



Effects of Rosemary Oil on Osteoarthritis Symptoms in the Elderly: A Double-Blind Randomized Control

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Abstract

Background: Despite anti-inflammatory effects of rosemary, there is no broad consensus on the effects of rosemary on osteoarthritis symptoms, being among the most common causes of disability. This study aimed to determine the effects of rosemary ointment on osteoarthritis symptoms in the elderly.

Materials & Methods: In this double-blind randomized trial, 75 elderly patients with knee osteoarthritis were selected from comprehensive health service centers based on inclusion criteria and assigned by the random minimization method to three groups equally. In the intervention and placebo groups, 4 cm of rosemary and Vaseline ointment were applied twice a day, respectively, for 10 days. The control group received no intervention. In addition, the Western Ontario and McMaster Universities Arthritis Index (WOMAC) was measured for the three groups, before, immediately after, and one month after the intervention. Data were analyzed using the Mann Whitney U test, a repeated measures ANOVA, and statistical modeling.

Results: There were no significant differences among the study groups based on demographic characteristics. In the rosemary and placebo groups, the mean score of the WOMAC and pain improved significantly ($p = 0.001$) immediately and one month after the intervention. In terms of intergroup comparisons, the WOMAC and pain scores, immediately after the intervention, were significantly higher in the rosemary group than in the other two groups ($p < 0.05$). However, joint performance and stiffness scores had no significant differences.

Conclusions: The results showed that shortly after the intervention, WOMAC and pain scores improved in the rosemary group. However, no improvement was observed in joint stiffness and function.

Keywords: Osteoarthritis, Rosemary, Pain, Elderly.

Introduction

Osteoarthritis (OA) is the leading cause of disability, which is associated with considerable costs in the elderly. With population aging and growing obesity, this syndrome has become more

prevalent globally in the current decade than in previous decades [1]. Osteoarthritis is a disease of the entire joint, which involves structural changes in the articular cartilage, subcutaneous bones, ligaments, capsules, synovial membrane, and

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muscles around joints [2]. Pain is the predominant symptom and the main stimulus for clinical decision making, with healthcare services being provided using a socio-psychological model [3]. Clinically, knees are the most common site of osteoarthritis, followed by hands and the pelvis [4]. In the Eastern Mediterranean Region (EMRO), women over 30 had the highest risk of developing musculoskeletal disorders among other regions. According to a study, in this region, Bahrain, Iran, and Morocco had the highest incidence rate of musculoskeletal disorders [5]. Results of a systematic review showed that the prevalence of OA in low- and middle-income countries was so high that approximately one sixth of the study participants reported a history of OA [6]. Research estimates that, in some western countries, the proportion of people over 45 to be diagnosed with knee osteoarthritis will increase to 15.7% by 2032 [7]. The prevalence of this disease in Tehran, i.e. the capital of Iran, is reported to be 15.1% [8].

The results of a study showed that 81% of OA patients had a reduced ability to perform their basic life activities [9]. In knee osteoarthritis, knee-related disability is highly affected by cognitive factors and impaired body perception [10]. This disease places a significant burden on individuals and society, being associated with complications, costs, and increased mortality rates [11]. Additionally, it is associated with decreased quality of life and adverse psychological impacts [12].

According to researchers, there is no known cure for OA. However, people with knee OA can benefit from appropriate management strategies [13]. Accordingly, the goals of the current treatment are to relieve pain and maintain the function. In this context, education, weight loss [14], heating/cooling therapies [15], focal vibration, and intra-articular oxygen–ozone therapy [16] could be effective. Drug options, in this case, include topical and oral non-steroidal anti-inflammatory drugs [14], duloxetine [17], glucocorticoids, periodic intra-articular hyaluronans [16], and total joint replacement [14]. New targets, such as the nerve growth factor, are being considered, which may be confirmed for OA pain in the future. Although OA is significantly affected by placebos [18], complementary medicine and herbs [19] as well as non-pharmacological interventions are necessary, having been shown to produce desirable outcomes [20].

In traditional medicine, *Rosmarinus officinalis* L. (rosemary) is used to treat asthma [21] and dysmenorrhea [22]. In a review, in addition to therapeutic uses of rosemary in treating inflammatory diseases, researchers alluded to other applications, such as healing wounds,

treatment of skin cancer and mycosis, potential uses in cosmetic formulations, as well as treatment of pathological and non-pathological conditions, such as cellulite, alopecia, ultraviolet damage, and aging [23]. Therapeutic effects of rosemary are related to the main components isolated from rosemary essential oil, which have anti-inflammatory, antioxidant, and analgesic effects [24]. Researchers in the existing literature evaluated the effects of rosemary combined with other plants and reported anti-inflammatory effects for them [25-28]. Positive effects of rosemary on articular cartilage were reported in some studies as well [29, 30]. However, the researchers in the present study found no study to have measured unique effects of rosemary on osteoarthritis symptoms. The present study aimed to determine the effects of rosemary ointment on osteoarthritis symptoms in the elderly.

Materials and Methods

This study, being a double-blind randomized controlled trial, was performed at comprehensive healthcare centers from February 2021 to July 2021, Rafsanjan, Iran.

The Research Council of Rafsanjan University of Medical Sciences approved the project. In addition, the deputy of the research and technology at this university obtained the code of ethics (IR.RUMS.REC.1398.201) from the Ethics Committee. Next, the letter was presented to the comprehensive health service centers of Rafsanjan by one of the researchers. At the next stage, she prepared a list of the elderly ($n = 85$) with a history of knee osteoarthritis in the health electronic files of the Iranian health integrated system (SIB). Next, they were briefed on the purpose of the study through making a call; accordingly, if they gave consent and met the primary inclusion criteria, they would be invited to attend the center and would be included in the study. Almost all of those who were invited agreed to participate in the study. After attending the center, one of the researchers who was a nurse and had received adequate training in this field from a rheumatologist examined them for clinical classification criteria of the American College of Rheumatology. These criteria were approved in the case of the existence of knee joint pain, with at least three of six items for knee joint osteoarthritis [31].

Following the implementation of the Health Transformation Plan (HTP) in 2014, the Iranian Ministry of Health, Treatment and Medical Education (MOHME) launched the Integrated Health System (SIB) in 2016. The SIB system

pursues vital goals, including implementation of the electronic health records system, creation of a national health information database, and provision of referral systems in the family physician plan [32]. In this study, the inclusion criteria were having no experience of damage to the knee skin, having no allergies to rosemary ointment (initially, a small amount of ointment was tested in the patients' arm), having no alcohol and drug addiction, not having used other complementary and alternative methods, such as acupuncture and physiotherapy, having no history of knee surgery, having no arthroscopy in 30 days prior to the intervention, not being a smoker, receiving a moderate to severe score on the WOMAC scale, being insensitive to rosemary ointment (among the intervention group participants), having phone numbers for follow-up calls, and having no cognitive impairment, like Alzheimer's disease. On the other side, the exclusion criteria included having received aggressive therapies or surgical interventions during the intervention, withdrawal from keeping participating in the study, as well as forgetting to use the ointment more than twice for the intervention and placebo groups.

Given the standard error of less than or equal to 0.05, the power of 0.90, the standard deviation of 10.3, the effect size of 11.4 for the WOMAC score after 4 weeks of the intervention [25], and using the following equation, the sample size was calculated at 19. However, we assigned 25 people to each group.

Formula 1.

$$n = 2(Z_{1-\alpha} + Z_{1-\beta})^2 (S_1^2 + S_2^2) / d^2 \times \sqrt{3-1}$$

Sampling was initially performed purposefully, based on the inclusion criteria and using the SIB system. Eligible samples were randomly allocated to the three groups of the intervention (the rosemary ointment group), the control (without any intervention), and placebo (hygienic Vaseline ointment) by the random minimization method, based on gender classes (male and female) and the WOMAC score in two middle (score 60-80) and severe (scores over 81) classes [33]. The purpose of the placebo group was to modify the effects of massage and the presence of the therapist. The first samples were randomly entered into one of the groups. Randomization units were included in the study individually. The allocation status of the first sample in each class of one of the study groups was randomly sealed by an envelope. The next sample was entered with the same pre-test class between the two remaining groups by lottery. In addition, the third sample with the same feature

was assigned to the last group in the same category. This process continued until the sample size of the study was obtained.

Data collection tools included demographic characteristics, including the age, gender, level of education, duration of the disease, and type of the drugs (oral or injectable) used. The second tool was the WOMAC index that was developed in 1982 at Western Ontario and McMaster Universities, being available in over 65 languages. This scale is used to assess patients with hip and knee joint arthritis, which consists of 24 questions and the three subscales of pain (5 questions), joint stiffness (2 questions) and physical performance within the last 48 hours (17 questions). The original scale is available in the two forms of Likert and VAS. In this study, the Likert form (no pain, low pain, moderate pain, strong pain, a lot of pain) was used with the scoring of 0-4. In addition, the minimum and maximum scores of the WOMAC index were 0 and 96, respectively, while the corresponding values for the pain index were 0 and 20, respectively, as well as 0 and 8, respectively, for the joint stiffness index. Additionally, the minimum and maximum scores of the physical performance index were 0 and 68, respectively. Reliability of the Persian version of the WOMAC index has been approved at a Cronbach's alpha of 0.917 and the R value of 0.964 for the interclass correlation coefficient. Besides, score reliability of global WOMAC was determined to be 0.68 for the Likert version and 0.64 (Kendall's tau) for the VAS version [33]. In addition, randomization units were included in this study individually.

In the intervention group, the rosemary ointment produced by the Goldaroo Company was used in the form of a thin layer of ointment (1.5 gr), having been equal to 4 cm of ointment on the affected knee joint. It should be noted that the ointment was applied twice a day (8 am and 8 pm) for 10 days. In fact, no intervention was applied to the control group other than routine treatments. In addition, the placebo group received the hygienic Vaseline ointment produced by the Goldaroo Company with the same pattern applied to the intervention group. It is noteworthy that all routine treatments of the patients were respected, with the time and manner of the intervention monitored every day on phone.

The primary outcome was the standard scale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). In addition, the pain, stiffness, and physical function of knee joints, as the subscales of WOMAC, were the secondary outcomes. For all participants in this study, WOMAC was measured before, immediately after, and one month after the intervention (the minimum

expected time lasting for the intervention from the researchers' point of view). It was done through a face-to-face interview by the researcher's colleague at 10:00 am, given that at least 8 hours had passed from the use of painkillers at the measurement time. The study was double-blind, so the patients and the person who filled out the questionnaire did not know how the samples would be assigned to the study groups.

For ethical considerations, as mentioned before, approval for the trial was received by the deputy of the research and technology at Rafsanjan University of Medical Sciences from the Ethics Committee of this university. Moreover, ethical considerations, including voluntary enrollment, being free to leave the study, obtaining informed written consent forms to participate before entering the study, and ensuring that treatments were not harmful, were taken into account. Additionally, all therapies were respected, with all conditions probably affecting osteoarthritis symptoms emphasized and monitored. The study did not inflict any financial, spiritual, or physical complications to the participants.

Data were analyzed by SPSS software V22.0 using descriptive statistics, the Fisher's exact test (to compare ratios), the Mann-Whitney U test (to compare means between the two groups), and a repeated measures ANOVA (to compare mean changes in WOMAC scores and its subscales at consecutive measurements in the three groups). In addition, statistical modeling was performed to test the group-time interaction at a significance level of 0.05. To reduce the effects of the gender and time of measurements as confounding factors at the time of sampling, the groups were matched for

gender categories and the baseline WOMAC score, with all measurements performed at the same time.

Results

According to the Shapiro-Wilk test, the distribution of some variables was not normal, but in terms of the coefficient of skewness and Kurtosis, all variables were within the range of 1 and -1. In addition, results of the Mauchly's sphericity test showed that the correlation coefficients of the consecutive measurements were significantly different, so the Greenhouse-Geisser correction coefficient was used to report p-values. Data analysis results showed that the mean and standard deviation of the patients were 66.76 ± 8.01 with a minimum of 60 and a maximum of 95 years. Additionally, the results of the Mann-Whitney U test showed that the median and the interquartile range of age in the intervention, placebo, and control groups were 62 ± 90 , 65.5 ± 10.75 , and 67 ± 10.75 , respectively. Besides, there were no statistically significant differences among the studied groups in age. Furthermore, there were no significant differences among the three groups in demographic variables, such as the gender, education, type of drug (oral drug or topical ointment, or the combination of these two types of treatments for managing knee osteoarthritis symptoms), and duration of the disease. Table 1 shows results for the comparison of the groups in terms of some important variables. As the study groups included the elderly, which matched in terms of gender at the time of assignment to the study groups as well as similarities of the treatment protocols, it is expected that the groups be similar in terms of these features.

Table 1. Comparison of demographic characteristics of the elderly with osteoarthritis

		Intervention n = 25 (100%)	Placebo n = 25 (100%)	Control n = 25 (100%)	Pearson's chi- squared test P-Value
Gender	Male	3(12)	2(8)	4(16)	0.685
	Female	22(88)	23(92)	21(84)	
Education	Illiterate	14(56)	16(64)	12(48)	0.938
	High school diploma	2(8)	2(8)	2(8)	
	Under high school diploma	9(36)	7(28)	10(40)	
	Academic	0(0)	0(0)	1(4)	
Drugs	Ointment	0(0)	1(4)	5(20)	0.069
	Oral	10(40)	10(40)	11(44)	
	Combined (oral & ointment)	15(60)	14(56)	9(36)	

*Significance was considered at 0.05.

The repeated measure ANOVA was used to examine the trend of the WOMAC score and its subscale changes for consecutive measurement times (time effects) among the study groups (group effects). In addition, the effects of the groups (interactions between times and groups) were taken into account over time (Table 2).

WOMAC score: In terms of WOMAC scores, the

results of the Mauchly’s sphericity test showed that the correlation coefficients of the consecutive measurements were significantly different among the groups (P = 0.038). Therefore, the precondition for the correlation equation was not accepted, so the Greenhouse-Geisser correction coefficient was used to report p-values.

Table 2. The mean and standard deviation of the WOMAC score and its subscales across the study groups for the three times of measurements

Variable		Intervention Mean ± SD n = 25	Placebo Mean ± SD n = 25	Control Mean ± SD n = 25	Time effect P-value	Time* group effect P-value	Group effect P-value
WOMAC score	Before the intervention	70.88 ±8.34	68.08±6.81	67.88±6.58	*0.001	*0.001	*0.023
	Immediately after the intervention	56.20±9.94	62.72±10.24	71.80±7.22			
	One month after the intervention	66.48±12.13	66.00±11.18	72.52±8.11			
Pain score	Before the intervention	14.32±3.13	14.60±2.27	14.20±2.30	*0.001	*0.001	*0.018
	Immediately after the intervention	10.28±3.51	12.76±2.78	14.80±2.14			
	One month after the intervention	13.20±2.95	13.76±2.57	14.96±2.26			
Joint stiffness score	Before the intervention	6.96±1.06	5.88±1.98	6.12±1.53	*0.001	*0.001	0.414
	Immediately after the intervention	5.28±1.69	5.76±1.78	6.52±1.22			
	One month after the intervention	6.32±1.40	5.96±1.88	6.60±1.22			
Joint performance score	Before the intervention	48.96±6.91	47.60±5.47	47.56±4.70	*0.001	*0.001	*0.041
	Immediately after the intervention	40.64±6.86	44.20±7.95	50.48±5.44			
	One month after the intervention	46.96±9.28	47.96±8.28	50.96±5.81			

*Significance was considered at 0.05.

Table 2 shows the results of the multivariate test for the examination of times, groups, and interactions between time and group effects for WOMAC and its sub-scale scores. Firstly, we try to explain WOMAC score changes within each group. Accordingly, the results showed that in the intervention group, the WOMAC score decreased significantly immediately after the intervention compared to the baseline and one month after the intervention (p = 0.001). Moreover, the WOMAC score increased significantly one month after the intervention compared to the

baseline (p = 0.024). Table 3 shows the results of pairwise comparisons between placebo and control groups. According to inter-group comparisons, the WOMAC score was the same for the groups before and one month after the intervention (P > 0.05). In addition, the WOMAC score was significantly lower in the intervention group than in placebo (p = 0.045) and control groups immediately after the intervention (p = 0.001). Table 4 shows the results of intergroup pairwise comparisons.

Table 3. Results of the intergroup paired comparisons of the WOMAC score

Group		Before the intervention		Immediately after the intervention		One month after the intervention	
		Mean±SE	P-value	Mean±SE	P-value	Mean±SE	P-value
Intervention	Placebo	2.80±2.06	0.536	-6.52±2.61	0.045	0.48±3.00	1.000
	Control	3.00±2.06	0.450	15.60±2.61	0.001	-6.04±3.00	0.144
Placebo	Intervention	-2.80±2.06	0.536	6.52±2.61	0.045	-0.48±3.00	1.000
	Control	0.20±2.06	1.00	-9.08±2.61	0.003	-6.52±3.00	0.100
Control	Intervention	-3.00±2.06	0.450	15.60±2.61	0.001	6.04±3.00	0.144
	Placebo	-0.20±2.06	1.00	9.08±2.61	0.003	6.52±3.00	0.100

Pain score: The results of the analysis of changes in the pain subscale score within each group were obtained. Accordingly, the pain score had an immediate significant improvement compared to before and one month after the intervention ($p = 0.001$) in the intervention group. However, it increased significantly one month after the intervention compared to the baseline ($p = 0.012$) and immediately after the intervention ($p = 0.001$). According to the results, there was no significant change in the pain score in the control group in the three stages ($P > 0.05$). The pain score in the placebo group was significantly lower immediately after and one month after the intervention than the baseline ($p = 0.001$). However, there was no significant difference between the baseline and one month after the intervention ($P > 0.05$). In the intergroup comparisons, pain scores were the same for the three groups in the pre-intervention phase ($P > 0.05$). Nevertheless, in the immediate period, the pain score of the intervention group was significantly lower than that of the control ($p = 0.001$) and placebo groups ($p = 0.010$). Besides, the pain score was lower in the placebo group than that in the control group ($p = 0.043$). However, one month later, the measurements were not significantly different ($P = 1.00$).

Joint stiffness score: The results of analyzing

changes in stiffness subscale scores within each group were obtained. Accordingly, in the intervention group, the stiffness score had a significant improvement immediately after the intervention compared to before and one month after the intervention ($p = 0.001$). In addition, it increased significantly one month after the intervention compared to the baseline ($p = 0.011$) and immediately after the intervention ($p = 0.001$). However, there were no significant changes in the scores of the control and placebo groups in pairwise comparisons ($P > 0.05$).

In the intergroup comparison, no significant differences were observed among the groups at the baseline and one month after the intervention ($P > 0.05$). However, the intervention group had a significantly lower score immediately after the intervention than the control group ($p = 0.022$). Nevertheless, no significant difference was observed among the placebo, intervention, and control groups ($P > 0.05$).

Joint performance score: Given the changes in the joint performance score in the intervention group, there was a significant improvement immediately after the intervention compared to before and one month after the intervention ($p = 0.001$). Besides, it increased significantly one month after the intervention compared to the immediate time after the intervention ($p = 0.001$).

Table 4. Results of paired comparisons of the WOMAC score among the groups

Time of measurement		Intervention		Placebo		Control	
		Mean±SE	P-value	Mean±SE	P-value	Mean±SE	P-value
Before the intervention	Immediately after the intervention	14.68±1.42	0.001	5.36±1.42	0.001	-3.92±1.42	0.022
	One month after the intervention	4.40±1.61	0.024	2.08±1.61	0.608	-4.64±1.61	0.016
Immediately after the intervention	Before the intervention	-14.68±1.42	0.001	-5.36±1.42	0.001	3.92±1.42	0.022
	One month after the intervention	-10.28±0.84	0.001	-3.28±0.84	0.001	-0.72±0.84	1.000
One month after the intervention	Before the intervention	-4.40 ±1.617	0.024	-2.08±1.61	0.608	4.64±1.61	0.016
	Immediately after the intervention	10.28±0.84	0.001	3.28±0.84	0.001	0.72±0.84	1.000

However, no significant differences were observed between one month after the intervention and the baseline ($P > 0.05$). In the placebo group, no significant difference was observed ($P > 0.05$). In the control group, the joint performance score was significantly lower immediately and one month after the intervention than that at the baseline. Nevertheless, no significant difference was observed in other comparisons ($P > 0.05$).

According to the intergroup comparisons, no significant differences were observed among the groups at the baseline and one month after the intervention ($P > 0.05$). However, the control group had a significantly higher score than the intervention ($p = 0.001$) and placebo groups ($p = 0.005$) immediately after the intervention.

Discussion

The results of the study showed that WOMAC and pain scores improved in the rosemary group in a short time after the intervention. Similarly, such an improvement was observed in the placebo group in contrast to the control group, yet all the three groups were similar one month later. However, no improvement was observed in terms of joint stiffness and function among the groups. According to the results, WOMAC score correction was more strongly affected by pain score changes than by stiffness and joint function scores. According to the available reports on anti-inflammatory effects of rosemary [34], one can attribute effectiveness of this drug in improving pain and WOMAC scores to anti-inflammatory effects, the reduction in joint inflammatory reactions, and soothing effects of joint massage. The correction of WOMAC and pain scores in a short time in the placebo group, in addition to the intervention group, suggests the possibility of a placebo effect or a massage effect rather than a therapeutic effect for rosemary. In fact, the difference in the number of therapist contacts with the intervention and placebo groups, compared to the control group, might have affected the results.

Review of the available literature shows that limited studies have been conducted on the independent effect of rosemary ointment on osteoarthritis symptoms. Besides, the researchers' focus on the combinatory effect of this plant derivative with other herbal drugs was limited. In a study, Ghannadi et al evaluated WOMAC, pain, physical activity, and joint stiffness scores in osteoarthritis patients in a three-month topical treatment with a combination of rosemary and lavender. Accordingly, the results showed a significant improvement in WOMAC, pain, and physical activity scores after 4, 8, and 12 weeks,

yet the joint stiffness score did not change significantly [25]. Although the effectiveness of the intervention in improving pain and WOMAC scores was similar to that of our study, there were some methodological differences in the design of this study with ours; accordingly, only 33% of the samples of this study were the elderly, it had no control group, and it was performed on a limited number of samples (15 people); thus, its results have limited validity and generalizability.

Mohammadifar et al evaluated the effect of nanoemulsion containing peppermint and rosemary essential oils in rats with osteoarthritis. The results showed that after receiving the nanoemulsion containing rosemary essential oil, osteoarthritis pain decreased through increasing the antioxidant capacity and improving histopathological properties of the knee joints of the rats [35]. Similar to our study, analgesic effects of rosemary were reported in animal samples, in the aforementioned study. The researchers attributed this state to antioxidant effects.

In a pilot study, Lukaczer et al showed that the standardized combination of reduced iso-alpha-acids from hops, rosemary extract, and oleanolic acid significantly reduced pain in patients with rheumatic disease [27]. Although in this study rheumatic patients were the target group (fibromyalgia, osteoarthritis, and rheumatoid arthritis) and the pain assessment tool was the Visual Analogue Scale, analgesic effects of peppermint and rosemary essential oils were similar to those of our study. The improvement in the patients' pain could be attributed to the possible reduction in inflammatory joint reactions. In addition to anti-inflammatory effects, researchers in some studies have found that rosemary significantly reduces bone loss caused by calcium deficiency and concluded that the plant could be considered a promising candidate for preventing bone resorption and osteoporosis [36].

Paixão et al (2021) published a review article that evaluated the role of essential oil therapy in patients with rheumatic disease. There are few reports on the effects of essential oils on rheumatic disease, mainly osteoarthritis, rheumatoid arthritis, and fibromyalgia. All studies, apart from one study, reported the effectiveness of these complementary therapies [37]. The results of the existing studies indicate the need for future research with a more accurate methodology to determine possible effectiveness of rosemary in managing osteoarthritis symptoms and clarifying possible pathways.

In the present study, we tried to obtain valid results by comparing the three groups in terms of major

intervention variables, with the nature of the study having been double-blind, yet it had some limitations. Accordingly, the effect of the therapist's presence and massage on the way the elderly would respond to the questionnaire questions could not be ignored. In addition, the effects of the patients' lifestyle that could affect osteoarthritis symptoms were beyond our full control. In general, it can be deduced from the available texts that although rosemary ointment with anti-inflammatory effects has relieved pain in patients with osteoarthritis in some conditions and improved physical functions of affected joints, the placebo effect has not been considered by researchers in most of them. Therefore, more research is needed to comment with certainty on its effectiveness in correcting osteoarthritis symptoms. In addition, it is necessary to determine in future research in which patients and at what stage of the disease, this method could be used therapeutically. On that account, more research is recommended to be done in this field.

Conclusion

The results of this study showed that although rosemary oil could improve WOMAC and pain scores in patients with knee osteoarthritis in the short term, this improvement was not observed in the long term.

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References

- Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet*. 2019;393(10182):1745-59.
- Brandt KD, Radin EL, Dieppe PA, van de Putte L. Yet more evidence that osteoarthritis is not a cartilage disease. *Ann Rheum Dis*. 2006;65(10):1261-4.
- Neogi T. The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis Cartilage*. 2013;21(9):1145-53.
- Prieto-Alhambra D, Judge A, Javaid MK, Cooper C, Diez-Perez A, Arden NK. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: influences of age, gender and osteoarthritis affecting other joints. *Ann Rheum Dis*. 2014;73(9):1659-64.
- Dizaj JY, Soleimanifar M, Hashempour R, Karyani AK, Mohsen F, Zali ME, et al. The burden of musculoskeletal disorders in the countries of the Eastern Mediterranean region of the World Health Organization (EMRO): Study period 2000-2017. [Internet]. 2021. Available from: <https://doi.org/10.21203/rs.3.rs-144165/v1>
- Yahaya I, Wright T, Babatunde OO, Cprp N, Helliwell T, Dikomitil L, et al. Prevalence of osteoarthritis in lower middle-and low-income countries: a systematic review and meta-analysis. *Rheumatol Int*. 2021;41(7):1221-31.
- Turkiewicz A, Petersson IF, Björk J, Hawker G, Dahlberg LE, Lohmander LS, et al. Current and future impact of osteoarthritis on health care: a population-based study with projections to year 2032. *Osteoarthritis Cartilage*. 2014;22(11):1826-32.
- Jamshidi A, Kianifard T, Ghorpade R, Shayan M, Mahmoudi M, Chopra A. THU0708 Disparity in osteoarthritis knee prevalence-a tale of two cities in iran (TEHRAN) and india (PUNE): findings from who ilar copcord population survey (STAGE I). *Ann Rheum Dis*. 2018;77(2):546.
- Conaghan PG, Porcheret M, Kingsbury SR, Gammon A, Soni A, Hurley M, et al. Impact and therapy of osteoarthritis: the Arthritis Care OA Nation 2012 survey. *Clin Rheumatol*. 2015;34(9):1581-8.
- Nishigami T, Tanaka S, Mibu A, Imai R, Wand BM. Knee-related disability was largely influenced by cognitive factors and disturbed body perception in knee osteoarthritis. *Sci Rep*. 2021;11(1):5835.
- Cai X, Yuan S, Zeng Y, Wang C, Yu N, Ding C. New Trends in Pharmacological Treatments for Osteoarthritis. *Front Pharmacol*. 2021;12:645842.
- Mahir L, Belhaj K, Zahi S, Azanmasso H, Lmidmani F, El Fatimi A. Impact of knee osteoarthritis on the quality of life. *Ann Phys Rehabil Med*. 2016;59(Supplement):e159.
- Arthritis Foundation. Osteoarthritis. [Internet]. 2022. Available from: <https://www.arthritis.org/diseases/osteoarthritis>
- Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. *JAMA*. 2021;325(6):568-78.
- Ariana M, Afrasiabifar A, Najafi Doulatabad S, Mosavi A, Behnammoghadam M. The Effect of Local Heat Therapy versus Cold Rub Gel on Pain and Joint Functions in Patients with Knee Osteoarthritis. *Clin Nurs Res*. 2022;31(6):1014-22.
- Richardson C, Plaas A, Block JA. Intra-articular hyaluronan therapy for symptomatic knee osteoarthritis. *Rheum Dis Clin North Am*. 2019;45(3):439-51.
- Gao SH, Huo JB, Pan QM, Li XW, Chen HY, Huang JH. The short-term effect and safety of

- duloxetine in osteoarthritis: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2019;98(44):e17541.
18. Chen AT, Shrestha S, Collins JE, Sullivan JK, Losina E, Katz JN. Estimating contextual effect in nonpharmacological therapies for pain in knee osteoarthritis: a systematic analytic review. *Osteoarthritis Cartilage*. 2020;28(9):1154-69.
19. Żęgota Z, Goździk J, Głogowska-Szeląg J. Efficacy of herbal and naturally derived dietary supplements for the management of knee osteoarthritis: A mini-review. *Wiad Lek*. 2021;74(8):1975-83.
20. Block JA, Cherny D. Management of Knee Osteoarthritis: What Internists Need to Know. *Med Clin North Am*. 2021;105(2):367-85.
21. Stansbury J. Rosmarinic acid as a novel agent in the treatment of allergies and asthma. *Journal of restorative medicine*. 2014;3(1):121-6.
22. Tahoonian-Golkhatmy F, Abedian Z, Emami SA, Esmaily H. Comparison of rosemary and mefenamic acid capsules on menstrual bleeding and primary dysmenorrhea: A clinical trial. *Iran J Nurs Midwifery Res*. 2019;24(4):301-5.
23. de Macedo LM, Santos ÉMd, Militão L, Tundisi LL, Ataíde JA, Souto EB, et al. Rosemary (*Rosmarinus officinalis* L., syn *Salvia rosmarinus* Spenn.) and Its Topical Applications: A Review. *Plants (Basel)*. 2020;9(5):651.
24. González-Trujano ME, Peña EI, Martínez AL, Moreno J, Guevara-Fefer P, Déciga-Campos M, et al. Evaluation of the antinociceptive effect of *Rosmarinus officinalis* L. using three different experimental models in rodents. *J Ethnopharmacol*. 2007;111(3):476-82.
25. Ghannadi A, Karimzadeh H, Tavakoli N, Darafsh M, Ramezanloo P. Efficacy of a combined rosemary and lavender topical ointment in the treatment of patients with osteoarthritis of the knee. *Zahedan J Res Med Sci*. 2013;15(6):29-33.
26. Mohammadifar M, Talaei SA, Vakili Z, Bahmani F, Memarzadeh MR, Aarabi MH. Evaluating antinociceptive effect of nano-emulsion gel containing rosemary and peppermint essential oils in a rat model of osteoarthritis. *Scientific J Kurdistan Univ Med Sci*. 2018;23(4):100-9.
27. Lukaczer D, Darland G, Tripp M, Liska D, Lerman RH, Schiltz B, et al. A Pilot trial evaluating meta050, a proprietary combination of reduced iso-alpha acids, rosemary extract and oleanolic acid in patients with arthritis and fibromyalgia. *Phytother Res*. 2005;19(10):864-9.
28. Rosenbaum CC, O'Mathána DP, Chavez M, Shields K. Antioxidants and antiinflammatory dietary supplements for osteoarthritis and rheumatoid arthritis. *Altern Ther Health Med*. 2010;16(2):32-40.
29. Scalfo F, Davis S, Lai A, Karsdal M, Offord E, Ameye LG. Rosemary extract slows down cartilage degeneration in bovine articular cartilage explants. *J Hum Nutr Diet*. 2009;22(3):270.
30. Horcajada M-N, Sanchez C, Scalfo F, Ameye L, Henrotin Y, Offord E. 071 Effect of Rosemary Extract and Related Flavonoid Carnosol on Chondro-Protection and on the Bone-Cartilage Crosstalk. *Osteoarthritis Cartilage*. 2010;18(2):S38-9.
31. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum*. 1986;29(8):1039-49.
32. Setoodehzadeh F, Khammarnia M, Peyvand M. Health Integrated System in Iran: Opportunities and Constraints. *J Health Sci Surveill Syst*. 2021;9(3):206-7.
33. McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. *Arthritis Rheum*. 2001;45(5):453-61.
34. Guo Y, Xie J, Li X, Yuan Y, Zhang L, Hu W, et al. Antidepressant Effects of Rosemary Extracts Associate With Anti-inflammatory Effect and Rebalance of Gut Microbiota. *Front Pharmacol*. 2018;9:1126.
35. Mohammadifar M, Aarabi MH, Aghighi F, Kazemi M, Vakili Z, Memarzadeh MR, et al. Anti-osteoarthritis potential of peppermint and rosemary essential oils in a nanoemulsion form: behavioral, biochemical, and histopathological evidence. *BMC Complement Med Ther*. 2021;21(1):57.
36. Elbarnasawy AS, Valeeva ER, El-Sayed EM, Rakhimov II. The Impact of Thyme and Rosemary on Prevention of Osteoporosis in Rats. *J Nutr Metab*. 2019;2019:1431384.
37. Barão Paixão VL, Freire de Carvalho J. Essential oil therapy in rheumatic diseases: A systematic review. *Complement Ther Clin Pract*. 2021;43:101391.