

# Effects of aromatherapy on pain in patients with musculoskeletal disease: A systematic literature review

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## Abstract

**Background/Objectives:** The purpose of this systematic review was to examine aromatherapy interventions for patients with musculoskeletal diseases, and to determine the effectiveness of these interventions on patients' pain.

**Methods/Statistical analysis:** Six national and international databases were reviewed to retrieve and collect literature, published up to March 4, 2020, describing randomized controlled trials (RCTs) and clinical controlled trials (CCTs) of aromatherapy interventions for patients with musculoskeletal diseases. Two reviewers independently selected the studies and performed data abstraction and validation.

**Findings:** Of a total of 11 analyzed articles, 3 articles whose effect size was analyzable were analyzed for the effect size of aromatherapy on pain in patients with musculoskeletal disease. Compared with a control group receiving no treatment, the pain score was reduced by 2.09 points (MD=-2.09; 95% CI -2.72 to -1.46), there was a statistically significant difference in effect size between the experimental and control groups ( $Z=6.52$ ,  $p<.001$ ), and there was no heterogeneity between the groups (Higgin's  $I^2=0\%$ ). And it was found that musculoskeletal pain and fatigue were significantly reduced in the experimental group receiving massage with aroma oils, and that daily life was easier.

**Improvements/Applications:** This study analyzed the effects of aromatherapy on pain in patients with musculoskeletal disease through a meta-analysis, and demonstrated that aromatherapy had an alleviating effect on pain and fatigue.

**Keywords:** aromatherapy, musculoskeletal disease, pain, systematic review

## 1. Introduction

Musculoskeletal disease is one of the major causes of disease burden worldwide, and results in major consequences for individuals and society. Its prevalence is high especially among elderly people [1, 2]. A typical aging-associated musculoskeletal disease is osteoarthritis, which is the most common disease causing damage and pain in joint function. The prevalence of hip osteoarthritis in elderly people was 3-8%, and the prevalence of knee osteoarthritis was 14-30%, accounting for a greater proportion [3]. The Korea Centers for Disease Control and Prevention (Korea CDC) disclosed that the prevalence of osteoarthritis in adults aged 50 years or older in South Korea was 12.5% with 5.1% in male adults and 18.9% in female adults. In particular, it was reported that 3 out of 10 women (36.1%) aged 70 years or older had osteoarthritis, and that knee osteoporosis was the most common [4]. According to the national health insurance statistics in 2017, the number of patients with arthrosis of knee who visited hospitals every year reached approximately 3.7 million, and the related medical expenses amounted to approximately KRW 1.6 trillion, posing a serious health problem with a large socioeconomic disease burden. [5].

Rheumatoid arthritis is less common than osteoarthritis, but it is a chronic autoimmune disorder in which inflammations occur in joints and surrounding tissues, and can invade the entire body system, and thus has a greater impact on individuals [6]. In addition, the most common types of musculoskeletal system diseases

include fibrous tumor syndrome characterized by extensive pain and tenderness in joints, muscles, and other soft tissues, chronic low back pain, and trauma [7].

Impaired musculoskeletal health can cause a number of problems, and its most common symptoms include acute and chronic pain, leading to functional limitations and disability [2, 8, 9]. These impairments can affect the overall quality of life in the long term [10]. The treatment of musculoskeletal disease involves mainly pain relief, and includes not only medical treatments such as medications or surgery, but also non-pharmaceutical treatments such as massage, aromatherapy, hot and cold therapy, exercise, aquatic therapy and educational programs, and physical therapy such as ultrasound therapy [11]. However, since pharmacological treatments and surgery have many side effects, and are expensive [12], complementary treatment methods, which are inexpensive and easily accessible with minimal side effects, can be helpful [12].

Aromatherapy has been used historically for various purposes, including medical purposes in the various forms of massage, inhalation, and bathing. In addition, aroma oils can be easily used by anyone in general public places, and have potential therapeutic properties, thus providing positive effects to users. In particular, many essential oils used in aromatherapy are reported to have anti-inflammatory, relaxation, anti-microbial, anti-stress, anti-depressant, and immunity enhancing effects [13].

For this reason, studies involving various subjects have been reported to measure the effects of aroma essential oils on various health problems using various techniques. Studies have reported that massage using aroma oils had positive effects on pain reduction in patients with knee osteoarthritis and rheumatoid arthritis [14, 15], and a study reported that massage with aroma oils was effective in reducing pain, depression, anxiety, and stress levels in community-dwelling elderly people [16].

However, the types of aroma oils are very diverse, and aroma oil blends are often used [13]. In addition, because there are differences in intervention modality and duration between previous studies, there are limitations to applying the results of such studies to actual clinical practice.

In this regard, this study aimed to investigate the effects of aromatherapy on pain in patients with musculoskeletal disease, and analyze the difference in its effects according to intervention modality through a systematic literature review of related articles, and provide a basis for using aromatherapy in patients with musculoskeletal disease in nursing practice.

## **2. Methods**

### **2.1. Study Design**

This study is a systematic literature review of experimental studies regarding the effects of aromatherapy on pain in patients with musculoskeletal disease. This study was conducted after submitting the research proposal to the Institutional Review Committee (IRB) at Konyang University, and receiving approval of IRB exemption (KYU-2019-358-01).

### **2.2. Search strategy**

The PICO (Patients, Intervention, Comparator, Outcome, Study design), specific questions for systematic literature review, are as follows:

#### 1) Patients

The subjects of this study were patients with musculoskeletal disease.

#### 2) Intervention

Studies using aromatherapy were selected for this study. Aromatherapy is a complementary and alternative therapy that uses the extracts of aromatic plants or essential oils to be absorbed into the body through the skin or respiratory tract.

#### 3) Comparator

As a comparator in this study, a control group who received aromatherapy was selected and analyzed.

#### 4) Outcome

The outcome was to determine the effects of aromatherapy on musculoskeletal system. Pain was selected as the primary outcome, and fatigue associated with musculoskeletal diseases was selected as the secondary outcome for analysis.

### **2.3. Literature review, data collection, and screening procedures**

#### **2.3.1. Literature review**

A literature search was conducted to identify all related articles that were searchable before March 4, 2020. The international databases used for the search included the Pubmed, CINAHL, and Cochrane Central Register of Controlled Trials (CENTRAL), and the domestic databases for searching related domestic articles included the Research Information Service System (RISS), Korean Studies Information Service System (KISS), and DBpia. The search formula was made based on MeSH (medical subject headings) terms and text words with appropriate use of the Boolean operators AND/OR and truncation. For intervention modalities, all articles using the terms 'aroma\*', 'aromatherapy [MeSH]', 'Oils, Volatile [MeSH]', and 'essential oil' were retrieved. For searching for subjects, the articles using "Musculoskeletal [MeSH]" were retrieved. In order to increase the sensitivity of the literature, the outcomes were not limited. In summary, the search formula was '(aroma\* OR aromatherapy [MeSH] OR Oils, Volatile [MeSH] OR essential oil) AND Musculoskeletal [MeSH]'. Since aromatherapy is also being used as the term '*hyanggi*' therapy in South Korea, we searched the domestic databases in the same way by using the conceptual words such as aroma, aromatherapy, '*hyanggi*' therapy, aroma oil, musculoskeletal system, and arthritis.

#### **2.3.2. Data collection and screening**

A The article selection criteria for a systematic analysis are as follows. (1) Aromatherapy intervention studies involving patients with musculoskeletal disease, (2) randomized controlled trials (RCTs) and nonrandomized controlled clinical trials (CCTs), (3) articles published in academic journals, and (4) studies published in Korean and English was included.

The exclusion criteria are as follows: (1) studies in which aroma oils were not absorbed into the body through the skin or respiratory tract, (2) animal studies or pre-clinical studies, (3) non-comparative studies, (4) unpublished dissertations, and (5) observational studies, and review articles.

In this study, the retrieved articles were selected based on the key questions, and selection and exclusion criteria. The flow chart of PRISMA was used to describe the status of the step-by-step literature selection process [17]. As a result of the literature search, 308 articles were retrieved from the Pubmed, and 106 articles from the CINAHL, 150 articles from the CENTRAL, 12 articles from the RISS, 11 articles from the KISS, and 10 articles from the DBPIA, totaling 597 retrieved articles. Two researchers reviewed the titles and abstracts of a total of 420 articles, excluding 177 duplicated articles, based on the key questions and selection and exclusion criteria. As a result, 27 articles, excluding 393 articles which were not related to the key questions, whose study design did not meet the selection criteria, or which were not published in Korean and English, were primarily selected.

As a result of reviewing the full texts of a total of 27 primarily selected articles according to the same criteria and process, a total of 11 articles were secondarily selected, excluding 6 studies whose study design did not meet the selection criteria, 6 studies that did not involve patients with musculoskeletal diseases, and 2 animal studies, and 2 studies in which the intervention modalities of using aroma oils did not meet the selection criteria. Among the controlled trials, 3 studies in which outcome variables included pain in patients with musculoskeletal disease and were presented as mean and standard deviation [Figure 1] were analyzed quantitatively using a meta-analysis [Figure 1].

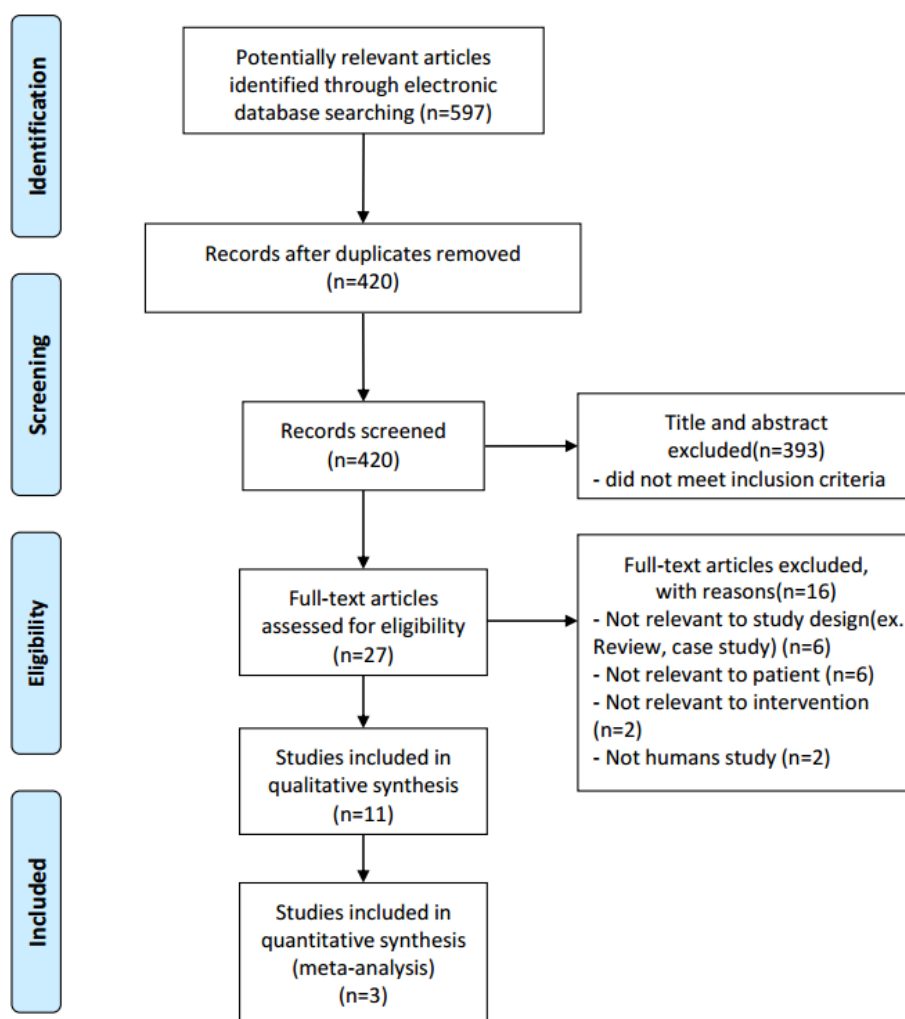


Figure 1. Study flow chart of study selection process.

### 2.3.3. Quality assessment of articles

In this study, a critical review of the articles was performed using the Cochrane Risk of Bias (RoB), a tool for assessing the quality of randomized controlled clinical trials, and the Risk of Bias Assessment Tool of Non-randomized Study (RoBANS), a tool for assessing the quality of non-randomized trials. As for the assessment method, the risk of bias for each quality assessment item was assessed as low, uncertain, and high. Two researchers independently evaluated the finally selected articles. If there was any item of disagreement between the researchers, they reached a consensus after listening to opinions from a third party researcher, and having sufficient discussion. The RoB, a tool for assessing the quality of randomized controlled clinical trials, consists of 7 items regarding random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. The RoBANS, a tool for assessing the quality of non-randomized trials, consists of 6 items regarding selection of participants, confounding variables, measurement of intervention, blinding of outcome assessment, incomplete outcome data, and selective reporting.

### 2.3.4. Data analysis

The systematic confirmation, data synthesis, merging statistics, and outcome reporting of the selected articles were analyzed based on the Cochrane guidelines [17], and the effect size was analyzed by meta-

analysis

### **2.3.5. Data extraction**

After the characteristics of the 11 articles included in this systematic literature review were analyzed, they were coded and tabulated. The coded table consists of author, year of publication, study design and number of samples, intervention modalities for experimental and control groups, type of aroma oils, outcome variables, differences between groups, and author's conclusion

### **2.3.6. Selection of the analysis model**

In this study, the studies were analyzed using a fixed-effects model, if there is no heterogeneity in intervention methods, time, and duration between the studies, whereas the studies were analyzed using a random-effects model if it was judged that there was a heterogeneity between the studies. The random-effects model is based on the premise that the true values of the effects can vary greatly depending on sampling and individual studies, and on the assumption that the difference in the effect size of each study is due to sampling error and between-study variation. Therefore, this model is used when there is evidence that there is an inexplicable heterogeneity between studies. In addition, this random-effects model is used when studies cannot be assumed to be homogeneous even if there is a low heterogeneity between the studies

### **2.3.7. Effect size calculation**

The effect size of this study was analyzed by means and standard deviation because the characteristics of the described outcome variables were continuous variables. When the same outcome was measured using the same measurement tool, the mean difference (MD) was calculated using the final mean value of each experimental group and each control group. When the same outcome was measured using different measurement tools, the standardized mean difference (SMD) was calculated. The effect of each outcome variable and the 95% confidence interval (95% CI) were analyzed using the inverse variance method

### **2.3.8. Heterogeneity test**

Heterogeneity refers to the difference that appears due to diversity between individual studies to be integrated in a meta-analysis. There are two ways to determine the presence or absence of heterogeneity is a visual method of confirming the common part of the confidence intervals and effect estimates between studies using the forest plot in the meta-analysis, and a method of confirming statistical values. The  $I^2$  is a representative value in testing heterogeneity using statistical values. In this study, the heterogeneity between studies was evaluated by Higgins  $I^2$ -statistic. When the  $I^2$  value was 25%, 50% and  $\geq 75\%$ , it is judged that the heterogeneity was low, moderate, and high, respectively

### **2.4. Publication bias test**

Publication bias refers to a bias that appears when there is a relationship between the statistical significance of study results and a possibility of publication. The propensity and characteristics of publishing process can lead to a result that the results of a meta-analysis, which is to reanalyze published study results, may be estimated to be larger than the actual ones. To test publication bias in this study, it was visually assessed using a funnel plot. The funnel plot refers to a visually drawn dot plot by setting an estimate of intervention effects, such as odds ratio or relative risk, obtained from each study on the horizontal axis, and the reciprocal number of standard error representing the precision of an estimation or the number of study samples on the vertical axis. The possibility of publication bias decreases when the funnel plot is visually symmetric, whereas the possibility of publication bias increases when the funnel plot is visually asymmetric.

## **3. Results**

### **3.1. General characteristics of the systemically reviewed articles**

The characteristics of 11 articles [18-28], which were included in the systematic literature review according to the article selection and exclusion criteria in this study, are as follows [Table 1, 2].

The study subjects included in the analysis were adults and elderly people with musculoskeletal health problems in 4 randomized controlled trials [18, 24, 27, 28], and 7 controlled clinical trials [19-23, 25, 26]. In terms of aromatherapy intervention modalities used, there were 8 aromatherapy massage modalities by which aroma oils are to be absorbed through the skin, 1 hot pack aromatherapy, 1 ultrasound aromatherapy, and 1 aromatherapy for nasal absorption. The types of aroma oils used varied; the number of studies regarding aromatherapy using lavender oil was the highest with 10 studies, followed by 5 studies using rosemary oil, 3 studies using peppermint oil, 3 studies using chamomile oil, and 3 studies using juniper oil, and other studies using ylang-ylang, bergamot, Jasmin, eucalyptus, ginger, clary sage or marjoram oils. There were 9 studies using aroma oil blends [18, 19, 21-23, 25-28], and 2 studies using a single aroma oil [20, 24], and the aroma oil used in the studies using a single aroma oil was lavender. In terms of intervention time, the massage modality took 5-20 minutes, the ultrasound aromatherapy took 5 minutes, and the inhalation modality took 45 minutes. The duration of intervention was mostly 2-4 weeks. The ultrasound aromatherapy was performed 6 times, and the inhalation aromatherapy was performed 3 times. In 10 studies included in the analysis, pain was measured to examine the effects of aromatherapy using the visual analogue scale (VAS) and the WOMAC (Western Ontario and McMaster Universities OA Index), and joint function, fatigue, depression, sleep, and so on were measured.

### **3.2. Quality assessment of articles**

In this study, two researchers assessed the quality of the selected articles using Cochrane risk of bias assessment tools such as the RoB and the RoBANS [Figure 2].

#### **3.2.1. RoB (Risk of Bias)**

The items with a high risk of bias included items regarding random sequence generation and allocation concealment, and its high risk of bias for the random sequence generation and allocation concealment items was found in 1 study (15%) and 1 study (15%), respectively. The risk of bias for the blinding of participants and personnel item was low in 2 studies (50%), whereas its risk was not mentioned in 2 studies, so that it could not be determined. In addition, the risk of bias for the incomplete outcome data, selective reporting items, and other bias items was low [Figure 2-A-1]. Looking at each study [Figure 2-A-2], each study had no more than one item with a high risk of bias, and thus all four studies were included in the analysis

#### **3.2.2. RoBANS (Risk of Bias Assessment tool of Non-randomized Study))**

The item with a high risk of bias included the blinding of outcome assessment item, which was found to be high in 3 studies (42.9%), whereas its risk was not mentioned in 2 studies (28.6%), and it could thus not be determined. In addition, the confounding variable item was not mentioned in 1 study, and the risk of bias for other items regarding selection of participants, measurement of intervention, incomplete outcome data, and selective reporting [Figure 2-B-1] was low. Looking at individual studies [Figure 2-B-2], each study had no more than one item with a high risk of bias, and 7 studies were thus included in the analysis

### **3.3. Publication bias**

In this study, there were 3 studies included in the meta-analysis. An interpretation of whether or not the funnel plot was asymmetric was not feasible based on evidence [29] that it is applicable only when the number of included studies is more than 10.

### **3.4. Effects of aromatherapy on pain among patients with musculoskeletal diseases**

Of a total of 11 analyzed articles, 3 articles whose effect size was analyzable were analyzed for the effect size of aromatherapy on pain in patients with musculoskeletal disease [Figure 3].

There were a total of 9 studies measuring pain, consisting of 3 RCTs and 6 CCTs. However, in view of the fact that an effect size cannot be calculated by combining the RCTs and CCTs, the effect size for the 3 RCTs was calculated. The results of investigating the homogeneity between the 3 studies revealed that they were not homogeneous in the experimental treatment. Therefore, the effect size of pain was analyzed using a random-effects model. Compared with a control group receiving no treatment, the pain score was reduced by 2.09 points (MD=-2.09; 95% CI -2.72 to -1.46), there was a statistically significant difference in effect size between the experimental and control groups ( $Z=6.52$ ,  $p<.001$ ), and there was no heterogeneity between the groups (Higgin's  $I^2=0\%$ )

**Table 1. Summary of Randomized Controlled Trials examining Aromatherapy in Musculoskeletal patients**

First author (years)	Study design Sample size age	Intervention group(regime)	Control group (regime)	Aromatherapy	Main outcome measures	Intergroup difference	Author's conclusion
Gok Metin, 2016	RCT 51 adults with rheumatoid arthritis	(A) aroma massage (n=17)	(B) Reflexology (n=17) (C) No treatment (n=16)	Lavender, Juniper, Ylang-ylang, Rosemary (3:3:2:2) (A) Duration 15min(Rt/Lt), 3times/week, 6weeks (B) Duration 20min(Rt/Lt), 1time/week, 6weeks	(1) Pain-VAS (2) Fatigue-FSS	(1) $p=.001$ (2) $p=.001$	"Aromatherapy massage and reflexology are simple and effective non-pharmacologic nursing interventions that can be used to help manage pain and fatigue in patients with rheumatoid arthritis."
Nasiri, 2018	RCT 80 adults with knee osteoarthritis	(A) aroma massage (n=27)	(B) almond oil massage(n=27) (C) No treatment (n=26)	Lavender Duration 20min, 9times, 3weeks	(1) ADL- WOMAC	(1)-1. immediately $p<.001$ (1)-2. after 1week $p<.01$ (1)-3. after 4week NS	"Aromatherapy massage with lavender essential oil may reduce the incidence of activities of daily living disability in patients with osteoarthritis of the knee."
Park, 2017	RCT 53 elderly women with total knee arthroplasty	(A) aroma inhalation (n=26)	(B) No treatment (n=27)	Bergamot, Lavender, Jasmine (5:3:2) Duration 45min,	(1) Pain-VAS (2) Anxiety-NRS (3) Anxiety-BP	(1) $p<.001$ (2)-1. 1 <sup>st</sup> $p<.001$ (2)-2. 2 <sup>nd</sup>	"Aroma inhalation was effective in decreasing pain and anxiety and changing HRV among



					1time/day, 3days	(4) HRV-SNS (5) HRV-PNS (6) Heart rate	$p<.01$ (2)-3. $p<.001$ (3) SBP $p<.001$ (4) $p<.01$ (5) NS (6) $p<.05$	elderly women with TKA during CPM exercise.”
Won, 2011	RCT 42 adults with knee osteoarthritis	(A) aroma massage (n=21)	(B) No treatment (n=21)	No	Peppermint, Eucalyptus, Rosemary (5:2:3) Duration 20min, 1time/day, 2days/week, 4weeks	(1) Pain-VAS (2) Sleep (3) Stride length(cm)	(1) $p=.001$ (2) NS (3) $p<.01$	“Aromatherapy massage could be recommended as an effective intervention to decrease pain and to increase stride length in the elderly with knee osteoarthritis.”

VAS=Visual Analogue Scale; FSS=Fatigue Severity Scale; ADL= Activities of Daily Living; WOMAC = Western Ontario and McMaster Universities OA Index; HRV=Heart Rate Variability; SNS=Sympathetic Nerve System

**Table 2. Summary of Clinical Controlled Trials examining Aromatherapy in Musculoskeletal patients**

First author (years)	Study design Sample size age	Intervention group(regime)	Control group (regime)	Aromatherapy	Main outcome measures	Intergroup difference	Author’s conclusion
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Han (2010)	CCT 43 adults with rheumatoid arthritis	(A) aroma massage (n=24)	(B) treatment (n=19)	No	Chamomile, Rosemary, Juniper, Lavender, Ginger (1:1:1:1:1) Duration 5min, 1time/day, 4-weeks	(1) Pain-VAS (2) Inflammatory response- Tender joint count (3) Inflammatory response- Swollen joint count (4) Inflammatory response-ESR	(1) $p<.05$ (2) $p<.05$ (3) $p<.05$ (4) NS	“These findings joint suggest that aromatherapy could decrease pain, tenderness, and swelling in patients with rheumatoid arthritis...”
Hwang (2011)	CCT 45 elderly with osteoarthritis	(A) aroma heat(45°C) therapy (n=21)	(B) treatment (n=24)	No	Lavender Duration 20min, 3time/day, 3-weeks	(1) Pain-VAS (2) Knee flexibility- goniometer (3) Sleep-QOS (4) Depression-	(1) $p=.001$ (2) $p<.001$ (3) $p<.05$ (4) $p<.05$	“Heat therapy combined with aromatherapy may be an effective nursing intervention and self- care technique to ameliorate pain and depression and to improve flexibility and sleep in elderly suffering from osteoarthritis.”
Kim (2009)	CCT 41 adults with knee osteoarthritis	(A) aroma massage (n=20)	(B) almond oil massage (n=21)		Lavender, Chamomile, Ginger (2:1:1)	(1) Pain-GRS (2) Pain- WOMAC	(1) $p<.001$ (2) $p<.001$ (3) $p<.001$	“Based on these results, aroma massage could be recommended as a self-

						Duration 5~10min, 2time/day, 2weeks	(3) ADL- WOMAC (4) Fatigue-MAF	(4) $p<.01$	managed intervention for the patients with knee osteoarthritis."
Kim (2013)	CCT 62 elderly women with osteoarthritis	(A) aroma foot reflex (n=31)	(B) No treatment (n=31)			Lavender, Bergamot, Clary Sage (1:1:1) Duration 40min, 3time/week, 2weeks	(1) Depression- POMSB (2) Vigor- POMSB (3) Fatigue- POMSB (4) Tension- POMSB (5) Anger- POMSB	(1) $p<.05$ (2) $p<.05$ (3) $p<.05$ (4) NS (5) NS	"Aroma foot reflexology massage can be utilized as an effective intervention to decrease depression of mood states, increase of $\alpha$ , and $\beta$ brain wave on woman elderly with osteoarthritis."

ESR=Erythrocyte sedimentation rate; QOS=Quality of Sleep; GRS=Graphic Rating Scale; WOMAC=Western Ontario and McMaster Universities OA Index; MAF=Multidimensional Assessment of Fatigue; POMS-B=Profile of Mood States-Brief

(continued)

**Table 2. Summary of Clinical Controlled Trials examining Aromatherapy in Musculoskeletal patients**

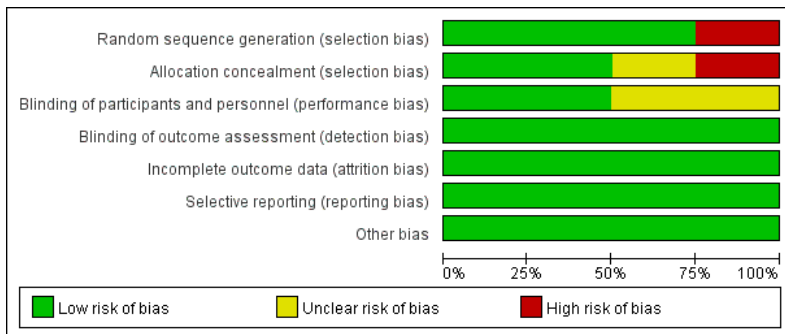
First author (years)	Study design Sample size age	Intervention group(regime)	Control group (regime)	Aromatherapy	Main outcome measures	Intergroup difference	Author's conclusion
Kim, 2005	CCT 40 adults with osteoarthritis or rheumatoid arthritis	(A) aroma massage (n=20)	(B) No treatment (n=20)	Lavender, Marjoram, Eucalyptus, Rosemary, peppermint	(1) Pain-VAS (2) Depression- CESD (3) Life satisfaction	(1) $p=.05$ (2) $p<.05$ (3) NS	"The result of this study clearly shows that aromatherapy has major effects on decreasing pain and depression

					(2:1:2:1:1) Duration 10~15min, 2time/day, 4weeks			levels”
Park, 2008	CCT 58 adults with rheumatoid arthritis	(A) aroma massage + heat therapy (n=19) (B) aroma massage (n=20)	(C) No treatment (n=19)	No	Lavender, Rosemary, Peppermint, Juniper berry (5:3:3:2) Duration 20min, 3times/week, 4weeks	(1) Pain(knee)- VAS (2) Pain(ankle)- VAS (3) ROM- goniometer (4) ADL	(1) $p<.001$ (2) $p<.001$ (3) $p<.001$ (4) $p<.001$	“On the basis of results, aroma-therapy can be applied as a nursing intervention to reduce pain for not only rheumatoid arthritis patients but also for other patients with other diseases.”
Park, 2005	CCT 90 women with shoulder pain	(A) aroma + U/S (n=30) (B) aroma (n=30)	(C) U/S (n=30)		Chamomile, Marjoram, Lavender (1:2:3) Duration 5min, 6times	(1) Pain-VAS (2) Pain-McGill (3) Pain- Algometer	(1) $p<.001$ (2) $p<.001$ (3) $p<.001$	“...it has been found out that Aromatic oil has bigger effect on McGill and visual pain scale examining subjective and emotional pains, but that it has less effect on the algometer value examining the threshold of algometer increasing from tissue recovery...”

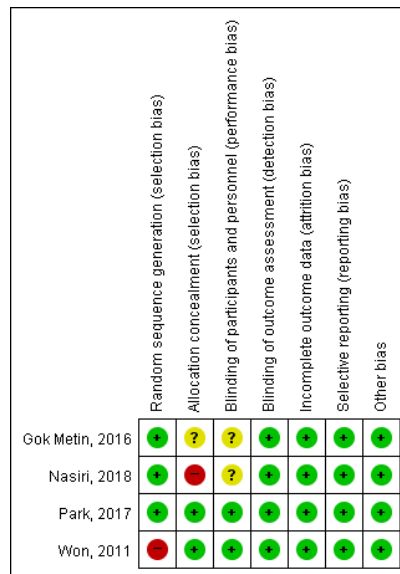
CESD=Centers for Epidemiologic Studies Depression; ROM=Range of Motion; ADL=Activities of Daily Living; U/S=Ultra-Sound



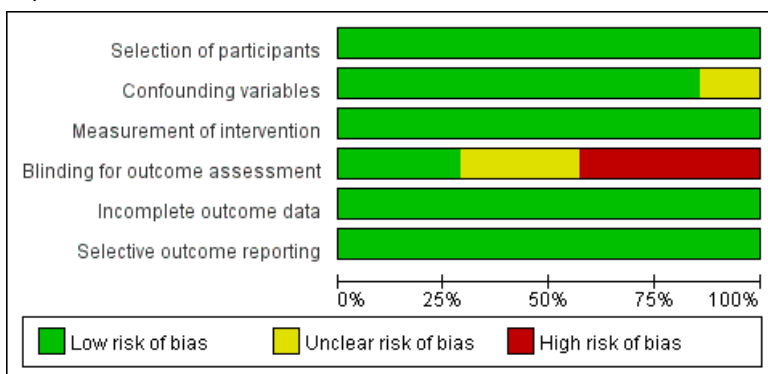
A-1)



A-2)



B-1)



B-2)

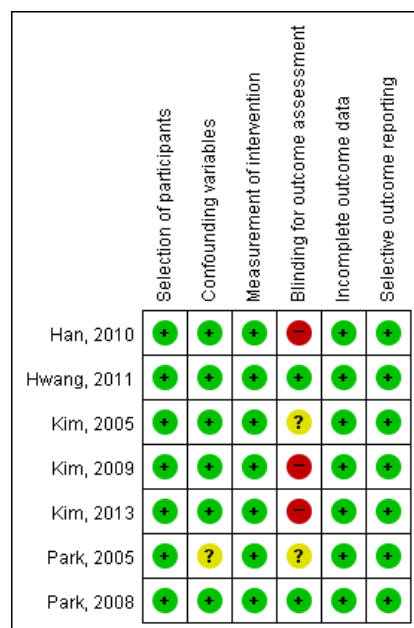
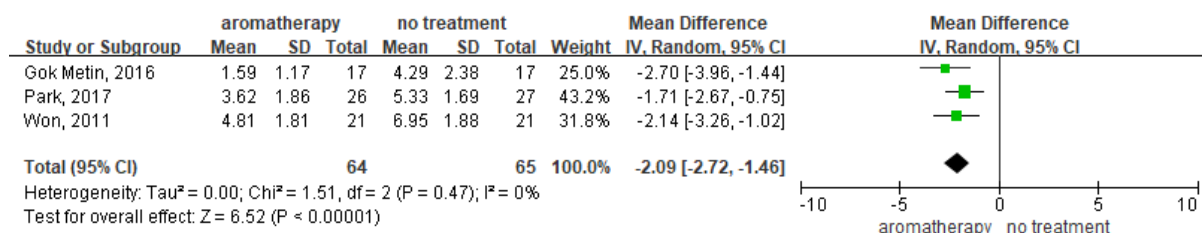


Figure 2. Reviewing authors' judgements about each risk of bias item presented as percentages across all included studies. (A) RoB 1) Risk of bias graph, 2) risk of bias summary and (B) RoBANS 1) Risk of bias graph, 2) risk of bias summary.



**Figure 3. Funnel plot of standard error by standardized mean difference: aromatherapy versus No treatment outcome, pain**

**SMD=standardized mean difference; SE=standard error**

**4. Discussion**

This study conducted a systematic literature review aimed at investigating the effects of aromatherapy on pain, fatigue, sleep, and daily life in patients with musculoskeletal disorders. Based on a total of 11 articles on experimental studies that were obtained as a result of the literature search, a systematic review of aromatherapy intervention contents, modalities, and outcome were conducted, and then the effects of aromatherapy on pain reduction was analyzed through a meta-analysis. Looking at the intervention modalities in the 11 articles included in this analysis, the number of articles on aromatherapy massage modality was the highest with 8 articles, and the massage area was the site of musculoskeletal disease. As the other intervention modalities, inhalation, hot pack, and ultrasonic aromatherapy modalities were used in 3 articles. In terms of aroma oils, 12 aromatic oils were used alone or in blends, of which lavender was the most commonly used. Aromatherapy can be seen to have overall positive effects on pain and fatigue as the outcome variables in this study, supporting the common sense that aroma oils are effective for various health problems [13, 30].

A meta-analysis was performed with 3 studies measuring pain among RCT-related articles. In comparison with the control group receiving no treatment, musculoskeletal pain was found to be significantly reduced in the experimental group receiving aromatherapy. The aroma oils used in the studies included in the meta-analysis included lavender, rosemary, juniper, ylang-ylang, bergamot, jasmine, peppermint, and eucalyptus oils, and aroma oil blends were used in all the 3 studies. Among them, lavender has been reported to help to balance and harmonize our body, and have antispasmodic and analgesic effects [13, 31]. In addition, rosemary, juniper, peppermint, and ylang-ylang are known to have the effects of reducing pain perception. In addition, rosemary is effective in promoting circulation and relieving fluid retention, juniper has the effects of promoting toxin removal, and peppermint has sedative effects [13, 31]. Such effects seem to contribute to relieving pain in patients with musculoskeletal disease. However, it was reported that the effects of aroma oils may vary depending on how aroma oils are blended even if the same types of aroma oils are used, and using 2 to 3 aroma oil blends rather than using a single aroma oil has a synergistic effect that can maximize the efficacy of aroma oils [32]. Therefore, studies regarding rationale for aroma oil selection, blending, application modalities, and time are needed to present standardized protocols. Among aromatherapy modalities using aroma essential oils, massage using aroma essential oils is assumed to have the effects of massage itself. Therefore, we tried to review the results of studies involving a placebo group, but no RCT-related article was identified, and an effect size was not analyzable, accordingly. However, there was a CCT-related article comparing with a placebo group receiving almond oil massage [21], and the analysis results showed that there was a statistically significant differences in pain, fatigue, and daily life scores between the two groups. In other words, it was found that musculoskeletal pain and fatigue were significantly reduced in the experimental group receiving massage with lavender, chamomile, and ginger oils, and that daily life was easier. Such effects are thought to relieve pain and inflammation of the joints in patients with musculoskeletal disease, thereby having positive effects on their daily life and having effects on fatigue, considering the results of a study indicating that azulene, a major component of chamomile, had anti-inflammatory effects [33], and the results of a study indicating that ginger extract had anti-inflammatory, analgesic and antipyretic effects [34].

The results of this study is significant in that it verified the effects of aromatherapy on pain in patients with musculoskeletal disease in a more integrated and scientific way through a systematic literature review and meta-analysis of individual controlled studies using aromatherapy in patients with musculoskeletal disease. However, because the number of randomized studies included in this study was very small and

non-equivalence control studies were also included, a possibility of bias in randomization and blinding-related areas was high in terms of the quality of the literature. In addition, the number of studies used for the meta-analysis was very small, which is also a limitation of this study, suggesting that rigorous experimental studies are needed in the future.

The aromatherapy modalities identified during this study were diverse, and such non-standardized intervention protocols are thought to be a barrier to being used as an effective nursing intervention in clinical practice despite the positive effects of aromatherapy as reported in many studies. In addition, almost all studies lacked evidence for pharmacological or causal relationships in the selection of aroma oils and also lacked the explanation of the mechanism of action. A lack of evidence for this mechanism or scientific backgrounds is thought to pose a problem in standardizing aromatherapy intervention protocols. Therefore, repetitive studies regarding aroma oils used for intervention, and duration of experimental treatment, and repetitive studies using control of exogenous variables, and strict control of experimental design are needed in the future. Resultantly, it is necessary to increase the level of related evidence through randomized controlled trials using standardized protocols.

## **5. Conclusion**

This study analyzed the effects of aromatherapy on pain in patients with musculoskeletal disease through a meta-analysis, and demonstrated that aromatherapy had an alleviating effect on pain and fatigue. Since only 4 out of the 11 studies included in the analysis were randomized controlled trials, and the remainders were non-equivalent controlled trials, there may be a certain risk of bias in the quality of the included literature itself. In addition, a lack of studies regarding the pharmacological mechanism of aromatherapy in humans and the resulting lack of standardized intervention protocols was found to be a problem. However, this study is significant in that it presented in an integrated way the outcome of studies regarding the effects of aromatherapy on pain in patients with musculoskeletal disease.

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## **7. References**

1. Brooks P. Musculoskeletal medicine: the challenge of the Bone and Joint Decade. *APLAR Journal of Rheumatology*. 2004;7(3):272-7.
2. Song J, Chang RW, Dunlop DD. Population impact of arthritis on disability in older adults. *Arthritis Care & Research: Official Journal of the American College of Rheumatology*. 2006;55(2):248-55.
3. Petersson IF, Jacobsson LT. Osteoarthritis of the peripheral joints. *Best Practice & Research Clinical Rheumatology*. 2002;16(5):741-60.
4. Woo K, Oh K. Prevalence of Osteoarthritis among Adults over 50 years old in Korea, 2010-2013. *Public Health Weekly Report*. 2015;8(4):82-4.
5. Kim Y-I, Kim ST. 2017 National health insurance statistical yearbook: National Health Insurance Service & Health Insurance Review & Assessment Service; 2017. p. 397-628
6. Palazzo C, Ravaud J-F, Papeard A, Ravaud P, Poiraudeau S. The burden of musculoskeletal conditions. *PLoS one*. 2014;9(3):e90633.
7. Bremander A, Bergman S. Non-pharmacological management of musculoskeletal disease in primary care. *Best Practice & Research Clinical Rheumatology*. 2008;22(3):563-77.



8. Björnsdóttir S, Jónsson S, Valdimarsdóttir U. Functional limitations and physical symptoms of individuals with chronic pain. *Scandinavian journal of rheumatology*. 2013;42(1):59-70.
9. Gatchel RJ. Musculoskeletal disorders: primary and secondary interventions. *Journal of Electromyography and Kinesiology*. 2004;14(1):161-70.
10. Park PW, Dryer RD, Hegeman-Dingle R, Mardekian J, Zlateva G, Wolff GG, et al. Cost burden of chronic pain patients in a large integrated delivery system in the United States. *Pain Practice*. 2016;16(8):1001
11. Connelly LB, Woolf A, Brooks P. Cost-effectiveness of interventions for musculoskeletal conditions. Washington DC: Oxford University Press; 2006. p. 963-80
12. Pagnano M, Westrich G. Successful nonoperative management of chronic osteoarthritis pain of the knee: safety and efficacy of retreatment with intra-articular hyaluronans. *Osteoarthritis and cartilage*. 2005;13(9):751-61.
13. Buckle J. *Clinical aromatherapy-e-book: Essential oils in practice*: Elsevier Health Sciences; 2014.
14. Metin ZG, Ozdemir L. The effects of aromatherapy massage and reflexology on pain and fatigue in patients with rheumatoid arthritis: a randomized controlled trial. *Pain Management Nursing*. 2016;17(2):140-9.
15. Nasiri A, Mahmodi MA, Nobakht Z. Effect of aromatherapy massage with lavender essential oil on pain in patients with osteoarthritis of the knee: A randomized controlled clinical trial. *Complementary therapies in clinical practice*. 2016;25:75-80.
16. Tang SK, Tse M. Aromatherapy: does it help to relieve pain, depression, anxiety, and stress in community-dwelling older persons? *BioMed research international*. 2014;2014:1-12.
17. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. *Cochrane handbook for systematic reviews of interventions*: John Wiley & Sons; 2019.
18. Gok Metin Z, Ozdemir L. The Effects of Aromatherapy Massage and Reflexology on Pain and Fatigue in Patients with Rheumatoid Arthritis: A Randomized Controlled Trial. *Pain Management Nursing*. 2016;17(2):140-9.
19. Han S, Nam E, Uhm D, Kim K, Paek S, Park S. Effects of aromatherapy on pain and inflammatory responses in patients with rheumatoid arthritis. *Journal of Muscle and Joint Health* 2010;17(1):25-34.
20. Hwang JH, Lee SO, Kim YK. Effects of thermotherapy combined with aromatherapy on pain, flexibility, sleep, and depression in elderly women with osteoarthritis. *Journal of Muscle and Joint Health*. 2011;18(2):192-202.
21. Kim I, Kim EK. Effects of aroma massage on pain, activities of daily living and fatigue in patients with knee osteoarthritis. *Journal of Muscle and Joint Health* 2009;16(2):145-53.
22. Kim IS, Yang HJ, Im ES, Kang HY. The effects of aroma foot reflex massage on mood states and brain waves in women elderly with osteoarthritis. *Korean J Adult Nur*. 2013;25(6):644-54.
23. Kim M-J, Nam E-S, Paik S-I. The effects of aromatherapy on pain, depression, and life satisfaction of arthritis patients. *Journal of Korean Academy of Nursing*. 2005;35(1):186-94.
24. Nasiri A, Mahmodi MA. Aromatherapy massage with lavender essential oil and the prevention of disability in ADL in patients with osteoarthritis of the knee: A randomized controlled clinical trial. *Complementary therapies in clinical practice*. 2018;30:116-21.
25. Park JE, Kim MA, Oh DH. The effect of aroma-therapy combined with heat application on the pain, range of motion of lower limb Joint, and discomfort of activities of daily living among patients with rheumatoid arthritis. *Korean J Adult Nur*. 2008;20(6):839-51.
26. Park KS, Han DW. The effects of aromatic oil on shoulder pain in the middle-aged woman patients. *The journal of Korean academy of physical therapist* 2005;12(4):11-24.
27. Park SY, Kim TI. The effects of aroma inhalation on pain, anxiety, and heart rate variability among elderly women with total knee arthroplasty during continuous passive motion exercise. *The Korean Data*

and Information Science Society. 2017;28(6):1383-402.

28. Won SJ, Chae YR. The effects of aromatherapy massage on pain, sleep, and stride length in the elderly with knee osteoarthritis. *Journal of Korean biological nursing science* 2011;13(2):142-8.
29. Kim S, Park J, Seo H, Lee Y, Jang B, Son H, et al. NECA's guidance for undertaking systematic reviews and meta-analyses for intervention. Seoul: National evidence-based healthcare collaborating agency. 2011. p. 173.
30. Umezu T. Anticonflict effects of plant-derived essential oils. *Pharmacology Biochemistry and Behavior*. 1999;64(1):35-40.
31. Battaglia S. *The complete guide to aromatherapy: International Centre of Holistic Aromatherapy*; 2003.
32. Lee H-J, Lee Y, Shin H, Song E, Son H, Kim I. Comparative analysis on the effects of abdominal massage using aroma oil and ordinary oil on nurses' dysmenorrhea and painful menstruation. *Clinical Nursing Research*. 2006;11(2):121-33.
33. Sakai H, Misawa M. Effect of Sodium Azulene Sulfonate on Capsaicin-Induced Pharyngitis in Rats. *Basic & clinical pharmacology & toxicology*. 2005;96(1):54-9.
34. Ali BH, Blunden G, Tanira MO, Nemmar A. Some phytochemical, pharmacological and toxicological properties of ginger (*Zingiber officinale* Roscoe): a review of recent research. *Food and chemical Toxicology*. 2008;46(2):409-20.