAIDs are not suggestable for management of arthritis pain alone or patients comorbid with cardiovascular, gastrointestinal, hypertension, and renal diseases. This highlights the need for a suitable alternative medicine to minimize NSAID-related side effects.

For thousands of years, plants have been utilized for their medicinal properties across diverse cultures and traditional healing practices, forming the basis of herbal medicine or phytotherapy. This approach leverages plant-based materials and extracts to prevent and treat various ailments, often with minimal side effects, offering a natural and time-tested alternative for health management (14). *Commiphora myrrha* is predominantly found in the arid and semi-arid regions of northeast Africa and the Arabian Peninsula. Its native range includes Somalia, Ethiopia, Kenya, and parts of Yemen and Oman, which are the primary sources of commercial myrrh resin. Although the *Commiphora* genus has a wider distribution, including India, the majority of myrrh resin comes from these East African and Arabian regions (15, 16).

The health benefits of *Commiphora myrrha* proven for its such as analgesic, anti-inflammatory, anti-diabetics, anti-septic, anti-spasmodic, and cardio and reno protective might be due to the presence of following chemical constituents such as Sesquiterpenes (Furanodienes, Curzerene, Lindestrene, Elemene (α, β, γ, δ-elemene), Germacrene D, and β-Caryophyllene), Monoterpenes (Limonene, α-Pinene, β-Pinene, Myrcene, and Sabinene), Diterpenes (Abietic acid and Communic acid), Triterpenoids, Guggulsterones (Dammaranes, Lupeol, and β-Amyrin), Volatile Oils (Eugenol, Methyl Eugenol, Sesquiterpene lactones, and Curcumene), Phenolic Compounds (Gallic acid, Ellagic acid, Ferulic acid, and Caffeic acid), Polysaccharides (Arabinogalactans and Glucans), Flavonoids (Quercetin, Kaempferol, and Luteolin) (17-20).

Unlike previous studies that compared *Commiphora myrrha* to a placebo, this study directly compares it to Etoricoxib, a standard pharmacological treatment. This design enables evaluation of short-term efficacy and safety, providing valuable clinical insights not previously explored. Therefore, the main objective of present study was to evaluate the safety and efficacy of *Commiphora myrrha* in osteoarthritis pain as alternative to the conventional NSAIDs therapy.

Methodology

Study Site and Design

An open-label, randomised, active-controlled, and parallel-group trial was conducted at Aditya Research Centre, Aditya Multispeciality Hospital, Guntur, Andhra Pradesh, India. This clinical trial evaluated the safety and efficacy of *Commiphora myrrha* (Myrlimax® capsule) in patients with osteoarthritis pain compared with Etoricoxib (Retoz Neo 90). Recruitment commenced on August 2, 2024, and was completed on December 2, 2024. A total of 102 newly diagnosed subjects with mild to moderate osteoarthritis, who hadn't received other treatments in the past three months, were

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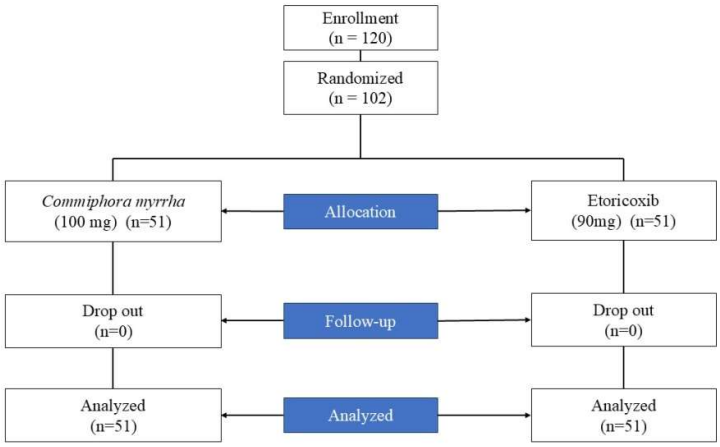

Fig. 1: Schematic representation of study design of *Commiphora myrrha* and Etoricoxib

randomly assigned (1:1) to receive either *Commiphora myrrha* or Etoricoxib. Subjects self-administered two 100 mg tablets of *Commiphora myrrha* daily or Etoricoxib one time for 30 days (Fig. 1). No concomitant medications were allowed.

Ethical Approval

This clinical study was conducted strictly according to the rules and regulations of the New Drugs and Clinical Trials Rules, 2019, India, and ICH-GCP guidelines. The study was approved by the Institutional Ethics Committee (IEC) of Aditya Multispeciality Hospital, Guntur, Andhra Pradesh, India (Approval no. IEC/AMSH/2024/026) and registered with the Clinical Trial Registry of India (Approval no. CTRI/ 2024/ 07/ 070087).

Sample Size and Screening of subjects

This study screened 102 subjects. Screening depended purely on the inclusion and exclusion criteria of the study protocol. subjects who didn't meet the study criteria were not enrolled in the present study.

Inclusion Criteria

In this trial, subjects fulfilled the following eligibility criteria: (1) age between 40 and 75 years, regardless of gender (male or female); (2) provisionally diagnosed with osteoarthritis; (3) a visual analogue scale (VAS) score > 4 on walking in one or both hands or knees during the 24 hours preceding the requirement; and (4) subjects should provide compulsory written informed consent and be willing to attend regular follow-up.

Exclusion Criteria

Subjects with the following criteria were not eligible: (1) A known history of hypersensitivity to herbal extracts or dietary supplements, pregnant or lactating women, or women of childbearing potential not using adequate contraception (with a positive urine pregnancy test); (2) Incapacitated or bound to a wheelchair/bed, unable to self-care, or received intra-articular corticosteroid injection in the knee within 3 months; (3) Pre-existing demyelinating disorders, type I diabetes, or treatment with anticoagulants, hydantoin, lithium, steroids, methotrexate, or colchicine; (4) Evidence of renal, hepatic, haemopoietic, or severe cardiac issues via lab investigations; (5) Congestive heart failure, hypertension, or untreated hyperlipidaemia with cardiovascular risk; (6) Participation in another clinical trial in the past month or use of ayurvedic/ complementary alternative medicine therapy in

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the past 2 months; (7) A non-cooperative attitude or any condition justifying exclusion per the investigator's opinion.

Informed Consent Form (ICF)

The study procedure, follow-up visits, treatment plan, importance of study medications, and study outcomes were explained thoroughly before subjects were given informed consent forms (ICFs). Two versions of the ICF were prepared for this study, in Telugu and English. subjects or their legal guardians wrote the ICF based on the subjects' language understanding.

Objectives

The primary objective of the study was to evaluate the safety and efficacy of *Commiphora myrrha* in osteoarthritis using the WOMAC scale. The secondary objective of the study was to evaluate the PGA scale, VAS scale, 6MWT, and monitoring adverse drug event during the treatment period.

Investigational Products

The Myrlimax® capsule containing 100 mg of *Commiphora myrrha* powder extract (equivalent to at least 4 mg of bioactive furanodienes) is a delayed-release gastro-protectant hydroxypropyl methylcellulose capsule with excipients like microcrystalline cellulose, magnesium stearate, talc, and silicone dioxide; or Retoz Neo 90 containing Etoricoxib 90 mg and titanium dioxide. Myrlimax® capsules and Retoz Neo 90 were purchased from Tarun Aditya Pharmacy, Aditya Multispeciality Hospital, Guntur, Andhra Pradesh, India.

Study Procedures

In this trial, the screening day (Day -5) occurred 5 days before investigational product administration, involving vital checks and informed consent (ICF) from subjects. After 5 days of screening visit, the investigational products were randomly assigned to the subjects. The randomisation numbers were generated by the computer (https://www.calculator.net/random). The subjects were randomly assigned either the *Commiphora myrrha* with a dose of 100mg or Etoricoxib with a dose of 90mg. These medications were dispensed by the Head of the Clinical Research Department (HCRD) at the Aditya Research Centre. Those subjects who received *Commiphora myrrha* one in morning and evening after the meal, whereas subjects who received Etoricoxib one in the morning after intake of food only. After completion of the treatment period, the subjects submitted their medication empty sheet to the HCRD. The study comprised a 30-day treatment period followed by a 15-day residual efficacy observation period, spanning a total of 50 days. Participants attended 5 scheduled visits: one screening day (Day -5), three treatment/follow-up days (Days 0, 15, and 30), and one total residual efficacy day (TRE) (Day 45) and visit-wise assessment scales were shown in (Fig. 2).

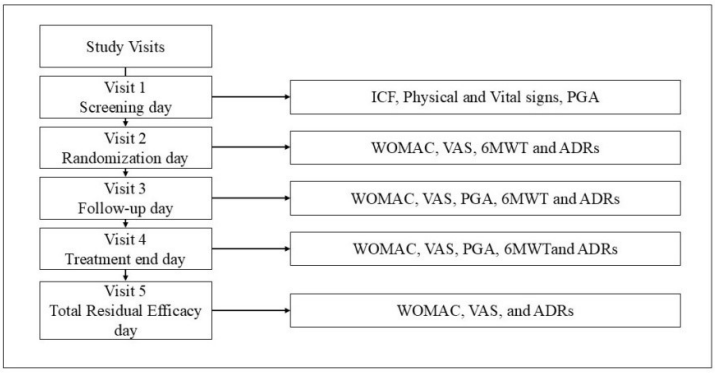

Fig. 2: visit-wise assessment scale

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Study Outcomes Measures

Efficacy was measured using scales such as the WOMAC scale (pain, stiffness, physical function), VAS scale, PGA, and 6MWT. WOMAC and 6MWT were assessed at follow-up visits on days 0, 15, and 30. VAS and PGA were assessed on days -5 (screening visit), 15, and 30. EQ-5D assessed quality of life on days 0 and 30. Safety was assessed via vital signs, physical exam, and adverse drug events on days 0, 15, and 30. VAS and WOMAC were assessed on day 45 (TRE visit) to determine long-term benefits of the investigational products.

Statistical Analysis

The values were presented as Mean ± SD, and statistical analysis was carried out using one-way ANOVA, followed by Bonferroni test with graph pad prism 5.0. Error bars represent 95% confidence interval. ***p<0.001, **p<0.01, *p<0.05 Vs Day 0.

Results and Discussion

Results

Demographics characteristics

Table 1 presents the demographic and anthropometric characteristics of the *Commiphora myrrha* and Etoricoxib groups (n = 51 each). No significant changes in demographic and anthropometric characteristics were observed between the *Commiphora myrrha* and Etoricoxib groups at baseline or day 30.

WOMAC and 6MWT Scale Outcomes

Figure 3 demonstrates the effects of *Commiphora myrrha* and Etoricoxib on WOMAC pain, stiffness, function scores, and the 6MWT over three time points (days 0, 15, and 30). WOMAC pain, stiffness, and function scores decreased from day 0 to day 30 with *Commiphora myrrha* compared to Etoricoxib. For the 6MWT, distance significantly increased from day 0 to day 30 with *Commiphora myrrha* compared to Etoricoxib.

PGA and VAS Scales Outcomes

The effects of *Commiphora myrrha* and Etoricoxib on PGA pain, inflammation, overall health status, and VAS across three time points (days -5, 15, and 30). PGA pain and inflammation scores decreased, and overall health status significantly increased with *Commiphora myrrha* compared to

Table 1: Demographics Characteristics

Variable	*Commiphora myrrha* (n = 51)	Etoricoxib (n = 51)	Overall (n = 102)
Age (years)	61.6 ± 8.41	61.3 ± 7.58	61.5 ± 7.97
Weight (kg)	70.6 ± 13.4	68.5 ± 12.7	69.6 ± 13.0
Height (cm)	164 ± 6.41	162 ± 6.42	164 ± 5.89
BMI (kg/m²)	26.4 ± 5.54	25.4 ± 4.95	25.9 ± 5.25
Gender			
Male	27 (52.9%)	19 (37.3%)	46 (45.1%)
Female	24 (47.1%)	32 (62.7%)	56 (54.9%)
Alcohol consumption			
With alcohol	12 (23.5%)	21 (41.2%)	33 (32.4%)
Without alcohol	39 (76.5%)	30 (58.8%)	69 (67.6%)
Smoking status			
With smoking	18 (35.3%)	16 (31.4%)	34 (33.3%)
Without smoking	33 (64.7%)	35 (68.6%)	68 (66.7%)

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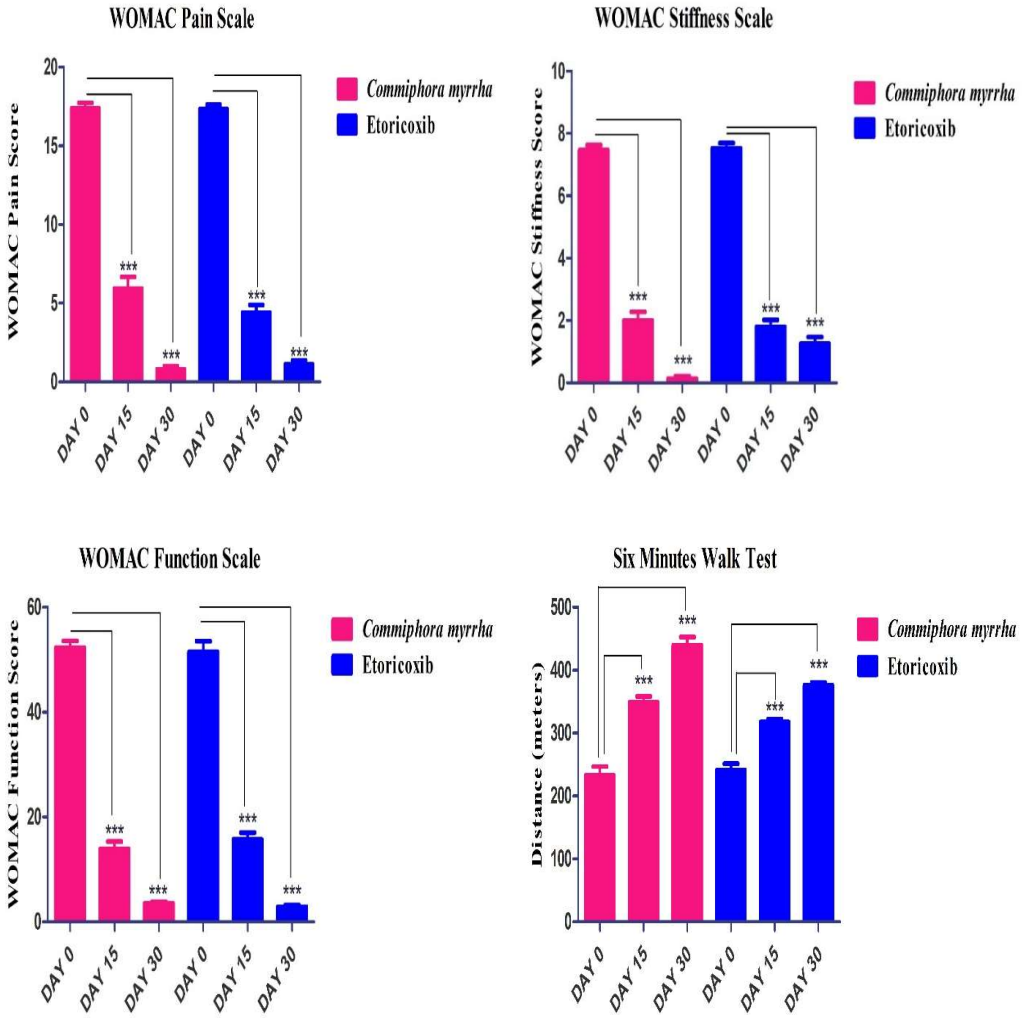

Fig. 3: Efficacy of *Commiphora myrrha* and Etoricoxib on WOMAC scale and 6MWT. Statistical analysis was performed using one-way ANOVA followed by post hoc Bonferroni test. ***p<0.001, **p<0.01, *p<0.05 Vs Day 0

Etoricoxib from day -5 to day 30. On the VAS scale, a significant decrease in osteoarthritis pain was observed with *Commiphora myrrha* compared to Etoricoxib from day -5 to day 30, as shown in (Fig. 4).

Total Residual Efficacy

The effects of *Commiphora myrrha* and Etoricoxib on WOMAC and VAS at days 30 and 45 are specified in (Fig. 5). In WOMAC and VAS scales, significant TRE improvement was observed with *Commiphora myrrha* treatment compared to Etoricoxib from day 30 to day 45.

Safety and Adverse events

The safety profile of both *Commiphora myrrha* and Etoricoxib was

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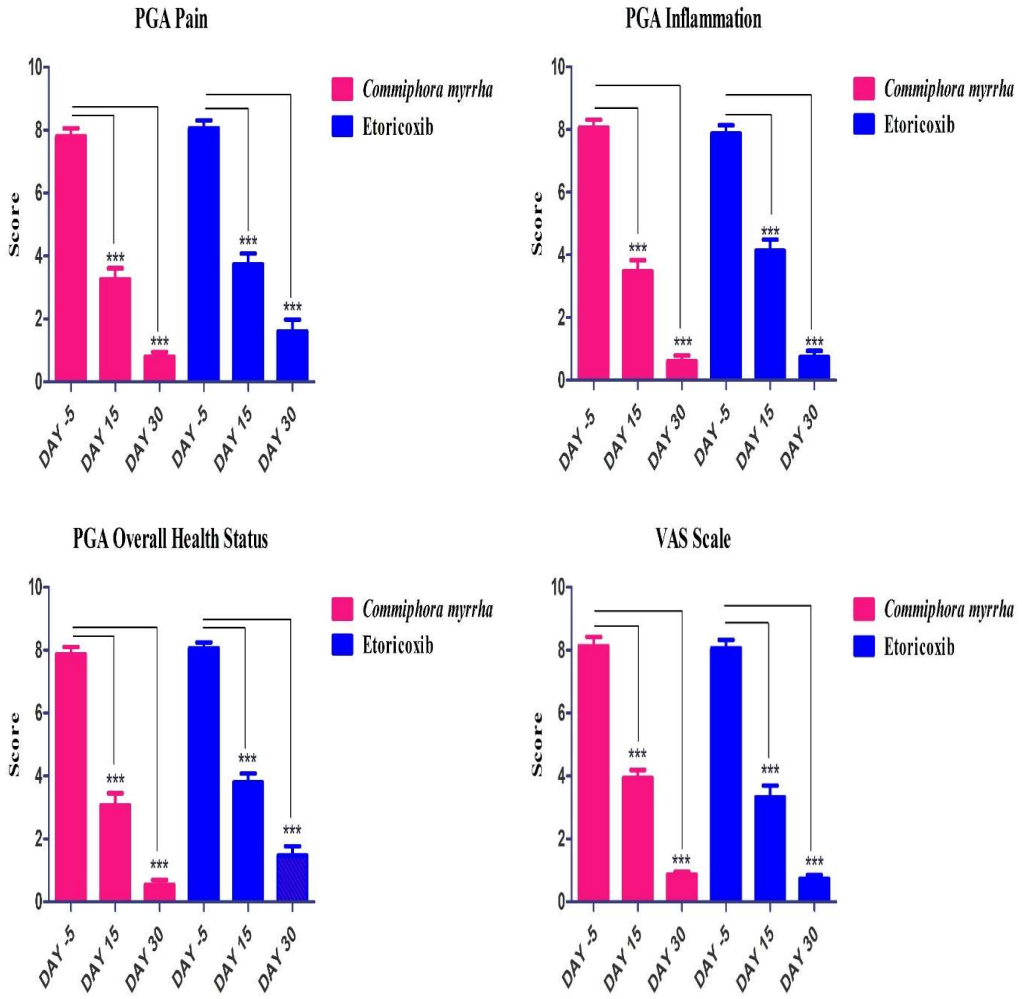

Fig. 4: Efficacy of *Commiphora myrrha* and Etoricoxib on PGA and VAS scales. Statistical analysis was performed using one-way ANOVA followed by post hoc Bonferroni test. ***p<0.001, **p<0.01, *p<0.05 Vs Day 0

closely monitored, revealing notable findings regarding adverse events. Subjects received *Commiphora myrrha* reported no adverse events during or after treatment. In contrast, the Etoricoxib treatment experienced adverse events: out of 51 subjects, 07 experienced issues including hypertension (3 subjects), epigastric pain (2), and heartburn (2), as highlighted in (Fig. 6).

Discussion

The present clinical study was evaluating the safety and efficacy of *Commiphora myrrha* compared to the standard drug Etoricoxib, belonging to the class of NSAID. Antonio Germano et al., 2017 reported a pilot study on the bioactive profile and analgesic effects of MyrLiq, a *Commiphora myrrha* extract rich in furanodiene. The extract's

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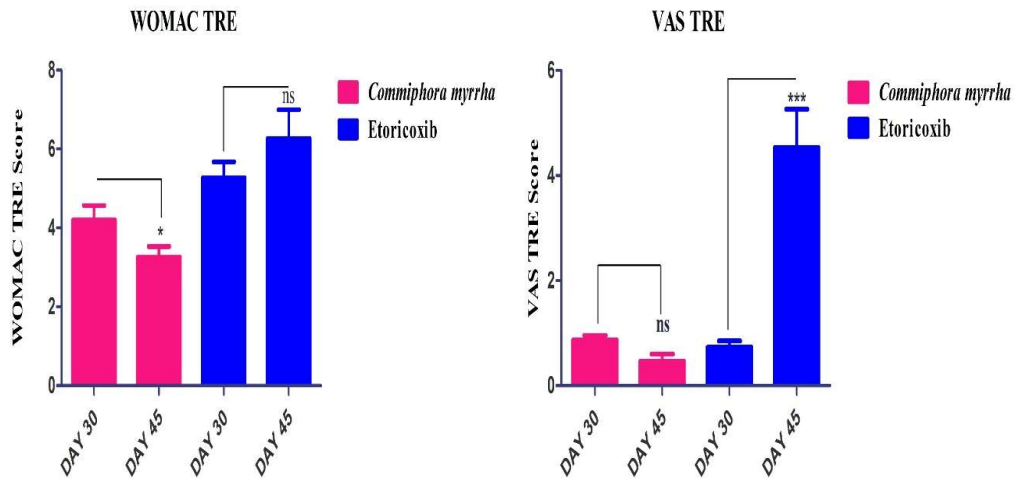

Fig. 5: Efficacy of *Commiphora myrrha* and Etoricoxib on WOMAC TRE and VAS TRE. Statistical analysis was performed using one-way ANOVA followed by post hoc Bonferroni test. ***p<0.001, **p<0.01, *p<0.05 Vs Day 0

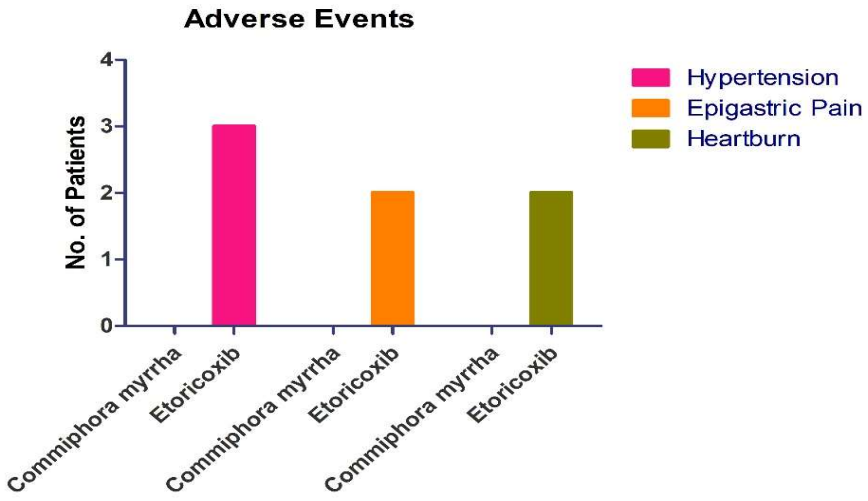

Fig. 6: Safety assessment of *Commiphora myrrha* and Etoricoxib

major chemical constituents included curzerene, lindestrene, and furanoeudesma-1,3-dienes, with a high content of furanodienes known for anti-inflammatory and analgesic properties. The study found MyrLiq exhibited significant analgesic activity against headaches, muscle aches, joint pains, lower back pain, fever-related pain, and menstrual cramps. Notably, in male volunteers, 400 mg/day of MyrLiq was effective for all pain

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types; in female volunteers, 200 mg/day alleviated lower back pain and fever-related pain (21).

A six-month clinical study was conducted on MyrLiq and ginkgo extracts along with supplements of Q10, vit B6, and riboflavin for a duration of 6 months in patients suffering with headaches and the study confirms the analgesic and anti-inflammatory activity of *Commiphora myrrha* (22). Sureja et al., 2021 conducted on 204 subjects over a period of 20 days by open label, multicentric, observational, post-marketing surveillance study to evaluated the safety and efficacy of MyrliMax® capsules containing *Commiphora myrrha* on lower back pain through VAS pain score, rescue medicine requirement, therapy satisfaction scores and safety parameters. The study concluded that MyrliMax® capsules potentially effective for reduction of pain in chronic lower back pain and also useful to treat subjects who were intolerant to NSAIDs (23).

A combination of *Commiphora myrrha* with alpha-lipoic acid and palmitoylethanolamide was used to treat endometriosis in women. this study reported the combination of nutraceutical reduces chronic pelvic pain, dyspareunia, and dysmenorrhoea (24). Pierro FD et al. reported that the ability of the drug myrrh to reduce pain perception in patients with chronic muscle, joint, and back pain (25). A prospective study over 6 months was conducted on DAIGO Artiplus, a combination of *Commiphora myrrha* and chondroprotective agents (glucosamine, bromelain, curcuma, and chondroitin), which significantly reduces joint pain and stiffness. This study also evaluates the safety of *Commiphora myrrha* over a 6-month period and reports it has no significant side effects (26). Existing studies on *Commiphora myrrha* have compared it to placebo, with no studies comparing it to NSAIDs. In the present study, the safety and efficacy of *Commiphora myrrha* (100 mg capsules containing 4 mg of furanodienes) were compared with Etoricoxib in patients with osteoarthritis pain.

The clinical outcomes of present study were assessed by using globally validated pain, inflammation and mobility scales such as the WOMAC, VAS, 6MWT, and PGA scale (27, 28, 29, 30). Both *Commiphora myrrha* and Etoricoxib treatments exhibited improvements in WOMAC scores such as pain, stiffness, and physical function over the 30-day treatment period. However, the between group analysis revealed no statistically significant difference in overall WOMAC score reduction, indicating comparable symptomatic relief in terms of joint pain, stiffness, and function. *Commiphora myrrha* and Etoricoxib reduces pain, stiffness and improves the physical function.

Mobility was evaluated by using the 6MWT, a validated and objective measure of functional capacity in subjects with osteoarthritis (31). Notably, subjects receiving *Commiphora myrrha* demonstrated a greater improvement in walking distance compared to those in the Etoricoxib group. This finding suggests superior enhancement in physical performance and joint mobility with the *Commiphora myrrha*. Importantly, this represents a novel outcome of the present study, highlighting the potential of *Commiphora myrrha* to improve functional mobility beyond symptomatic pain relief.

The PGA scale, which captures subjects-reported outcomes related to pain, inflammation, and overall health status (32). showed improvement in both treatment groups. However, subjects in the *Commiphora myrrha* arm reported marginally better global health status, indicating a trend toward improved overall quality of life with the herbal formulation.

VAS scores, which serve as a direct measure of pain intensity (33), showed a significant reduction from day 0 to day 30 in both treatment groups, confirming the analgesic efficacy of both *Commiphora myrrha* and Etoricoxib. During the initial treatment phase (day 0 to day 15), Etoricoxib demonstrated a more pronounced reduction in pain compared to *Commiphora myrrha*, suggesting a faster onset of analgesic action. However, from day 15 to day 30, both groups

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exhibited comparable reductions in VAS scores, indicating that *Commiphora myrrha* achieved similar pain control in the later phase of treatment. Notably, a slightly greater overall decline in VAS scores was observed in the *Commiphora myrrha* group by the end of the study, further supporting its potential as an effective phytotherapeutic agent for long-term pain management in osteoarthritis.

The WOMAC TRE score showed a statistically significant decrease in the *Commiphora myrrha* group from day 30 to day 45. This reduction indicates a sustained therapeutic effect, suggesting that the benefits of *Commiphora myrrha* persisted even after discontinuation of treatment. In contrast, the Etoricoxib group exhibited a progressive increase in WOMAC TRE scores during the same period, reflecting a rebound in symptoms particularly pain, stiffness and physical functional following cessation of therapy. These findings highlight the potential long-term efficacy of *Commiphora myrrha* in maintaining symptom control in osteoarthritis subjects, surpassing that of Etoricoxib in terms of sustained relief.

Similarly, VAS TRE analysis was showed a contrasting trend between the two treatment groups. Although both groups exhibited low residual pain at day 30 and 45, the Etoricoxib group showed a statistically significant increase in VAS TRE at day 45, suggesting a rebound in pain and a shorter duration of analgesic effect following treatment cessation. In contrast, the *Commiphora myrrha* group exhibited a continued decline in VAS TRE from day 30 to day 45, indicating sustained pain relief and a prolonged therapeutic effect. These results reinforce the potential of *Commiphora myrrha* to provide longer-lasting analgesic benefits compared to the conventional NSAIDs.

Rajeshwary Gosh et al., 2015 prolonged taking of NSAIDs induces gastric ulcers, increases the risk of internal bleeding and damage to the kidney, and enhances the possibility of causing cardiac arrest and a brain stroke. NSAIDs induce the ROS pathway in different cells, including renal and cardiovascular cells (34). Jean – Pascal Fournier et al., 2012 study was conducted on 5710 hypertensive subjects. Finally, the study reported causes of blood pressure alterations in those patients taking angiotensin receptor blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors. This study suggests not prescribing NSAIDs along with the ARBs and ACEIs. In present studies, the Etoricoxib treatment group reported 3 subjects with hypertension, 2 subjects with epigastric pain, and 2 subjects who noticed a heartburn sensation (35).

The key limitation of the current research was duration and sample size but it gives the new avenues for long term safety and efficacy of *Commiphora myrrha* in the treatment of osteoarthritis as comparison with Etoricoxib.

Conclusion

Commiphora myrrha showed promise as an alternative to Etoricoxib for managing osteoarthritis pain and improving mobility. While Etoricoxib provided better short-term pain relief, *Commiphora myrrha* demonstrated comparable efficacy, a favorable safety profile, and notable benefits in overall health, joint discomfort, and quality of life. Integrating *Commiphora myrrha* into arthritis management may offer a safer and more tolerable option, complementing existing therapies.

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Conflict of Interest

All authors declared the no conflict of this research work.

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