



## Effects of Galbanum Oil on Patients with Knee Osteoarthritis: A Randomized Controlled Clinical Trial

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### Abstract

Knee osteoarthritis is considered as a major public health issue causing chronic disability worldwide with the increasing number of aging people. Many sufferers with knee osteoarthritis are using complementary and alternative medicine including herbal drug, herbal patch, etc. This research aimed to compare the efficacy of galbanum oil in the management of knee osteoarthritis with diclofenac gel using parallel randomized controlled design. In this randomized controlled trial (RCT), 32 patients with chronic knee pain due to osteoarthritis were randomly allocated into two equal groups. The intervention group received topical galbanum oil and control group received topical diclofenac gel. The drugs were given for 1 month, 3 times per day. Outcomes were assessed using Persian version of Western Ontario McMaster University Osteoarthritis Index (WOMAC) and visual analog scale (VAS). No statistically significant difference was observed between the topical galbanum oil and topical diclofenac gel regarding knee pain, morning stiffness and physical function over the 1- and 2-months follow-up period. It seems that using topical galbanum oil is clinically effective for patients suffering from knee osteoarthritis in order to decrease their pain, morning stiffness and limited function; its effect is comparable with topical diclofenac gel. Considering lesser side effects of galbanum and its herbal base, it may be a better choice compared to topical diclofenac in management of the pain of knee osteoarthritis at least in short term.

**Keywords:** Ferula gummosa; Galbanum oil; Knee osteoarthritis; Pain; Morning stiffness

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## 1. INTRODUCTION

Osteoarthritis (OA), the most common form of arthritis, is a chronic, degenerative, joint disease that affects mostly middle-aged and older adults. Osteoarthritis is characterized by a series of pathological changes in the whole joint, including cartilage loss, bone remodeling, excess synovial fluid secretion, capsular swelling, inflammation in the synovium (synovitis), bone marrow lesions, muscle weakness, and atrophy resulting in bone thickening and formation of bone growths or spurs that interfere with joint movement [1], [2].

The symptoms of the knee osteoarthritis are pain, morning stiffness and knee limited motion [3]. In the past few years, there is not much progress in treating the disease and it is limited to some analgesic anti-inflammatory drugs [4], [5]. There are various curing methods including oral medicines, topical drugs, intra-joint injection, complementary drugs and surgery [6], [7], [8], [9]. Nonsteroidal anti-inflammatory drugs (NSAID) such as aspirin or ibuprofen are extensively used for treatment [4], [8]. Based on the current and predicted estimates of knee osteoarthritis rates, an increase in the number of people suffering side effects of analgesics and NSAIDs will also occur. Consequently, with the frequency and severity of side effects of NSAIDs and analgesics, suggestions for less toxic treatment of osteoarthritis are warranted [10].

Evidence gathered from a systematic review show that herbal medicines, which appear relatively safe, may offer a much-needed alternative, and merit further attention [11]. Natural remedies, because of their relative safety, may reduce the dependency on NSAIDs and analgesics and could have important role in the treatment of osteoarthritis, even if they are only moderately effective [10]. These drugs are very prevalent and popular in some countries [12].

*Ferula gummosa* Boiss (Persian name, "Baridje") is one of the most well-known medicinal plants in Iran [13]. Its root has

glandular tissues rich in oleo-gum-resin (commercially known as galbanum) [14], [15]. Among the traditionally reported medicinal uses of *Ferula* species in Iran are treating convulsion, neurological disorders, diabetes, joint pain and inflammation [16], [17], [18], [19], [20], [21], [22], [23], [24], [25].

The present study aimed to investigate the analgesic effects of galbanum oil as a topical medicine compared to topical diclofenac gel in patients with knee osteoarthritis.

## 2. METHODS

Patients aged more than 18 years with knee osteoarthritis were included in the study and excluded if they had active infectious disease, skin lesion in knee, renal failure, history of knee surgery during 2 months before, alcohol or opioid abuse, pregnancy or breastfeeding, and allergy to galbanum oil.

The study protocol was approved by the local ethics committee at Iran University of Medical Sciences. The intervention was explained to the patients and written informed consent was signed by all patients before participation in the study.

The trial was registered at the Iranian Registry of Clinical Trials (IRCT) with the reference ID of IRCT2014102719699N1.

In view of the significant level of 0.05 and power of 0.8, at least 10 score difference between the two groups, and in regard to standard deviation (SD) of 8, the sample size was calculated 15 people for each group.

This single-blind randomized controlled trial investigated the efficacy of galbanum oil to treat knee osteoarthritis. Patients were allocated into galbanum or diclofenac treatment groups using a block randomization method. Participants and rater were both blinded to the treatment. Patients were told that they may receive topical galbanum or diclofenac (Figure 1). Study was done at Firoozgar hospital, Iran University of Medical Sciences, Iran, in 2014.

Essential oil of *Ferula gummosa* was prepared from the Barij Essence Co. (Iran). A hundred gram of solid paraffin (Farabi Co.,

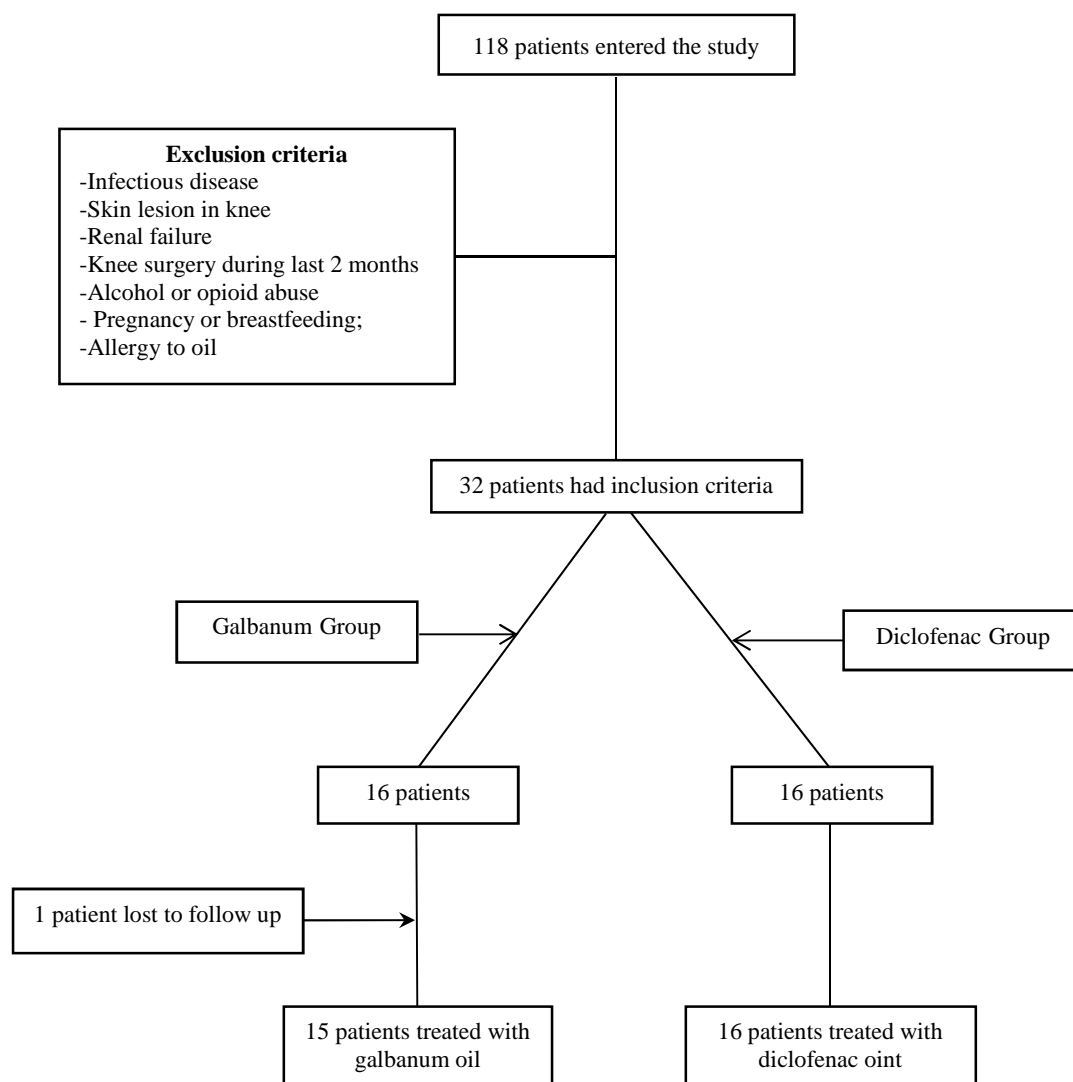


Figure 1. Study flowchart

Iran) was dissolved and five ml of essential oil was added to paraffin. Then, the mixture was interlarded by the mixer. Each gram contained 8.5 mg of 1, 8-cineole.

Sixteen patients were assigned to galbanum oil and 16 to diclofenac gel group. Patients took a knuckle of topical ointment three times per day and massaged it over the knee for one minute for four weeks. Patients were instructed to strengthen quadriceps muscles three times per day. If needed, patients were allowed to take oral acetaminophen and should inform the physician of the dose. In galbanum group, sixty grams of galbanum ointment and in diclofenac group, sixty grams of diclofenac gel were given to each patient. Each gram of

diclofenac gel contained 1 mg diclofenac sodium and created by Razak Co. (Iran).

Pain severity was rated using a 10-point visual analogue scale (VAS), where 0 was no pain and 10 was pain as severe as possible.

The Persian version of Western Ontario McMaster University Osteoarthritis Index (WOMAC) was used to evaluate the pain, morning stiffness and limited physical activity of the patients before initiation of treatment, and 1 and 2 months after it. The WOMAC score has 24 questions and 3 domain including pain, morning stiffness, and limited physical activity. Each domain is rated from 0 to 4; the higher rate in WOMAC score indicates the worse condition of patients.

Data were analyzed using SPSS statistical

software (SPSS Inc., Chicago, IL). The level of significance was set at  $P < 0.05$ . Distributional data characteristics were assessed; primary and secondary continuous variables were normally distributed. Descriptive statistics were used to describe baseline characteristics and outcomes measures at each time point; Separate confounding analyses were conducted for participant age, gender, body mass index (BMI), and radiographic grading.

The units of analysis in the VAS and WOMAC scores were the participants. Percent improvement in VAS and WOMAC score was calculated as the percentage change in total outcome measures from baseline to one- and two-months follow-up time. Data from outcomes were analyzed against baseline utilizing repeated-measure ANOVA test. For inter-group participants' analysis, repeated measure ANOVA test compared the change in outcome measures from baseline to one- and two-months follow-up.

### 3. RESULTS

Thirty-eight patients with knee osteoarthritis (6 males and 32 females) were recruited in this study with a mean age of 58.79 ranging from 38 to 79 years. Six patients discontinued participation in the study, two patients in galbanum group due to worsening of pain and four patients in diclofenac group because of

physiotherapy and acupuncture. Thirty two patients completed the study, mainly were female ( $n = 26$ , 81.2%). In this study, the written radiography reports of the patients' knee consisted of grade 1 ( $n = 6$ ), grade 2 ( $n = 15$ ), and grade 3 ( $n = 11$ ).

Comparison of patients' baseline clinical and demographic characteristics revealed no statistically significant difference between the two groups at the time of enrollment. Patients' pain characteristics and demographics are summarized in table 1.

One month after the treatment, there were no significant difference between the groups in patients' pain score in all subcategories. These results repeated in patients follow-up, two months after intervention. In patients follow-up with VAS score and WOMAC questionnaire, there were no significant differences between the groups two months after intervention (Table 2).

One month after the treatment, in galbanum group, there was significant difference in patients' VAS and WOMAC scores, in all categories; and in diclofenac group, significant differences were seen in patients' VAS and WOMAC scores. Two months after the intervention, in patients' follow-up, no significant differences were seen in any of the groups regarding VAS and WOMAC scores (Table 2).

**Table 1.** Patients' pain characteristic and demographics in two groups

Variable	Group	Galbanum oil	Diclofenac	P value
Sex [n(%)]				> 0.999
Men		3(18.8)	3(18.8)	
Women		13(81.2)	13(81.2)	
Age (Year)		60.89 ± 11.29	56.69 ± 11.01	0.297
BMI (kg/m <sup>2</sup> )		27.18 ± 3.83	29.48 ± 4.74	0.142
Education [n(%)]				0.209
Under diploma		5(31.3)	3(18.8)	
Diploma		6(37.5)	10(62.5)	
Associate degree		1(6.3)	0(0)	
Bachelor		2(12.5)	3(18.8)	
Master		2(12.5)	0(0)	
Radiology grade [n(%)]				0.924
Grade 1		3(18.8)	3(18.8)	
Grade 2		7(43.8)	8(50)	
Grade 3		6(31.5)	5(31.3)	

BMI: Body mass index

**Table 2.** Comparison of galbanum oil and diclophenac in different outcomes of knee osteoarthritis

Variable	Galbanum group	Diclophenac group
VAS		
Changes a month after the intervention	-0.56	-1.18
Changes two month after the intervention	+0.19	-0.56
Pain		
Changes a month after the intervention	-3.13	-1.69
Changes two month after the intervention	-0.82	+0.18
Joint stiffness		
Changes a month after the intervention	-0.57	-0.32
Changes two month after the intervention	-0.25	+0.12
Physical Function		
Changes a month after the intervention	-2.44	-6.37
Changes two month after the intervention	+1.13	-1.37
WOMAC		
Changes a month after the intervention	-6.12	-9
Changes two month after the intervention	+0.26	-1.06

VAS: Visual analog scale; WOMAC: Western Ontario McMaster University Osteoarthritis Index

No adverse effect was seen during the treatment.

#### 4. DISCUSSION

Presently, there is no effective treatment for osteoarthritis, much less a cure. The use of ethnomedical information has contributed to health care worldwide, even though efforts to use it have been sporadic [26]. A large number of herbal medicines have been traditionally used for the management of osteoarthritis such as *Achillea millefolium*, *Acorus calamus*, *Allium sativum*, and *Althaea officinalis*. These medicinal plants potentially alleviate inflammation and synovitis via suppression of nitric oxide (NO) and cartilage degradation by destructive matrix metalloproteinases (MMP-3 and MMP-9), down regulation of inflammatory cytokines such as interleukin (IL)-12, IL-2, IL-8, tumor necrosis factor (TNF)- $\alpha$ , IL-1 $\alpha$ , IL-6, IL-8, interferon (IFN)- $\gamma$ , and nuclear factor (NF)- $\kappa$ B as well as their antioxidant, analgesic, and anti-nociceptive activities [27].

This study aimed to investigate whether galbanum oil could induce relief in pain in patients with knee osteoarthritis. For this purpose, the effect of galbanum oil on severity of pain was compared with diclofenac gel.

In this study, the mean of age, the duration of disease, height, weight, BMI, gender

distribution, type of knee were similar in both groups. Based on the results, pain, morning stiffness and limited activity of daily living had reduction in both groups in 1 month after intervention. This difference was statistically significant. While these indexes never reached the level of statistical significance after 2 months and difference was not significant between the two groups as well.

One of the limitations of this study was the small sample size. Another limitation was the lack of placebo group.

Galbanum is a well-known herb in traditional Persian medicine and had been used for management of joint pain and inflammation. In the present study, the analgesic and anti-inflammatory properties of galbanum oil was considered for the first time and these pharmacological activities have not previously evaluated in any other studies. However, some studies performed on other topical herbal drugs support effectiveness of natural remedies. A study of topical capsaicin in hands osteoarthritis found tenderness to be reduced by 40% compared to the control group [28]. In another study, the effect of topical herbal cream on hand and knee osteoarthritis was compared with placebo and patients' pain score was significantly improved after the treatment [29].

One of the proposed mechanisms to explain the effect of galbanum oil on knee

pain is 1,8-cineole which has anti-inflammatory effect [30].

Therefore, we can say galbanum oil could have an outcome at least equal to diclofenac gel in the management the symptoms of knee osteoarthritis. However, due to the small sample size of this study, further studies with larger groups are required to confirm this finding.

This study showed that there is no difference between the pain improvement rate and quality of life in one month and two

months from either consumption of the topical galbanum or diclofenac. Considering lesser side effects of galbanum and its herbal base, it may be a better choice compared to topical diclofenac for management of the pain of the knee osteoarthritis at least in short term.

## 5. CONFLICT OF INTERESTS

Authors have no conflict of interests.

## 6. ACKNOWLEDGMENTS

None.

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