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RESEARCH ARTICLE

Effectiveness of Phlai Mixed Cannabis Leaf Oil for The Treatment of Chronic Pain in Elderly Patients: A Double-Blind Randomized Controlled Trial

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ARTICLE INFO	ABSTRACT
	This study investigated the effectiveness of a traditional Thai herbal remedy, Phlai (*Zingiber montanum*), combined with Cannabis Leaf Oil
	(PMCL), in relieving pain in elderly person. The goal was to compare its efficacy with that of conventional treatment, specifically topical diclofenac, for chronic pain relief, and to determine whether PMCL is non-inferior to topical diclofenac. In a randomized trial, participants
	aged 60–75 years with chronic neck, shoulder, or back pain were assigned to receive either PMCL or topical diclofenac using a randomized method. The primary endpoint of the study was to compare pain intensity reduction between the two groups using a Numerical Rating Scale (NRS) for up to 14 days after treatment. The study ensured that the person measured the NRS and the participants were blinded. Of these 80 participants, 73 completed the study. The primary endpoint measurements were taken at 30 min and on days 1, 3, 7, and 14 in both groups receiving medication. The Mann-Whitney U test revealed no significant differences in the NRS scores between the two medication groups. Non-inferiority was assessed by analyzing the median difference in pain-NRS of the two study groups using the Hodges-Lehmann estimator, with a non-inferiority margin of 0.84,
*Corresponding Author: Sribud.s@ku.th	which indicated that the median difference (with a 95% confidence interval) was -1.5 (-3.0 to - 0.5), falling within the non-inferiority range. This shows that favor is given to PMCL, meaning that it is non-inferior to topical diclofenac in reducing pain. No differences were observed between the two medication groups regarding adverse drug reactions; therefore, PMCL exhibited efficacy in alleviating chronic pain in the elderly, similar to topical diclofenac, without any significant adverse reactions. These findings indicate that PMCL may be a feasible and equally effective option for pain control in the elderly.

INTRODUCTION

Chronic pain, lasting for more exceeding three months, is becoming more prevalent among middle-aged and older individuals. The prevalence of this condition varies from 25% to 50% among elderly individuals living in the community, and can reach up to 80% in those who are institutionalized. The anomalous musculoskeletal system is the main factor contributing to

chronic pain in older individuals, affecting their daily functioning and imposing substantial strain on healthcare systems. In addition, elderly individuals frequently experience multiple chronic health conditions, which adds to the intricacy of pain management and the likelihood of polypharmacy.)Treede, et al., 2019; Cravello, et al. 2019; Stompór, et al., 2019; Dagnino and Campos, 2022(

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used to treat musculoskeletal disorders in older individuals. Nevertheless, the use of these medications is linked to significant and potentially perilous adverse reactions, particularly in elderly individuals with additional health conditions, such as cardiovascular disorders and deteriorating kidney function.)Monteiro, et al., 2022(

As a result of these potential dangers, there is increasing interest in alternative medicines, especially among individuals suffering from pain-related ailments. Researchers are currently investigating the pain-relieving properties of various herbs, such as St. John's Wort, ginger, and turmeric, due to their analgesic effects.)Jahromi, et al., 2021(*Zingiber montanum* (J.König) Link ex Dietr., commonly referred to as Phlai, is renowned for its diverse therapeutic properties and has a long history of use in traditional Asian remedies (The pthong, et al., 2023; Devkota, et al., 2021; Wisuitiprot, et al., 2019).

In the United States, alternative medicine is the most popular among patients with pain because of the adverse reactions and complications of conventional treatments, such as opioids (opium derivatives) or non-steroidal anti-inflammatory drugs (NSAIDs), especially for the elderly. Several herbs with analgesic effects reduce pain and inflammation, such as St. John's Wort, ginger, turmeric, capsicum, Chili Cinching, Thunder God Vine, Butterbur, Feverfew, and Willow Bark)Jahromi, et al., 2021(

Likewise, tetrahydrocannabinol (THC) and cannabidiol (CBD), which are cannabinoids, are more commonly used to treat long-lasting pain. They are often applied topically because their dosing and absorption characteristics differ from those of other oral medications (Hameed, et al., 2023; Patel & Lio, 2021; McClements, 2020).

This study used a solution of diclofenac sodium 1% w/w versus the PMCL cool recipe (Department of Thai Traditional and Alternative Medicine recipe). Diclofenac is an FDA-approved medication for the treatment of acute and chronic pain associated with inflammatory conditions, specifically those involving the musculoskeletal system. Diclofenac inhibits the activity of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) by inhibiting the synthesis of prostanoids such as prostaglandin-E2 (PGE2), prostacyclins, and thromboxanes)Alfaro and Davis., 2023(in PMCL, namely menthol, Borneo camphor, camphor, eucalyptus oil, peppermint oil, cinnamon oil, and clove oil. Previous studies on the synergistic analgesic effects of phlai and cannabis have not yet been established. However, the mechanisms of action of phlai and cannabis are different. Phenylbutanoid derivatives extracted from phlai exhibit anti-inflammatory activity with mechanisms similar to those of non-steroidal anti-inflammatory drugs (NSAIDs), with cyclooxygenase inhibition, resulting in a reduction in the synthesis of prostaglandins, which are composed of (E)-1-(3,4-dimethoxyphenyl) DMPBD, (E)-1-(3,4-dimethoxyphenyl) compound D, and curcumin, which are strong inhibitors of COX. The mechanism of the analgesic action of cannabis is related to the endocannabinoid system; the analgesic effect of internal or external cannabinoids is mediated by the activation of cannabinoid receptor 1 (CB1R) and cannabinoid receptor 2 (CB2R). (Wisuitiprot, et al., 2019, Shehata, et al., 2022)

Topical analgesics often contain menthol and camphor, either alone or in combination with salicylate. Menthol activates transient receptor potential melastatin 8 (TRPM8), also known as cold and menthol-sensitive receptors (CMR1), on the sensory nerves and vasculature. When applied to the skin, it cools and then warms, increasing blood flow and relieving pain by blocking Ca2+ channels. In addition, menthol binds to-opioid receptors and may confer an additional opioid analgesic effect. There is evidence that camphor produces analgesic effects by activating and desensitizing the capsaicin and garlic receptors TRPV1 and TRPV3.)Garg, et al., 2022(In an

ex vivo study, peppermint and eucalyptus oils were evaluated for their effects on drug penetration through the skin.)Sorathia, et al., 2021(Cinnamon oil and clove oil disturb the ordered intracellular lipid structure between corneocytes in the stratum corneum, thereby increasing intercellular diffusivity.)Caliskan and Karakus, 2020(

This study specifically examined the use of a topical preparation called Phlai mixed with Cannabis Leaf Oil (PMCL), which is derived from traditional Thai medicine. The objective of this study was to assess the effectiveness of PMCL in addressing chronic pain in the elderly, a population that is particularly affected by chronic pain, and the difficulties it presents in treatment.)Department of Thai Traditional And Alternative Medicine, 2021(

MATERIALS AND METHODS

Study designs and ethics

This was a Non-inferiority double-blinded randomized controlled trial. The Ethical Committee approved this study of Kasetsart University, Thailand (KUREC- HS64/051) and the clinical trials registry by the Thai Clinical Trials Registry (TCTR) Committee, Thailand TCTR20231014005.

Patient selection

Participants were recruited from the outpatient department of Wanonniwas Hospital in Sakon Nakhon Province, Thailand, specifically during June and July 2022. The patients were allocated into two groups using a stratification method based on the location of their pain and NRS pain scores, and a blocked randomization method. The sample size was determined using a non-inferiority design, with the Numeric Rating Scale (NRS) score as the main outcome measure.

Inclusion criteria

1. The study included individuals between the ages of 60 and 75 who provided their informed consent.)Dagnino and Campos, 2022(

2. Individuals experiencing persistent neck, shoulder, or back pain lasting longer than three months, with a recorded NRS score of 4 or above)Brutcher, et al., 2019; Dagnino and Campos, 2022(

Exclusion criteria

1. Refrain from using NSAIDs for 48 hours prior to the study and during its entirety.

2. Non-utilization of cannabis drug in the week leading up to and during the study.

3. Topical anaesthetics must not be used within 48 hours before and during the study.

4. All other pain relief treatments, except those given by the investigator, are not allowed 24 hours prior to and during the study.

5. Absence of preexisting conditions resulting in persistent pain, such as cancer or rheumatoid arthritis.

6. No history of allergy to cannabis or phlai (*Zingiber montanum* (J.König) Link ex Dietr.), or coconut oil.

7. No history of previous allergic reactions to Diclofenac or severe reactions to nonsteroidal anti-inflammatory drugs (NSAIDs).

8. No history of asthma, gastrointestinal bleeding, liver dysfunction, or kidney insufficiency.

9. Must not be receiving warfarin therapy.

Withdrawal criteria

1. Noncompliance with the treatment regimen.

2.Discontinuation of the study medication or preference for alternative treatments.

3. Encountering unfavourable drug reactions throughout the study.

Study interventions

Qualified patients were diagnosed by a physician or practitioner of traditional Thai medicine. Participants who met the specified criteria were randomly assigned to one of two treatment groups. The chemist administered the medications, which were unknown to both the patients and investigators. Both medications were contained in identical opaque spray bottles. Label 1 indicated the presence of topical diclofenac, specifically Diclofenac Sodium (1% w/w). Label number 2 indicated the presence of PMCL, which is a mixture of 19.23% v/v rhizomes of phlai and cannabis leaf oil, prepared according to traditional Thai medicinal guidelines. PMCL consisted 260 ml consisted of 1. Phlai mixed Cannabis Leaf oil)5 kg of fresh phlai rhizomes and 100 g of fresh cannabis leaves were traditionally prepared with 1 L of coconut oil using deep-frying methods.(50 ml, 2. Menthol 90 ml, 3. Borneo camphor 40 ml, 4. Camphor 20 ml, 5. Eucalyptus oil 30 ml, 6. Peppermint Oil 20 ml, 7. Clove oil 5 ml and 8. Cinnamon Oil 5 ml. Participants will not receive the intervention simultaneously to prevent interaction between the experimental and control groups.

Patients administered their designated medication by spraying 1-2 doses, four times per day, at specific intervals (7:00 AM, 11:00 AM, 3:00 PM, and 7:00 PM), while gently rubbing for 30 s. The duration of treatment was 14 days, during which the NRS scores were evaluated at specific intervals after the application. If any unfavorable incidents occurred, the patients were instructed to cease medication. Post-treatment follow-up assessments were performed 28 days later to monitor for any adverse reactions. During this period, the use of additional analgesics was prohibited. pre-existing treatments for other coexisting medical conditions remained unaltered. The study ensured that the person measured the NRS and the participants were blinded.

Outcome measures

The primary outcome of the study was to compare pain intensity reduction after the administration of medication between the two study groups, as measured by the difference in the numeric rating scale (NRS) between groups at various time points: baseline, 30 minutes, and days 1, 3, 7, and 14 after receiving medication. These assessments will be consistently conducted by the same investigator. The scale spans from 0, denoting the absence of pain, to 10, signifying the most excruciating pain conceivable.

Monitoring for Side Effects

Adverse events were observed and tracked from the start of drug administration to day 28. Participants were directed to disclose any possible negative occurrences encountered throughout the duration of the medication period. After reporting such incidents, participants were either instructed to stop taking the medication or removed from the study due to safety concerns.

Statistical analysis

The sample size estimation for this study was calculated using the non-inferiority design formula of Chow et al. (2017), using the online calculator available at https://riskcalc.org/samplesize/. The non-inferiority margin for sample size estimation between topical diclofenac and PMCL was determined using Numeric Rating Scale (NRS) scores in accordance with the guidelines established in a previous non-inferiority trial. The margin was specified as 0.84, and the standard deviation was 1.4, necessitating a minimum of 39 participants per group to attain a Type I error rate of 5% and a power of 80%. (Miki, et al., 2018)

The analysis included both per-protocol (PP) and intent-to-treat (ITT) populations according to the guidelines outlined in the Consolidated Standards of Reporting Trials 2010 (CONSORT 2010) for non-inferiority trials. Primary per-protocol (PP) analysis specifically examined patients who strictly followed the treatment regimen. In contrast, intention-to-treat (ITT) analysis included all patients who were randomly assigned to receive either topical diclofenac or PMCL for 14 days, regardless of their adherence to the treatment. Comprehensive information regarding patients

who were not included will be provided, and there were no scheduled evaluations conducted during the study.

The normality of the data distribution was verified using the Kolmogorov-Smirnov test. Eighty geriatric individuals with chronic neck, shoulder, or back pain were randomly assigned to receive either PMCL or topical diclofenac treatment. The changes in NRS scores, measured from the initial assessment to specific time intervals after treatment (30 min, days 1, 3, 7, and 14), were analyzed using the Friedman Test, and negative changes were defined as decreases in NRS scores from baseline at follow-up. The baseline characteristics of the patients were assessed using the Mann-Whitney U test and chi-square test. Additionally, the Hodges-Lehmann estimator was used to evaluate non-inferiority. This was done by comparing the location parameters of the treatment and control distributions, based on the following hypotheses:

The null hypothesis (H0) states that the difference between the median NRS score in the treatment group (MedT) and the median NRS score in the control group (MedC) was greater than or equal to the non-inferiority margin (M = 0.84).
The alternative hypothesis (H1) states that the difference between the mean of the treatment group (MedT) and the mean of the control group (MedC) is less than a certain value (M), specifically 0.84. Where Med T represents the median NRS score in the treatment group, MedC represents the median NRS score in the control group, and M represents the non-inferiority margin.
H_0: Med T - MedC $\geq$ M (0.84)
H_1 = Med T – MedC < M (0.84)

Med T: Median NRS score in the treatment group.
Med C: Median NRS scores in the control group.
M: Non – inferiority margin

RESULTS

Figure 1 illustrates the progression of the participants throughout the study. Eighty patients with chronic neck, shoulder, or back pain were randomly assigned to receive treatment. Of these, 73 patients (91.25%) successfully completed the study, with 35 patients receiving Phlai Mixed Cannabis Leaf Oil (PMCL) and 38 patients receiving topical diclofenac. Three participants (3.75%) dropped out of the study due to loss to follow-up, two (2.5%) switched to oral analgesics, and two (2.5%) were non-compliant with the treatment regimen. The dropout rate remained within the acceptable threshold of 10% based on the sample size calculation. Baseline characteristics, as indicated in Table 1, did not differ between the two groups. Pain intensity was assessed using the Numeric Rating Scale (NRS) at the initial assessment and at each subsequent follow-up. Friedman Test results showed changes in both the control and treatment groups. In the control group, the test statistic (χ^2) was 185.94 with five degrees of freedom (df). Similarly, in the treatment group, the test statistic was 172.98 with five degrees of freedom. The results are presented in Table 2.

The Mann-Whitney U test was used to compare pain NRS scores between the PMCL and diclofenac groups at different follow-up points. The analysis conducted on both ITT and PP data revealed no significant differences in scores ($p < 0.05$). This information is summarized in Table 3. Values of median difference, if positive, indicate that NRS scores in the PMCL group are higher than those in the topical diclofenac group. Positive values indicate that the NRS scores of the PMCL group are lower than those of the topical diclofenac group, and negative values indicate equal NRS scores. Thus, the null hypothesis, predicting PMCL's effectiveness of PMCL was less than that of topical diclofenac by a minimum of 0.84 points, was rejected at all follow-up stages. As a result, the alternative hypothesis was confirmed, stating that PMCL has an effectiveness comparable to that of topical diclofenac of at least 0.84 points.

Figure 2 and 3 visually illustrate this discovery. The median difference in NRS scores between the two groups fell within the non-inferiority range, with a non-inferiority margin of 0.84 points.

Neither PMCL nor topical diclofenac were significantly less effective than topical diclofenac at either follow-up point on the pain NRS. The alternative hypothesis was that PMCL has an effect similar to that of topical diclofenac on pain NRS, even within 0.84 points (Figures 2 and 3).

The study revealed no notable disparities in adverse drug reactions between the two medications, suggesting that both treatment options had comparable safety profiles.

DISCUSSION

(Thai Traditional Medicine Department's formula) consists of 2 warm and cool recipes. To prevent detection bias, we chose cool recipes of PMCL because it was more similar to that of the diclofenac topical solution than warm recipes. This study was conducted on patients aged 60–75 years with back or neck and shoulder pain for at least 3 months, measured using the numerical rating scale (NRS). A clinical study by Murray et al. (2021) found that older adults with chronic pain (age 65-75) had higher pain acceptance and self-efficacy and lower catastrophizing levels than middle-aged and young adults.)Dagnino and Campos, 2022(

It was found that after using the drug for 30 min on days 1, 3, 7, and 14, PMCL could reduce pain no different from that of diclofenac. Similarly, Wisuitiprot et al.)2019(compared 1.0% diclofenac gel, phlai oil, and placebo oil for relieving pain in patients with myofascial pain syndrome (n = 114) assessed by the visual analog scales (VAS) at 3 days and 6 days after using the drug and showed a significant difference in VAS within the group, but between groups there was no significant difference in VAS scores. (p-value<0.05) The placebo of this study consists of methyl salicylate and eucalyptus oil. In addition, Worasing et al.)2023(Six randomized controlled trials (RCTs) involving a total of 812 patients. There was a significant reduction in pain scores when using *Z. montanum* as a remedy compared with placebo (SMD = 0.63; 95% CI = 1.20, 0.06; I^2 = 90%). However, no significant difference was observed when compared with NSAIDs (SMD = −0.61; 95% CI = −1.41, 0.81; I^2 = 73%).

According to Xu et al. (2020), topical cannabidiol oil has the potential to alleviate symptoms of peripheral neuropathy in the lower extremities. In a study involving patients with symptomatic peripheral neuropathy of the lower extremities, the use of topical CBD oil resulted in statistically significant reductions in various pain domains assessed using the Neuropathic Pain Scale. These reductions included intense pain ($p = 0.009$), sharp pain ($p < 0.001$), itching ($p = 0.001$), and sensitivity to cold ($p < 0.05$) compared with patients who received a placebo. Based on a study conducted by Hall et al. (2023), topical cannabidiol is well tolerated by individuals with a history of elite physical performance and chronic lower extremity pain. The study reported a significant improvement in self-reported pain levels (mean intake $3.5 ± 0.29$; mean exit $1.7 ± 0.23$; $P < 0.001$) and a reduction in pain-related debility, encompassing family and home responsibilities, life support activities, occupational, social and recreational activities, self-care, and sexual function. All these factors and activities were $P < 0.001$.

It was found in this study that there were no adverse reactions, and the study was not discontinued. There were no adverse effects associated with topical CBD treatment according to a recent randomized controlled trial of thumb basal joint arthritis.)Heineman, et al., 2022(. In a study by Jatuten et al. (2023) on diabetic neuropathy pain, no adverse events were reported in either group. Topical diclofenac may cause local reactions such as dry skin, erythema, erythema, and pruritus, with minimal systemic effects.)Revel, et al., 2020(

Limitations of this study: This study compared two topical medications for pain relief. The non-inferiority margin was defined as 0.84 according to a previous study that compared oral analgesics (acetaminophen versus loxoprofen) for patients with acute low back pain and calculated from the mean difference. However, the data in this study are non-normally distributed and should be used to determine the non-inferiority margin based on the median difference. In addition, the data from this study had an abnormal distribution; therefore, future studies should determine the suitability of the Non-Inferiority Margin. In addition, increasing the sample size

and drug duration may have resulted in greater differences in the effectiveness of the control and treatment groups.

Therefore, although there were no significant differences in the effectiveness of the two medication groups, the safety information PMCL groups had more advantages than diclofenac. Satisfaction information showed the advantages of the PMCL groups, fragrance, freshness, relaxation, and coolness on the skin.

Furthermore, using PMCL, which promotes Thai herbs, can also help stimulate the economy in another way. As the world moves towards an aging society, in the long term, the use of PMCL to reduce pain will reduce the cost of managing adverse reactions that NSAIDs or other modern medicines may cause. The results of this study have piqued the interest of researchers' keen on investigating the efficacy and safety of PMCL compared to oral NSAIDs and its effects on patients with office syndrome. This will be pursued in future research.

CONCLUSION

This study established that Phlai Mixed Cannabis Leaf Oil is efficacious in relieving chronic neck, shoulder, or back pain in older individuals, demonstrating a comparable level of effectiveness to topical diclofenac and establishing its non-inferiority. Significantly, both groups receiving treatment showed a comparable level of safety, as no noteworthy negative reactions to medication were observed throughout the study. This discovery highlights the potential of Phlai Mixed Cannabis Leaf Oil as a practical substitute for pain management in the elderly population.
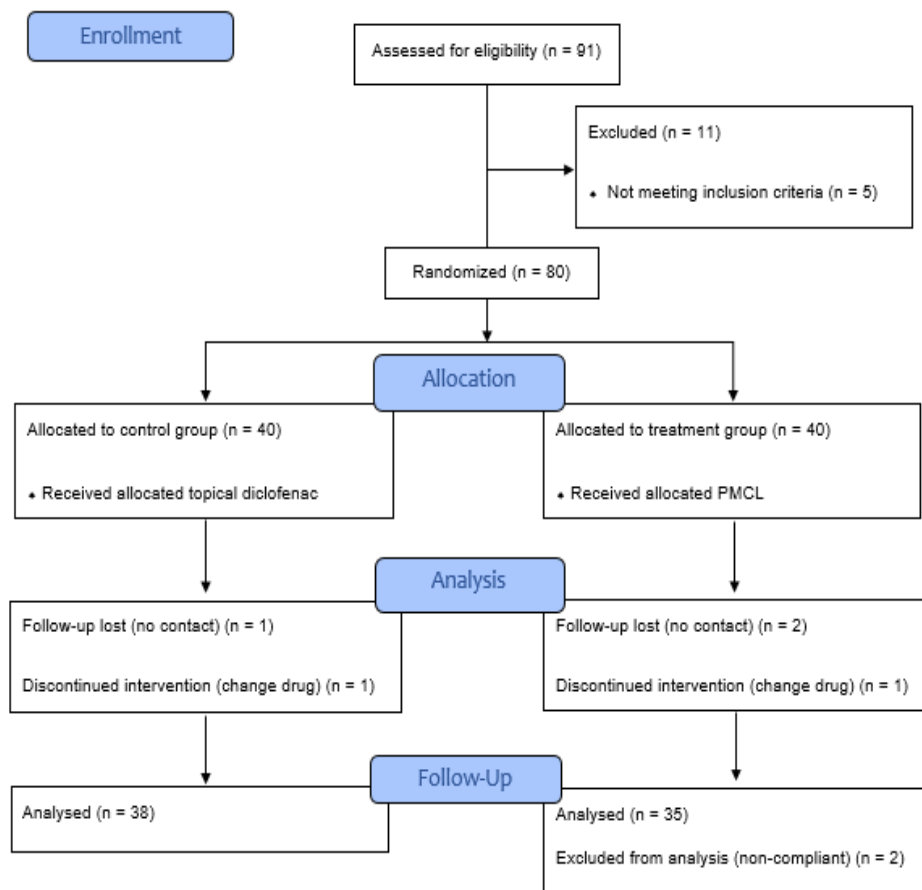

Figure 1: Flow diagram of the randomized trial comparing topical diclofenac or Phlai mixed Cannabis leaf oil groups.

Table 1 Baseline characteristics of treatment and control group

Demographics	Topical diclofenac		PMCL		Comparison (p-value)	
	ITT	PP	ITT	PP	ITT	PP
	(n = 40)	(n = 38)	(n = 40)	(n = 35)	(n = 80)	(n = 73)
Men (%) [1]	57.40	57.90	60.00	57.10	0.820	0.948
Age, Median (IQR([2]	67.00 (64.00-72.00)	66.50 (63.75-72.00)	67.00 (61.25-71.75)	66.00 (61.00-72.00)	0.478	0.543
Pain Location)%([1]					1.000	0.903
Back	50.00	50.00	50.00	48.60		
Neck and shoulder	50.00	50.00	50.00	51.40		
Pain Duration (%) [1]					0.364	0.230
3 months	30.00	31.60	30.00	31.40		
More 3 - 6 months	40.00	39.50	25.00	20.00		
More 6 months - 1 year	22.50	21.10	27.50	31.40		
More 1 year	7.50	7.90	17.50	17.10		
Working conditions (%) [1]					0.654	0.918
do not work	50.00	47.37	55.00	48.57		
still working	50.00	52.63	45.00	51.43		
Alcohol drinking (%) [1]					1.000	0.963
No	60.00	60.53	60.00	60.00		
Yes	40.00	39.47	40.00	40.00		
Smoking (%) [1]					0.576	0.672
No	77.50	78.95	82.50	82.86		
Yes	22.50	21.05	17.50	17.14		
Numerical rating scale baseline, Median (IQR([2]	6.50 (5.00-7.00)	7.00 (7.00-9.00)	6.50 (5.00-8.00)	6.00 (5.00-8.00)	0.341	0.076

Table 2 Summary of Friedman test results difference the NRS score before and after using the drug at 30 minutes, days 1, 3, 7, and 14.)Friedman test(

|	Mean NRS score	Study group	Before	After 30 min	After Day 1	After Day 3	After Day 7	After Day 14	X[2]	df
Intention-to-treat)ITT(	x̄	Topical diclofenac	6.20	5.88	4.70	3.95	2.89	1.66	185.94	5.00
		PMCL	6.40	5.80	5.02	4.00	3.06	1.80	172.98	5.00
	Mean Rank	Topical diclofenac	5.53	4.81	4.28	3.10	2.10	1.19		
		PMCL	5.53	5.24	3.93	3.10	1.96	1.25		

[1] Number of patients (%) with Chi-Square test.

[2] Median [IQR] with Mann–Whitney U test.

The p value < 0.05 was considered statistically significant

Per protocol (PP)	$\bar{x}$	Topical diclofenac	7.79	5.82	4.61	3.89	2.84	1.63	172.98	5.00
		PMCL	6.60	6.00	5.35	4.16	3.09	1.88	172.967	5.00
	Mean Rank	Topical diclofenac	5.56	4.84	4.17	3.10	2.14	1.19		
		PMCL	5.75	5.01	3.89	3.11	1.97	5.75		

Table 3 Comparison of NRS scores before and after using the drug at 30 minutes, days 1, 3, 7, and 14 between two medicine groups. (Mann-Whitney U test) (Non – inferiority margin = 0.84)

	Time	Median Difference[1]	95% CI	P-Value[2]
Intention-to-treat (ITT)	Before	-0.50	(-1.00,0.50)	0.339
	After 30 min	0.00	(-1.00,0.50)	0.729
	After Day 1	- 0.50	(-1.50,0.00)	0.217
	After Day 3	-0.50	(-1.00,0.00)	0.996
	After Day 7	- 0.50	(-1.50,0.50)	0.67
	After Day 14	- 1.50	(-3.00,-0.50)	0.472
Per protocol (PP)	Before	1.50	(1.00-2.50)	0.076
	After 30 min	0.00	(-1.00,0.50)	0.053
	After Day 1	-0.50	(-1.50,0.00)	0.437
	After Day 3	-0.50	(-1.50,0.50)	0.339
	After Day 7	-0.50	(-1.50,0.00)	0.182
	After Day 14	-1.50	(-2.50,-0.50)	0.067

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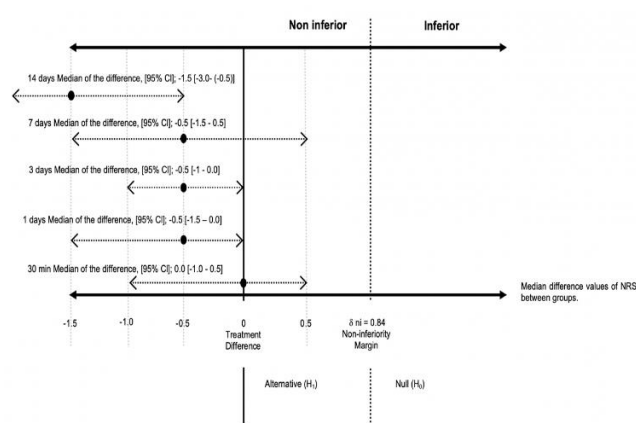
[1] The median Difference was calculated with the use of Hodges–Lehmann. Values of median difference; positive indicate that NRS scores in the PMCL group is higher than in the topical diclofenac group, negative values are present, it indicates that the NRS scores in the PMCL group is lower than that in the topical diclofenac group, 0.0, indicate there are the equal NRS scores.

[2] Adjusted p-values < 0.05 were considered statistically significant

Figure 2: Comparing Phlai mixed Cannabis leaf oil with the topical diclofenac group (ITT) in terms of pain numeric rating scale at 30 minutes, days 1, 3, 7, and 14 days at each follow-up(
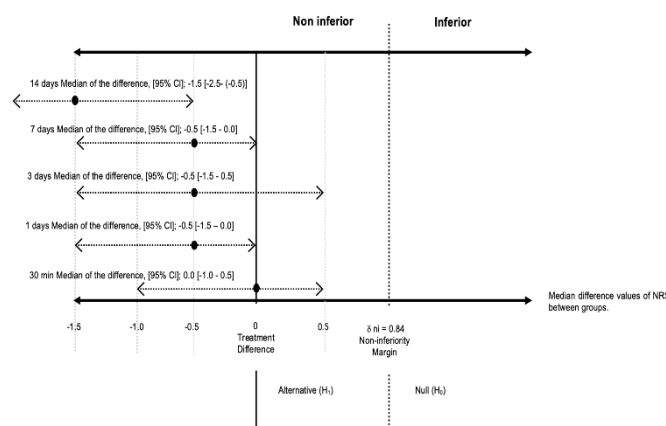

Figure 3. Comparing Phlai mixed Cannabis leaf oil with the topical diclofenac group (PP) in terms of pain numeric rating scale at 30 minutes, days 1, 3, 7, and 14 days at each follow-up(

AUTHORS' CONTRIBUTIONS

The project was conceptualized by M.L. and S.S., while the methodology was developed by M. L., S. S., N. T., M. C., S. T., and W. R. The original draft was written by M.L., and the review and editing process was undertaken by S.S. and N.T.

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