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## The Effects of *Kaempferia Galanga L.* Extract on Pain, Stiffness and Functional Physic in Patient with Knee Osteoarthritis: Double Blind Randomized Clinical Trial

Akmal Novrian Syahrudin<sup>1</sup>, Citra Kesumasari Dahlan<sup>2</sup>, Nurpudji A. Taslim<sup>3</sup>

<sup>1</sup>Graduate School Universitas Hasanuddin, <sup>2</sup>Department of Nutrition School of Public Health Universitas Hasanuddin, <sup>3</sup>Department of Nutrition School of Medicine Universitas Hasanuddin, Jalan Perintis Kemerdekaan Km. 10, PO Box 90245, Makassar, Indonesia.

Corresponding Author: Akmal Novarian Syahrudin

### ABSTRACT

**Background:** Osteoarthritis (OA) is a common disease of arthritis and one of the leading causes of disability in aged population specially on knee OA.

**Objectives:** This study was to determine the effect of *Kaempferia galanga L.* extracts in pain, stiffness, and functional improvement in patient with knee osteoarthritis (OA).

**Materials and Methods:** This study was Double Blind Randomized Clinical Trial. Forty (40) patients with primary knee OA based symptom and radiographic (K-L grading OA) diagnoses in Tamalanrea public health center, Makassar. Sample is divided into two group, the intervention group by giving *Kaempferia galanga L.* 160 mg/day and control group by giving meloxicam 15mg/day for 10 days. Outcomes measures using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) with a visual analog scale (0-10cm) for pain, stiffness, and physical function.

**Result:** The study found out, from 40 samples, 5 were dropped out and 35 samples completed the study (18 intervention and 17 control group). Both groups at the baseline did not show any differences. At the end of the study, there was a significant reduction both intervention and control group for the three WOMAC indicators (pain, stiffness and physical function) with  $p < 0.05$  and their reduction did not differ significantly for both groups.

**Conclusion:** *Kaempferia galanga L.* extract has the same effectiveness as meloxicam for the treatment of knee Osteoarthritis. Therefore, *Kaempferia galanga L.* as herbal medicine can be used for treatment for Osteoarthritis.

**Key words:** *Kaempferia galanga L.*; efficacy; WOMAC index; meloxicam; knee osteoarthritis

### INTRODUCTION

Knee osteoarthritis (OA) is a degenerative joint disease that is most common in old age. Pain is the most common symptom caused by OA and OA is expected to be the fourth cause of disability in old age. [1] OA is a progressive disease characterized by the degeneration of cartilage and joint tissue changes that result in pain, stiffness and disability. [2] Osteoarthritis is more common in the joints that support the body, especially the knee joint. OA knee contribute greatly to the burden of physically handicapped. [3]

The incidence of OA increases with age and is estimated about 80% of the population age 65 has some radiographic evidence of OA disease. [4] In the United States, estimated to affect more than 27 million people and cause disability and impaired quality of life of elderly. [5] In Asia, OA become the most common disease associated with various risk factors such as age, obesity and jobs. Cross-sectional study conducted in India the prevalence of OA according to the criteria ACR and EULAR 2009, respectively 17% and 5.6% in adults (<60 years) and 54.1% and 16.4% in the elderly (> 60 years). [6] The prevalence of knee OA in Thailand reported there were 31% male and 35% female while in China, the prevalence of knee OA 4% in men and 10% in women aged over 40 years. [7] Meta-

analysis of Prevalence of knee OA between women and men showed that the incidence of OA in men <55 years was lower than women. While women aged ≥55 years had more severe knee OA. This indicates that the incidence of knee OA of the difference between the sexes occur after the age of menopause. In Korea, the prevalence of knee OA men reach 38.1%, in Vietnam prevalence of radiographic knee OA was 34.2%, with women having a higher rate than men (35.3% vs 31.2%).

OA treatment management focuses on controlling pain and improving function and quality of life. Use of non-steroidal anti-inflammatory drugs (NSAIDs) is effective to overcome the chronic pain in the knee one Meloxicam which has the function of analgesic, anti-inflammatory and antipyretic. However, if its use in the long term will lead to gastrointestinal side effects.

The use of phytopharmaca (medicinal plants) for treatment has long been practiced and tends to increase. One of the plants used for traditional medicine is Kaempferia galanga l. Kencur (Kaempferia galanga L.) is also included in the Zingiberaceae family is an herbal medicine plant original from Indonesia. This finding is reinforced that Kaempferia galanga L. contains essential oils that can provide analgesic and anti-inflammatory effects, especially in arthritis disease.

The main content of essential oil from Kaempferia galanga L. is Ethyl p-methoxycinnamate (EPMC), and is the most important constituent responsible for most pharmacology of the Kaempferia galanga L. plant. including anti-inflammatory and analgesic. In addition, it was reported that Kaempferia galanga L. was hepatoprotective.

Several studies have shown that alcohol extract K. galangal l has analgesic activity as a painkiller as pain. In vitro studies also show the content of ethyl p-methoxycinnamate in Kaempferia galanga has antiinflammatory activity capable of inhibiting COX-1 and COX-2 as well as

some inflammatory mediators present in joints.

The findings show that the Kaempferia galanga l. extract can be used as an alternative medicinal plant for the reduction of symptoms and clinical signs of inflammation in OA patients such as pain, swelling, joint stiffness and disability in addition to pharmaceutical drugs such as Meloxicam. The purpose of this research is to know the effect of Kaempferia galanga l extract. Against symptoms and clinical signs of inflammation in the form of pain, joint stiffness and impaired physical function of knee OA patients.

## MATERIALS AND METHODS

### Location and Research Design

This study was Double Blind Randomized Clinical Trial, (RCT) and aim to see the effect of Kaempferia galanga L. extract compared with the control group of meloxicam in knee OA patients. The study was conducted after obtaining approval from the research ethics committee of the Medical Faculty of Universitas Hasanuddin. All procedures undertaken in this study are in accordance with the standards of the ethics committee.

### Method of Collecting Data

Sample Selection and Implementation this research was conducted in the working area of Tamalanrea Health Center, Makassar City. The inclusion criteria in the study were subjects with Knee-Lawrence (KL) age 40-80 years of age, both in men and women, who had not undergone analgesic and anti-inflammatory treatment at least seven days, willing to participate in the research by signing informed consent. The exclusion criteria is to have no history of liver and kidney disease and not allergic to Kaempferia galanga l. and meloxicam.

The extract from Kaempferia galanga L. used in this study is a product developed by the Center for the Development and Application of Traditional Medicine (SP3T), South Sulawesi Province,

under the auspices of the Ministry of Health of the Republic of Indonesia. A total of 40 knee OA samples are collected and have met the criteria and divided into two groups: the intervention group (n=20) who received *Kaempferia galanga L.* extract capsules 160mg / day and the control group

(n=20) were given meloxicam 15 mg / day and administered for 10 days, total of 20 samples were included in the intervention group and 20 samples into the control group. *Kaempferia galanga L.* extract capsules and meloxicam are made with the same sighting.

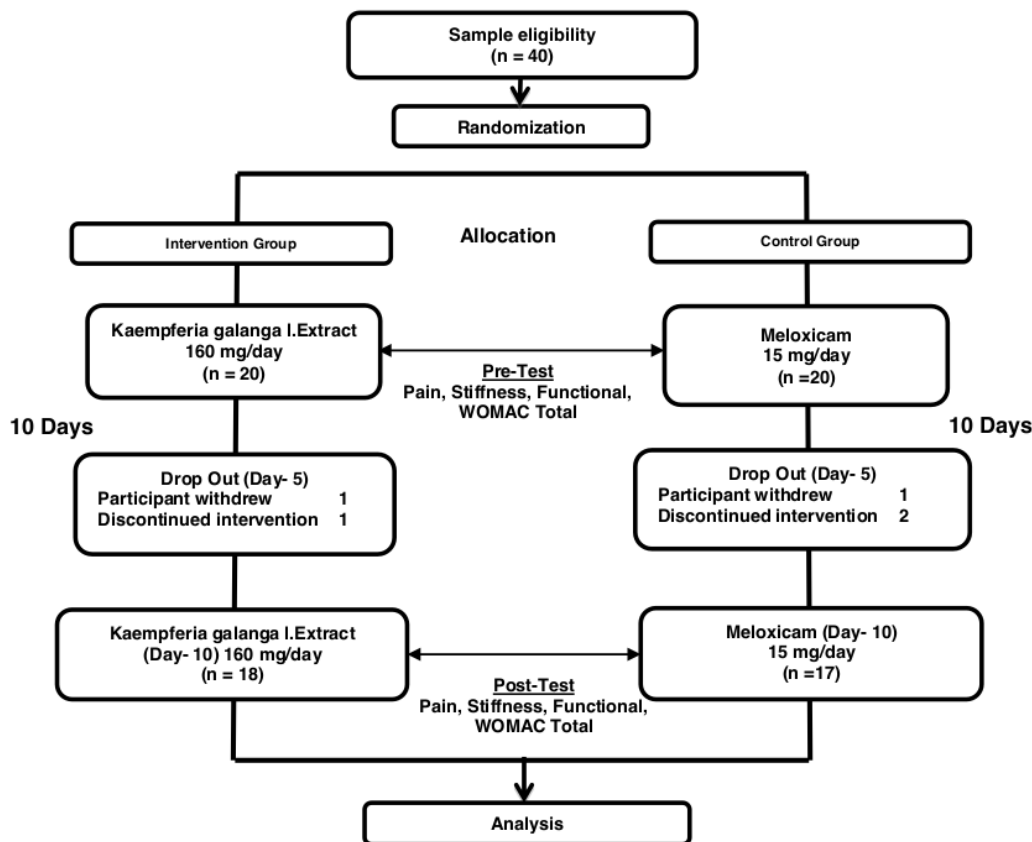


Figure1. Participant flow chart

### Data Analysis

Measurement outcomes were assessed based on the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) scores on day 0 and day 10, respectively. WOMAC Index consists of three subscales: pain, stiffness, physical function. The assessment of each scale using visual analog scale (VAS) is a horizontal line along the 10 cm with a range

from 0-10. The highest score ("10") represent poor or very painful functions; while the lowest score ("0") represents no pain or normal. [9] The data have been collected and then put into Microsoft excel, were analyzed using SPSS version 21. Independent t-test and paired t-test was used to compare the mean scores between groups and changes in scores before and after intervention

## RESULTS

### Characteristics of Sample

A total of 35 samples were completed the study. The majority sample were female in both the intervention group and the control group (94.4% vs 94.1%), the average age was 51-60 years (44.4% vs 35.3%), most of them had education at the elementary school (44.4% vs 25.7%). The majority worked as housewives in both samples (94.4% vs 76.5%). Intervention and control group were classified as obese (61.1%, 64.7%, respectively). Meanwhile, radiographic evidence that illustrates the severity of the disease based on OA grade according to KL criteria, most of the sample were in grade III for both sample (Table 1).

Table 2 shows the main outcome parameters in this study that is WOMAC score. Baseline values between both groups were pain, stiffness, physical function and total WOMAC score statistically did not show a difference ( $p > 0.05$ ). The pain scores, stiffness, physical function and total WOMAC score of both the intervention group and the control group on day 10 compared with baseline values significantly decreased ( $p < 0.05$ ) (12.06 vs 9.29), (5.39 vs 4.76), (37.50 vs 27.06) and (54.94 vs 40.88) respectively.

12 Table 1. Demographic characteristics of the samples

Variables	Intervention Group		Control Group		Total		P value
	n=18	%	n=17	%	n=35	%	
<b>Gender</b>							
Man	1	5.6	1	5.9	2	5.7	1.000
Women	17	94.4	16	94.1	33	94.3	
<b>Age</b>							
41-50	3	16.7	4	23.5	7	20.0	
51-60	8	44.4	6	35.3	14	40.0	0.843
61-70	6	33.3	5	29.4	11	31.4	
71-80	1	5.6	2	11.8	3	8.6	
<b>Level of education</b>							
No Education	3	16.7	6	35.3	9	25.7	
Elementary School	8	44.4	4	23.5	12	34.3	
Junior High School	3	16.7	2	11.8	5	14.3	0.325
Senior High School	4	22.2	3	17.6	7	20.0	
College	0	0.0	2	11.8	2	5.7	
<b>Occupation status</b>							
Housewife	17	94.4	13	76.5	30	85.7	
Entrepreneur	1	5.6	0	0.0	1	2.9	
Teacher	0	0.0	1	5.9	1	2.9	0.239
Retire	0	0.0	1	5.9	1	2.9	
Farmers	0	0.0	2	11.8	2	5.7	
<b>BMI</b>							
Normal	3	16.7	4	23.5	7	20.0	
Overweight	4	22.2	2	11.8	6	17.1	0.677
Obesity	11	61.1	11	64.7	22	62.9	
<b>Grade OA (KL)</b>							
Grade I	1	5.6	0	0.0	1	2.9	
Grade II	5	27.8	7	41.2	12	34.3	0.347
Grade III	10	55.6	10	58.8	20	57.1	
Grade IV	2	11.1	0	0.0	2	5.7	

Table 2 Effect of treatment on WOMAC scores between the groups

Variable	Pre Test Mean±SD	Post Post Mean±SD	Δ Mean±SD	P Value
<b>Pain</b>				
Intervention(n=18)	19.06 ± 8.09	12.06 ± 10.45	7.00 ± 5.97	0.001 <sup>d</sup>
Controls(n=17)	16.00 ± 5.18	9.29 ± 6.23	6.71 ± 4.39	0.000 <sup>a</sup>
P Value	0.195 <sup>b</sup>	0.643 <sup>c</sup>	0.870 <sup>b</sup>	
<b>Stiffness</b>				
Intervention(n=18)	8.22 ± 3.26	5.39 ± 3.12	2.83 ± 3.74	0.005 <sup>a</sup>
Controls(n=17)	8.82 ± 3.62	4.76 ± 3.401	4.06 ± 4.29	0.001 <sup>a</sup>
P Value	0.609 <sup>b</sup>	0.575 <sup>b</sup>	0.374 <sup>b</sup>	
<b>Physical Function</b>				
Intervention(n=18)	58.44 ± 26.89	37.50 ± 29.73	20.94 ± 18.45	0.000 <sup>a</sup>
Controls(n=17)	49.47 ± 25.85	27.06 ± 24.17	22.41 ± 14.85	0.001 <sup>d</sup>
P Value	0.322 <sup>b</sup>	0.254 <sup>c</sup>	0.798 <sup>b</sup>	
<b>Total WOMAC Score</b>				
Intervention (n=18)	85.72 ± 34.81	54.94 ± 41.80	30.78 ± 27.36	0.000 <sup>a</sup>
Controls(n=17)	74.29 ± 30.18	40.88 ± 33.10	33.41 ± 20.38	0.001 <sup>d</sup>
P Value	0.287 <sup>c</sup>	0.280 <sup>b</sup>	0.503 <sup>c</sup>	

<sup>a</sup>Paired t-test <sup>b</sup>Independent t-test <sup>c</sup>Mann Whitney <sup>d</sup>Wilcoxon

## DISCUSSION

OA is a degenerative joint disease, characterized by cartilage damage and inflammation of synovial tissue causing pain, joint stiffness and disruption of physical function. OA of the knee is

considered to be one causes of disability in old age.

Gender plays a role in the increased prevalence of OA of the knee, where women are more at risk than men OA. The risk of knee OA was significantly

reduced in males.<sup>[11]</sup> The increasing prevalence and incidence of knee OA increases with age, beginning at the age of 40 years and over.<sup>[20]</sup> Oxidative damage, thinning of the cartilage, muscle weakness, age of menopause for women (>50 years) and the production of the hormone estrogen decrease was associated with an increase in knee OA. Although the interaction effect of sex hormones and growth factors in old age with the risk of occurrence of OA is still poorly understood.<sup>[21]</sup> Another risk factor is the low level of education and socio-economic circumstances family effect on the incidence of knee OA.<sup>[22]</sup> Higher education will increase a person's ability to be more predictive of progression of the disease and aware of health.<sup>[23]</sup>

Pain is the main symptom of knee OA, research findings indicate the overall sample complained of pain in his knee has lasted a long time where pain lasting more than three months is classified as chronic pain.<sup>[24]</sup> Pain will gain weight because of the nutritional status of the majority of samples obesity. These results are consistent with other research that shows self reported knee pain was significantly associated with BMI.<sup>[9]</sup> Study meta-analysis where someone obesity risk is 2.63 times to undergo knee OA compared with normal nutritional status.<sup>[25]</sup> Other studies suggest that overweight and obesity significantly increases the risk of knee OA, respectively 2:45 and 4:55 fold times.<sup>[26]</sup>

Giving of Kaempferia galanga L extract on knee OA in the study sample had an effect on pain reduction, joint stiffness and improvement of physical function based on WOMAC score. These results consistent with previous research which states that Kaempferia galanga extract may reduce pain.<sup>[11,27]</sup> This is because Kaempferia galanga extract a substance that serves as an anti-inflammatory and analgesic.<sup>[15]</sup>

Stiffness is a common symptom of knee OA that arises as a result of inflammation of synovial tissue (synovitis). Synovitis will cause pain at rest or at night and cause joint stiffness in the morning that

lasted <30 minutes or when joints are not used within a certain period.<sup>[28]</sup> The decrease in stiffness with Kaempferia galanga L is indicated by its function as anti-inflammatory. Animal studies showed that the methanol extract of Kaempferia galanga l. able to reduce edema.<sup>[11]</sup> Two substances kencur rhizome (K. galangal l.) dominant that have pharmacological effects are ethyl p-methoxycinnamate and ethyl cinnamate.<sup>[29]</sup>

Mechanism of action of ethyl p-methoxycinnamate and ethyl cinnamate at Kaempferia galanga L. almost the same as the NSAID class of drugs by inhibiting cyclooxygenase (COX) enzyme through arachidonic acid metabolism causing decreased prostaglandin synthesis (PG) arising from injury to tissue. This prostaglandin is an inflammatory mediator that can cause tumors (swelling) and the onset of pain (dolor). Therefore, inhibition of COX synthesis, it can reduce the symptoms of OA due to the inflammatory process. In addition to the inhibition of PG synthesis, Kaempferia galanga L also inhibit several inflammatory mediators TNF- $\alpha$ , IL-1 $\beta$ , and Nitric Oxide (NO).<sup>[27]</sup>

Giving Kaempferia galanga L extract had an effect on the decrease of WOMAC score both pain score, stiffness and improvement of physical function. Risk factor controls such as weight loss management are required where weight gain is a major factor in the increased knee OA.

## CONCLUSION

This study concluded that there is not significant difference in pain score, stiffness, physical function and total score of WOMAC both intervention group and control group ( $p > 0.05$ ). Kaempferia galanga l. extract has the same effect as the administration of meloxicam to treat the symptoms and signs of knee OA.

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