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Evaluation of Safety and Efficacy of Cannaquic Oil In Comparison With Diclofenac Oil For The Management Of Osteoarthritis – A Double-Blind, Randomized Controlled Clinical Study

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ABSTRACT

Background:Osteoarthritis (OA) is the most prevalent type of arthritis in the globe. Considerable adverse effects of existing therapeutic agents have widened the scope of development of a new, safer and effective medicine for osteoarthritis. The present study aimed to evaluate the safety and efficacy of cannaquic oil in comparison with diclofenac oil for the management of osteoarthritis.

Methods:A randomized, double-blind, controlled trial was conducted to compare the efficacy and safety of Cannaquic and diclofenac in patients with knee osteoarthritis. Participants were randomly assigned to receive either Cannaquic oil or diclofenac oil for 30 days. clinical assessment and laboratory findings were compared between day 0 and day 30 and post study follow up was analyzed between day 0 and day 60.

Results:A total of 80 patients were enrolled in the study. Cannaquic oil reduces pain, stiffness, and inflammation, as seen in the decreased VAS, WOMAC, ESR, IL-1, IL-6, and TNF levels during the study period. No significant changes ($p > 0.05$) were observed in hematological, liver, renal, and blood glucose parameters, indicating safety. A total of 41 adverse drug reactions were reported, with gastrointestinal disturbances being the most common (34.15%). When comparing cannaquic oil and diclofenac oil, Cannaquic oil shows long term benefits in post study follow up.

Conclusion:The results demonstrated that the cannaquic oil was safe and efficacious for long time use for pain relief compared to diclofenac oil for OA.

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1. INTRODUCTION

Osteoarthritis (OA) is the most prevalent type of arthritis in the globe is a chronic degenerative disorder, characterized by the gradual breakdown of cartilage within joints, leading to pain, stiffness, swelling, and reduced range of motion present as localized, generalized or erosive arthritis It falls into two categories: primary osteoarthritis and secondary osteoarthritis [1]. Primary osteoarthritis is mostly related to aging, whereas secondary osteoarthritis is caused by another disease or condition [2].

The management of OA focuses primarily on pain relief and maintaining joint function through both pharmacological and non-pharmacological interventions. Among pharmacological treatments, nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used due to their anti-inflammatory and analgesic properties [3]. Topical NSAIDs, such as diclofenac oil, are frequently prescribed as they provide localized pain relief with a lower risk of systemic side effects. Diclofenac oil is a well-established treatment option for OA, reducing pain and inflammation in affected joints [4]. However, long-term use of NSAIDs, even in topical form, carries risks such as skin irritation, gastrointestinal disturbances, and cardiovascular

concerns [5]. As a result, there is a growing interest in alternative therapies that offer comparable or superior pain relief while minimizing adverse effects.

Cannabinoids have emerged as promising treatment options for chronic pain, especially OA-related pain [6]. Topical formulations bind to cannabinoid receptors (CB1 and CB2) in the skin and joints, providing regional pain relief and potentially lowering inflammation [7]. According to preclinical and clinical research, cannabinoids have neuroprotective, anti-inflammatory, and analgesic qualities, which make them a viable substitute for NSAIDs in the treatment of OA [8].

Cannaquic oil is a cannabinoid-based topical preparation designed to treat musculoskeletal pain, particularly OA. Cannabinoid receptors interacting with joint tissues, it is intended to reduce inflammation and offer regional pain relief [9]. Unlike oral NSAIDs, topical cannabis formulations may have a decreased risk of systemic side effects [10].

While diclofenac oil is a well-known treatment for OA, there is a growing demand for alternative medicines with higher safety profiles. Cannabinoid-based topical preparations may provide comparable or superior pain relief while avoiding the long-term hazards associated with NSAIDs [11]. This study aims to fill this knowledge gap by directly comparing Cannaquic oil and Diclofenac oil in the management of OA. The results could contribute to expanding treatment options for OA patients, particularly those at risk of NSAID-related adverse effects

2. . METHODOLOGY:

2.1 study design and study site

A double-blind, randomized controlled clinical study was conducted on participants diagnosed with osteoarthritis. They were recruited from the outpatient department of general medicine of SRM Medical college Hospital and Research Centre, Kattankulathur – 603203

2.2 Ethical consideration:

The Institutional Ethics Committee (IEC) approved the protocol, informed consent form and case record form of this study (IEC clearance number: ECR/8839/INST/TN/2013/RR-19). Written informed consent was obtained from the study participants and the study was conducted according to revised National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, Indian Council of Medical Research (ICMR) 2017. The study was registered with the Clinical Trials Registry India (CTRI) and approval number is CTRI/2024/08/072537.

2.3 Study criteria:

2.3.1 Inclusion criteria:

The study included participants of either sex aged 18 to 65 years who had been diagnosed with moderate to severe arthritis and had been suffering symptoms such as pain, swelling, soreness, and morning stiffness in one or more joints for more than three weeks. In accordance with established criteria, such as the American College of Rheumatology (ACR) criteria, participants who had musculoskeletal pain as their primary symptom and those who had been diagnosed with osteoarthritis based on clinical evaluation and radiographic findings consistent with OA in one or more joints (e.g., knee, hip, or hand) were eligible. Individuals with chronic pain who scored 6 or above on a 10-cm visual analog scale (VAS) for baseline pain intensity were included. Following a seven-day washout period, patients taking local medicine for symptomatic pain treatment were eligible. Written informed permission was obtained from each participant.

2.3.2 Exclusion criteria:

Participants with severe spinal pathology (e.g., cauda equina syndrome, trauma, fractures, malignancy) or aberrant hematologic function (hemoglobin < 8 g/dl, WBC count < 3000/mm³, platelet count < 100,000/mm³) were not allowed to participate. Those with acute inflammatory rheumatologic disease or those who had undergone lower limb, lumbar, or abdominal surgery in the previous 12 months were not eligible. Participants with severe concurrent conditions such hepatic dysfunction, CKD, CVD, lung diseases, or a history of cancer were not allowed to participate, neither were those with deformities or open wounds in the afflicted area. Individuals with psychiatric disorders (e.g., schizophrenia, suicidal tendencies), seizure disorders, or cognitive/emotional impairments that could interfere with study participation were not included. Pregnant or lactating women, heavy smokers, chronic alcoholics, drug users, and people with known cancers, HIV/AIDS, or other serious diseases were also excluded. Finally, those who refused to give informed consent or consistently adhere to the protocol were not allowed to participate in the study.

2.4 Study procedure:

Patients diagnosed with osteoarthritis who met the inclusion criteria were screened at the study site. Following a complete baseline examination, eligible patients were randomly assigned to one of two groups to receive either Cannaquic oil or Diclofenac oil. Each patient was instructed to apply 5 ml of the assigned oil topically twice daily for 30 days. Patients

demographic details were collected in a specially designed data collection form. During the trial, patients were advised not to use any extra topical or systemic anti-inflammatory drugs. Hematological and biochemical parameters, IL-1, IL-6, TNF values as well as pain and functional assessments (VAS and WOMAC ratings), were measured at baseline (Day 1) and at the end of the trial (Day 30). Throughout the study, adverse events and compliance were observed, and all findings were recorded for final analysis. After the study's completion, subjects were followed up for an additional 30 days to reassess the effectiveness of Cannaquic and Diclofenac oil. The follow-up evaluation included WOMAC and VAS scores to measure sustained improvements in pain and functionality.

2.5 Efficacy assessment:

The efficacy of Cannaquic oil and Diclofenac oil was evaluated through ESR, IL-1, IL-6, TNF, WOMAC, and VAS scores. ESR levels were measured at baseline and Day 30 to assess systemic inflammation. WOMAC scores were recorded at baseline, Day 30, and the 30-day follow-up. Similarly, pain intensity was assessed using the VAS scale at these time points. The deduction in ESR level, IL-1, IL-6, TNF values, WOMAC Score, and VAS points from baseline was considered as clinically significant.

2.6 Safety assessment:

Hematological, liver, renal function tests and random blood glucose levels were compared before and after treatment. During the study period, all of the recruited patients were thoroughly monitored for the incidence of any ADRs. Patients reported ADRs were documented in an ADR documentation form.

2.7 POST-STUDY FOLLOW UP:

After the study's completion, subjects were followed up for an additional 30 days to reassess the effectiveness of Cannaquic and Diclofenac oil. The evaluation included the WOMAC score and the Visual Analogue Scale (VAS) to measure improvements in pain and functionality

2.8 Statistical analysis:

The data were analyzed as per protocol. The continuous data were measured in mean and standard deviation. The categorical data were measured in frequency distribution. P values of less than 0.05 was considered statistically significant.

3. RESULTS:

3.1 Demographic and clinical examination:

A total of 93 patients were screened for eligibility. of them,80 was enrolled in the study. The maximum number of cases were in the age range of 31-40(58%), followed by the ages of 41-50(20%), 20-30(18%) and 51-60(4%). 60% of the patients were male and 40% of the patients were female. Assessment of patients at the end of treatment showed no gross changes in clinical symptoms in all the patients. No significant differences were found in the mean values of body weight, systolic and diastolic blood pressure between day0 and day30.

3.2 Efficacy assessment:

Tables 1 and 2 present the mean efficacy parameter change between day 0 and day30. Statistically significant ($p<0.05$) reduction in ESR, WOMAC, VAS SCORE were observed in both cannaquic oil and diclofenac oil. IL-1, IL-6, TNF values were showed statistically significant reduction in cannaquic oil whereas diclofenac oil showed no significant difference in inflammatory markers.

3.3 Safety assessment:

The effect of cannaquic oil and diclofenac oil on the serum parameter of Hematological, liver, renal function tests and random blood glucose levels in tables 3 and 4. The levels of all the parameters were approximately stable during the period of study with no statistically significant ($p>0.05$) changes in both cannaquic and diclofenac oil.

A total of 41 adverse drug reactions (ADRs) were documented. Gastrointestinal disturbances were the most frequently occurred ADR (34.15%), followed by Fever (17.07%), headache (14.63), cold (14.63). Nausea /vomiting (12.20%) and sore throat (7.32%).

3.4 POST-STUDY FOLLOWUP:

Tables 5 present the mean efficacy parameter change between day 0 and day60. Statistically significant ($p<0.05$) reduction in WOMAC, VAS SCORE were observed in cannaquic oil. Table 6 shows that no significant difference (>0.05) in

WOMAC, VAS SCORE were observed in diclofenac oil. When comparing cannaquic oil and diclofenac oil, cannaquic oil shows long term benefits in post study follow up.

4. DISCUSSION:

In this present study, we observed that efficacy of cannaquic oil in comparison with diclofenac oil on ESR, IL-1, IL-6, TNF values, WOMAC, and VAS score in osteoarthritis patients. we found a significant reduction in ESR, IL-1, IL-6, TNF values, WOMAC, and VAS from baseline to day 30 in patients receiving cannaquic oil. The pronounced decrease observed with Cannaquic Oil suggests its superior efficacy in lowering inflammatory markers compared to Diclofenac Oil. This suggests that Cannaquic Oil may have a more pronounced anti-inflammatory effect.

Cannaquic Oil demonstrated a significant ability to reduce inflammation by decreasing inflammatory markers, as evidenced by a reduction in IL-1, IL-6, TNF levels. Cannaquic proved effective in reducing symptoms due to its unique formulation of cannabinoids delivered through a nano liposomal system. It has an effect on the endocannabinoid system (ECS) , targeting CB1 and CB2 receptors that regulate pain, inflammation, and immune responses. The nano liposomal delivery system enhances the bioavailability of these active ingredients, ensuring better absorption and targeted action. It also has antioxidant properties that reduce oxidative stress, which is often linked to chronic inflammation. These mechanisms explain the significant symptom relief and improvement in patient well-being observed in the study [12].

Diclofenac Oil showed no significant change, with levels remaining nearly the same. Diclofenac oil relieves pain and inflammation in osteoarthritis by inhibiting COX-1 and COX-2, hence lowering prostaglandin synthesis. This helps to increase mobility and minimize stiffness by lowering inflammation in the synovium. [13].

Abbasifard et al. (2025) [14] studied 90 patients and found that hemp seed oil helped reduce pain and improve joint function compared to a placebo, but it wasn't more effective than diclofenac gel. Current study on *Cannaquic Oil* (80 participants) showed similar short-term relief but stood out in the long run, with a much greater reduction in symptoms over time (*WOMAC score: 13.7 vs. 0.67 for Diclofenac, $p < 0.05$*). Unlike Abbasifard et al., who found hemp seed oil worked about the same as diclofenac, current study suggests *Cannaquic Oil* offers longer-lasting relief. This could be due to its unique cannabinoid-based formula and better absorption. Both studies highlight the potential of plant-based treatments for osteoarthritis, but *Cannaquic Oil* seems to have a stronger long-term impact.

Cannabis oil considerably decreased pain ($p = 0.00015$) and improved daily activities and quality of life ($p = 0.01$) in 32 patients with severe knee osteoarthritis, according to Prucksikanont W. (2025) [15]. However, the effects did not reach the minimal clinically meaningful difference (MCID). A sustained WOMAC score reduction (13.7 vs. 0.67, $p < 0.05$) over 60 days was another indication of significant pain alleviation and functional improvement in trial on Cannaquic Oil (80 participants). current study showed both statistical and clinically significant long-term gains, in contrast to Prucksikanont et al., who discovered statistical improvements without significant clinical perception. Although both studies demonstrate the potential of cannabis-based therapies, Cannaquic Oil might offer more durable symptom alleviation.

Strengths of this study are its randomized controlled trial, double-blind design, which eliminates bias and allows for valid results. It has clinical relevance as it compares Diclofenac oil to Cannaquic oil and assesses an alternative treatment compared to a gold standard. Including both short- and long-term efficacy data as well as both objective and subjective outcome measures strengthens the study in terms of being comprehensive. A big sample, balanced distribution, and long-term safety evaluation enhance the conclusion even more. The possible long-term advantages of Cannaquic oil and the mechanistic clues to its role in reducing pain and inflammation also add worthy evidence to the effect of osteoarthritis treatment

The limitation of the study is that, Blood tests for inflammatory markers, such as C-reactive protein (CRP), were not included in this study. Incorporating these studies into future study could lead to a better understanding of Cannaquic oil's anti-inflammatory properties. A longitudinal study with a bigger sample size may also improve the dependability of the findings and increase trust in the conclusions.

5. CONCLUSION:

The study highlights the differing efficacy profiles of Cannaquic Oil and Diclofenac Oil in managing osteoarthritis. Diclofenac Oil provided short-term relief, particularly in easing pain and stiffness, but its effects gradually declined over time, showing little improvement during the follow-up period. In contrast, Cannaquic Oil demonstrated a significant effect, not only providing short-term benefits but also sustaining a notable reduction in inflammatory markers and pain levels. Cannaquic oil reduces pain, stiffness, and inflammation, as seen in the decreased VAS, WOMAC, ESR, IL-1, IL-6, and TNF levels during the study period. The sustained reduction in pain and inflammatory markers suggests that Cannaquic Oil not only relieves symptoms but also supports healing, making it a promising option for osteoarthritis treatment.

Table 1

Effect of efficacy parameter on Cannaquic oil

parameter	Day 0	Day 30	P value
ESR	7.325 ± 2.22	5.55 ± 1.33	<0.05
IL-1	20.44 ± 1.08	14.91 ± 1.13	<0.05
IL-6	10.05 ± 1.12	5.98 ± 0.65	<0.05
TNF	19.92 ± 1.15	12.98 ± 2.08	<0.05
VAS	7.105 ± 1.4355	6.184 ± 1.1980	<0.05
WOMAC Score	71.25 ± 3.002	67.14 ± 3.524	<0.05

Values are expressed as mean ± SD; p-value of independent *t*-test for comparison between day 0 and day 30

Abbreviations: ESR = erythrocyte sedimentation rate; VAS = Visual Analog Scale;

WOMAC = western ontario and mcmaster universities osteoarthritis index; IL-1 = Interleukin-1; IL-6 = Interleukin-6; TNF = tumour necrosis factor

Table 2

Effect of efficacy parameter on Diclofenac oil

parameter	Day 0	Day 30	P value
ESR	7.615 ± 2.51	5.743 ± 1.22	<0.05
IL-1	19.93 ± 1.08	19.87 ± 1.08	>0.05
IL-6	9.95 ±1.24	9.89 ± 1.24	>0.05
TNF	20.24 ± 1.10	20.17 ± 1.15	>0.05
VAS	6.975 ± 1.5248	5.675 ± 1.1651	<0.05
WOMAC Score	70.61 ± 3.192	65.02 ± 4.157	<0.05

Values are expressed as mean ± SD; p-value of independent *t*-test for comparison between day 0 and day 30

Abbreviations: ESR = erythrocyte sedimentation rate; VAS = Visual Analog Scale;

WOMAC = western ontario and mcmaster universities osteoarthritis index; IL-1 = Interleukin-1; IL-6 = Interleukin-6; TNF = tumour necrosis factor

Table 3

Effect of safety parameter on Cannaquic oil

parameters	Day 0	Day 30	P-Value
Hemoglobin	14.06 ± 1.256	14.82 ± 1.072	>0.05
RBC	4.11 ± 0.65	4.32 ± 0.60	>0.05
WBC	9357.23 ± 2340.74	8945.45 ± 1518.96	>0.05

Platelet Count	247224.3 ± 67468.53	239481.1 ± 64280.91	>0.05
Neutrophils	58.29 ± 8.86	56.16 ± 8.67	>0.05
Lymphocytes	28.06 ± 5.15	28.98 ± 4.91	>0.05
Basophils	0.92 ± 0.45	0.97 ± 0.37	>0.05
Eosinophils	2.79 ± 0.7582	2.58 ± 0.8130	>0.05
Monocytes	3.96 ± 1.1349	3.64 ± 1.0112	>0.05
Sr.Creatinine	0.9875 ± 0.3048	1.1425 ± 0.4031	>0.05
SGPT	31.97 ± 10.1463	33.02 ± 6.7310	>0.05
SGOT	34.875 ± 12.23	32.275 ± 5.69	>0.05
RBS	96.1 ± 15.85	94.6 ± 15.69	>0.05

Values are expressed as mean ± SD; p-value of independent *t*-test for comparison between day 0 and day 30

Abbreviations: RBC = red blood cells; WBC = white blood cells; SGOT = serum glutamic-oxaloacetic transaminase; SGPT = serum glutamic pyruvic transaminase; Sr. Creatinine = serum creatinine; RBS = random blood sugar.

Table 4

Effect of safety parameter on Diclofenac oil

parameters	Day 0	Day 30	P-Value
Hemoglobin	14.18 ± 1.087	14.45 ± 0.908	>0.05
RBC	4.33 ± 0.72	4.46 ± 0.68	>0.05
WBC	8247.02 ± 2417.68	7542.79 ± 1730.79	>0.05
Platelet Count	250620.9 ± 69465.53	227982.4 ± 69155.47	>0.05

Neutrophils	58.35 ± 9.89	56.20 ± 9.85	>0.05
Lymphocytes	28.94 ± 5.77	28.16 ± 4.58	>0.05
Basophils	0.97 ± 0.47	0.87 ± 0.36	>0.05
Eosinophils	2.65 ± 0.8537	2.46 ± 0.8775	>0.05
Monocytes	4.02 ± 0.93	3.83 ± 0.90	>0.05
Creatinine	1.0948 ± 0.2491	1.0641 ± 0.3842	>0.05
SGPT	31.745 ± 8.6075	30.660 ± 5.7524	>0.05
SGOT	34.769 ± 4.981	32.666 ± 7.164	>0.05
RBS	93.589 ± 17.737	95.179 ± 13.701	>0.05

Values are expressed as mean ± SD; p-value of independent *t*-test for comparison between day 0 and day 30

Abbreviations: RBC = red blood cells; WBC = white blood cells; SGOT = serum glutamic-oxaloacetic transaminase; SGPT = serum glutamic pyruvic transaminase; Sr. Creatinine = serum creatinine; RBS = random blood sugar.

Table 5

Effect of efficacy parameter on cannaquic oil (post study follow up)

parameter	Day 0	Day 30	P value
VAS	7.105 ± 1.3922	5.174 ± 1.1522	<0.05
WOMAC Score	71.25 ± 3.00	57.55 ± 7.334	<0.05

Values are expressed as mean ± SD; p-value of independent *t*-test for comparison between day 0 and day 30

Abbreviations: VAS = Visual Analog Scale; WOMAC = western ontario and mcmaster universities osteoarthritis index

Table 6

Effect of efficacy parameter on diclofenac oil (post study follow up)

parameter	Day 0	Day 30	P value
VAS	6.975 ± 1.3076	6.667 ± 1.2841	>0.05
WOMAC Score	70.61 ± 3.192	69.94 ± 3.605	>0.05

Values are expressed as mean ± SD; p-value of independent *t*-test for comparison between day 0 and day 30

Abbreviations: ESR = VAS = Visual Analog Scale; WOMAC = western ontario and mcmaster universities osteoarthritis index.

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