

Efficacy of a Combined Rosemary and Lavender Topical Ointment in the Treatment of Patients with Osteoarthritis of the Knee

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Article information	Abstract
<p>Article history: Received: 16 Nov 2011 Accepted: 12 Jan 2012 Available online: 29 Oct 2012 ZJRMS 2013; 15(6): 29-33</p> <p>Keywords: Knee osteoarthritis Topical products Rosemary Lavender Pain</p> <p>*Corresponding author at: Department of Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Centre, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: ghannadi@pharm.mui.ac.ir</p>	<p>Background: One of the preservative treatments of knee osteoarthritis is the use of topical medications. This study is aimed to clinically evaluate the effect of topical products containing essential oils of rosemary and lavender herbs on the treatment of patients with osteoarthritis of the knee.</p> <p>Materials and Methods: Rosemary and lavender essential oils were prepared by steam distillation method and inserted into the ointment with the hydrophilic base. In this study, 15 patients with knee osteoarthritis were treated with this ointment for three months. The results were assessed using WOMAC and Lequesne indices and were evaluated by the Wilcoxon statistical test.</p> <p>Results: At the week of admission to the hospital, mean WOMAC index was equal to 71.4, mean Lequesne index was equal to 18 and the average time of passing through the distance of fifty feet by patients was equal to 19.4. After 4, 8 and 12 weeks, all these indices significantly decreased ($p \leq 0.05$). The WOMAC questionnaire denotative survey also showed that the pain and physical function at the 4th, 8th and 12th weeks were significantly less than the first week of admission ($p \leq 0.05$), but there was no significant difference as far as joint stiffness is concerned.</p> <p>Conclusion: Topical application of essential oils of rosemary and lavender herbs in a hydrophilic ointment base can be useful as a preservative treatment for the patients with knee osteoarthritis.</p>

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Introduction

Osteoarthritis is the most common disease of the joints among humans; and knee osteoarthritis is the largest cause of disability among elderly in the most developed countries. The main pathological feature of osteoarthritis is the progressive destruction of articular cartilage. But in addition to cartilage, synovial joints and all associated tissues such as synovium and subchondral bone are also being involved by osteoarthritis.

The main complaint of patients is the pain that can be relieved by the rest early in the disease process. But with disease progression, the pain increases and becomes more resistant [1-4].

Among other symptoms, stiffness, swelling and inflammation of the joints can be mentioned and an enlargement of bone, deformities, limitation of motion, warmth, space and synovial thickening with weak muscles can also be seen in these patients [3, 5]. Risk factors for osteoarthritis are increasing age, repetitive movements, family history, obesity and joint injury [6].

Since there is no cure for this disease, one of the main goals of treatment is the reduction of abovementioned symptoms.

Treatments include training the patients, exercise, weight control, joint protection, physical therapy and physiotherapy and in some cases, pharmacotherapy such as prescription of non-steroidal anti-inflammatory medications, topical analgesics, intra-articular injection of glucocorticoids and hyaluronic acid, muscle relaxants, antidepressants; and different methods of operation are used [7-9].

Non-steroidal anti-inflammatory medications are associated with the gastrointestinal, cardiovascular, renal, liver and hematological side effects depended on the dose, duration of use and age factors. So it is recommended that the effective dose and duration of use (consumption) is reduced through topical medications [10].

For this reason, today topical treatments are also considered. In a study conducted on the effectiveness of topical piroxicam gel compared to the oral ibuprofen, it was observed that the topical treatment is as effective as the oral medication and it is also effective on acute musculoskeletal injuries with fewer side effects. A high concentration of piroxicam was seen in the skin underlying tissues and synovial fluid, using new measurable methods, while its plasma concentration was very low [11]. Natural alternative and supplementary

treatments can also reduce the need for synthetic analgesics through causing fewer side effects and sometimes they even have an important role in the treatment of osteoarthritis despite having less effectiveness. The most common treatments include oral consumption of glucosamine and chondroitine, vitamins, supplements, copper, manganese, zinc, niacinamide, n - acetyl cysteine, folic acid, vitamin B12, using the methods of acupuncture, homeopathy, leech therapy, music therapy, yoga and herbal medicines [12-16].

Some plants or herbs, effectiveness of oral or topical medications of which on the treatment of osteoarthritis has been observed include ginger (*Zingiber officinale*), turmeric (*Curcuma longa*), frankincense (*Boswellia serrata*), green pepper (*Capsicum annum*), Pomegranate (*Punica granatum*), Avocado (*Persea americana*), soybean (*Glycine max*), devil's claw (*Harpagophytum procumbens*), nettle (*Urtica dioica*), willow bark (*Salix* spp.), ashwagandha root (*Withania somnifera*) and sedge root (*Cyperus rotundus*) [13, 17, 18].

Today, for the aim of reducing the side effects of chemical drugs, topical ointments containing herbs with proven efficacy in the treatment of osteoarthritis are used to treat and relieve pain in patients with this disease. For example, an ointment containing extracts of *Symphytum officinale* has had a good effect on the reduction of knee pain and improvement of mobility [19]. Also it was found that massaging the area of pain with a mixture of ginger and orange essential oils can be useful for the short-term treatment of pain and improving physical function in patients with osteoarthritis [20]. Through evaluation of the analgesic effects of capsaicin ointment derived from green peppers, the mechanism of its effect on the substance P was specified [21, 22].

Rosemary (*Rosmarinus officinalis* L.) and lavender (*Lavandula angustifolia* L.) are two valuable medicinal herbs belonging to the Lamiaceae family. This study was conducted to evaluate the effectiveness of topical mixture of essential oils obtained from these herbs, considering the potential analgesic and anti-inflammatory effects of natural compounds found in the essential oils of these herbs. In some cases, the mentioned anti-inflammatory effects were equal to the effects of corticosteroid dexamethasone. These effects seem to occur with a lag in the migration of leukocytes [23-25].

Materials and Methods

Rosemary and lavender essential oils are obtained by steam distillation method using the Clevenger apparatus [23]; then they were inserted into the hydrophilic ointment base. Considering that the herbal active substance must pass through the skin, therefore, hydrated skin and durability of the hydration were considered as the important factors in this section. So, emulsion bases were chosen for topical formulation. Given the need for vegetable oils to enter into the oil phase, the external phase is mixed with sebum in an emulsion form and will be passed through the skin layers and the moisture found in the emulsion particles will hydrate the horny layer to

enable the passage of drug through the skin to be done easier. On the other hand, forming a film layer on the skin prevents separation of moisture from skin. Given that the pure fat bases are not well adopted by patients, hydrophilic ointment base was used in this study. To prepare the product, aqueous phase (containing compounds of methyl paraben, propylene glycol and purified water) was heated in the steam bath up to 80°C and was slowly added to the oil phase (containing propyl paraben, stearyl alcohol, white petrolatum, white and liquid paraffin) which was separately heated up to 75°C in the steam bath. When the mixture temperature reached 40°C, mixture of the essential oils heated to the same temperature, was added to them [26].

The basic ingredients of the ointment were provided from the German Merck and Roth Companies. In this study, patients with knee osteoarthritis (diagnosed by an advisor rheumatologist) were admitted to the Al Zahra Hospital in Isfahan. Sampling was done using simple consecutive method, based on the selection of volunteers willing to participate in the study who had relevant criteria for enrolling in this evaluation. All patients enrolled in this study had a full knowledge and consent of the study process and the method of treatment; and also an informed consent was obtained from them. The final number of patients participating in the study was 15 patients.

This study was performed within the framework of a research thesis having a code specified in 1997 which has been approved by the Research Council of the School of Pharmacy and Pharmaceutical Sciences of Isfahan University; and all ethical considerations were observed in it. WOMAC and Lequesne questionnaires were used in this study. WOMAC (Western Ontario and McMaster Universities) questionnaire has been developed by the Western Ontario and McMaster Universities and is used for the evaluation of patients with osteoarthritis of the knee and hip which includes three parts of pain levels, stiffness of the knee and the ability to perform some actions. Each question in this questionnaire contains five options which are scored by the patient from one to five, based on the Likert scale. Higher scores indicate more pain and poorer work performance and lower scores represent less pain and better function in daily activities [27-29].

Lequesne or Lequesne Algofunctional Index questionnaire has also been developed by a person with the same name and is used for the evaluation of patients with osteoarthritis of the hip and knee which includes area of pain during sleep, morning stiffness or progressive pain after getting up, pain when moving, the patient's maximum walking distance even with the pain and performing daily activities and its numerical answers are at the range of 0-20 or 0-60 [30].

Patients' inclusion criteria were pain, morning stiffness, limitation of motion in the knee joint, lesion degree equal to or greater than 2 (obvious osteofit and possibility of narrowing) and up to 4 (obvious osteofit, obvious narrowing, severe sclerosis and deformation detected at the end of the bones). The exclusion criteria included the

followings: Articular lesions associated with the rheumatoid arthritis or simple exhaustion of the joint and dislocation of the joints, joint injections close in time to the study, sensitivity and allergy to the topical herbal products and the increase in the severity of symptoms [31].

Fifteen patients participated in this study used this ointment on the area of pain twice a day for three months and they were referred to the hospital for evaluation at 4th, 8th and 12th weeks after their admission in the hospital. Possible side effects during these visits were questioned from patients. The mentioned pilot study was conducted on a small sample of the society before and after the treatment and the level of recovery of patients compared to the time of patient's admission was evaluated using two-sequence Wilcoxon statistical test. Significant level was considered as CI 95% and the probability of $p < 0.05$ for all tests [32, 33].

Results

The most important volatile natural compounds found in the essential oils of rosemary and lavender used in this study included tricycline, 1,8-cineol and camphor in the essential oil of rosemary and 1,8-cineol and borneol in the essential oil of lavender [23, 24].

Fifteen patients participated in this study, 12 patients of which were females and 3 patients were males. The average age of patients with knee osteoarthritis was 56.3 ± 7.9 years, mean disease duration was 4.7 ± 5.2 years and mean BMI (Body Mass Index) was 32.1 ± 4.9 . At the week of inclusion, they answered to the questionnaire with a mean value of 71.4 ± 13 (possible range of 0-96) and Lequesne Questionnaire (possible range of 0-24) with a mean value of 18 ± 3.6 and the average time of passing through the distance of fifty feet was 19.4 ± 3.6 seconds. All these patients were scrutinized 4, 8 and 12 weeks after using topical ointment mixture of rosemary and lavender twice a day. No certain side effect that may lead to the drug discontinuation observed in the patients. According to the results, during all the weeks after the first week of admission in the hospital, average scores of WOMAC and Lequesne indices and duration of passing through the fifty feet distance were significantly decreased.

As far as the WOMAC questionnaire is concerned, statistical analysis on its three components (The level of pain, morning stiffness of the joints and the ability to function of the organ suffered from disease) was performed. The results obtained at the week of admission in the hospital and at the 4th, 8th and 12th weeks have been shown in tables 1 and 2. Changes in the clinical results of WOMAC and Lequesne questionnaires and duration of passing through the 50 feet distance at the 4th, 8th and 12th weeks have been listed in table 3. According

to the results, the amount of pain and physical function significantly increased as opposed to the joint stiffness.

Discussion

Generally speaking, women suffer more from knee osteoarthritis than men due to their involvement in the affairs of home but the risk of this disorder in the knee joints in men is also possible because of handling heavy loads and there are relatively other factors in both sexes [34]. In this study, 80 percent of patients were female and factors such as high weight, non-proportional works at the home and accidentally blows (trauma) to the joint and aging, genetic and metabolic factors are possible causes of the disease in some patients.

For example, more than 50 percent of the patients in this study were equal to or greater than 80 kg and 33% of them were 60 years old or older. In a study, the association of osteoarthritis with the aging was evaluated and was found that in women, the osteoarthritis risk is higher with the passing of each decade of life after the age of 50. But in men with more than 60 years old, the relative risk of osteoarthritis increases [35]. Most of the patients enrolled in this study were complaining of too much work at the home and heavy jobs.

A study has proved that the obesity is a major risk factor for the progression of knee injury. This study emphasizes that weight reduction, is one of the ways to prevent arthritis [36]. In another study, exposure to the cold and wet weather is known to be associated with OA disease [37]. However, the majority of patients enrolled in this study, expressed one of the abovementioned underlying arguments in their explanation of disease.

This study was involved with limitations, the most important of which was too small a sample to be analyzed. Also, given that 80% of the patients participating in the study were female, the results might not be generalized to men. The results of the WOMAC questionnaire and VDI scale containing level of pain, level of morning stiffness of joints, and level of the patients' functioning show that the topical products prepared by the essential oil of the rosemary and lavender herbs are effective on the level of pain and the improvement in the level of patient's pain. But it had no great effect on morning stiffness.

This may be due to the less active muscles attached to the patient's knee. The little efforts of these patients to strengthen their muscles add to the occasion. It seems that if they use this ointment more than twice a day (e.g. once before hours of sleep), the effect of this ointment on morning stiffness is probable.

According to the results of Lequesne questionnaire and the reduction in the duration of passing through 50 feet, it seems that the level of the physical activity of patients was significantly improved.

Table 1. Denotative results of the WOMAC questionnaire at the week of patients' admission in the hospital

	Physical function	Amount of joint stiffness	Amount of pain
Mean±SD	51.4±11.1	6.7±1.6	14.1±2.8

Table 2. Denotative results of the WOMAC questionnaire at the 4th, 8th and 12th weeks

	Physical function			Amount of joint stiffness			Amount of pain		
	4week	8week	12week	4week	8week	12week	4week	8week	12week
Mean±S	-	-12.8±14.2	-10.3±13.2	-1.1±1.6	-0.5±0.9	-0.5±1.1	-2.5±2.8	-2.5±3.8	-2.9±1.4
D	8.4±13.7								
p value	≤ 0.05	≤ 0.05	≤ 0.05	>0.05	>0.05	>0.05	≤ 0.05	≤ 0.05	≤ 0.05

Table 3. Changes in the clinical results of WOMAC and Lequesne questionnaires and duration of passing through the 50 feet distance at the 4th, 8th and 12th weeks

	50-foot walk time (sec)			Lequesne index score			WOMAC index score		
	4week	8week	12week	4week	8week	12week	4week	8week	12week
Mean±SD	-1.5±1.9	-1.7±2.9	-2.3±1.9	-1.8±2.9	-2.6±3.5	-3.7±3.9	-11.4±10.3	-9±15.6	-15.9±8.2
p value	≤ 0.05	≤ 0.05	≤ 0.01	≤ 0.02	≤ 0.05	≤ 0.02	≤ 0.01	≤ 0.05	≤ 0.01

Of course it should be noted that the evaluation of the results of other studies on the effect of topical products of *Symphytum* [19] and essential oils of ginger and orange peel on patients with osteoarthritis in Germany and Hong Kong [20] showed similar results and these products had more significant analgesic effects on the pain and function of patients than being effective on the morning stiffness. It seems that it is possible to observe better effects on slany stiffness of patients with osteoarthritis of the knee through prolonged oral or topical applications of herbal medicines or a combination of these two ways. This, however, requires a separate study.

Another important point in this study was the lack of any specific adverse effect reported by patients. But the use of some herbal and topical analgesic and anti-inflammatory products containing extracts such as green peppers and capsaicin are associated with the severe skin irritation and patients usually stop using them [21,22]. The nice aroma of rosemary and lavender topical product and the lack of skin irritation are the benefits of this pharmaceutical form which was associated with the better acceptance by the patients.

Both of these herbs are used in the perfumery industries of the world. Due to the natural compound of 1, 8 - cineole as the main natural substance of both herbal volatile oils used in this study, it seems many of the topical anti-inflammatory and analgesic effects of this compound is due to the existence of this substance or composition. This natural substance forms almost half the percentage of the active ingredient in this herbal ointment. It should be noted that the composition of 1, 8 - cineole in

the in vivo and in vitro conditions is able to inhibit the formation of inflammatory mediators, prostaglandins, leukotrienes, cytokine and shows considerable analgesic and anti-inflammatory effects [23-25, 38, 39].

Both Rosemary and lavender plants are named or mentioned with other names in traditional Iranian medicine resources and their analgesic and anti-inflammatory effects have also been noted in these resources [23, 24]. Given the rational move toward evaluating the effects of medicinal plants started in Iran in recent years, one can certainly hope and expect that many of the techniques of experimental medicine hidden in Traditional Iranian Medicine Treasures are approved by the new methods. The results of these kinds of scientific studies will be resulted in the introduction of effective drugs in different fields of medicine and pharmacy.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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