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REVIEW ARTICLE

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Alleviating severity of limb trauma pain with coadministration of topical sesame oil and standard treatments: A GRADE-assessed systematic review and meta-analysis of randomised controlled trials

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Abstract

Recent randomised controlled trials (RCTs) have investigated the analgesic activity of sesame oil among patients with limb trauma; nevertheless, their findings are inconsistent. Hence, this review aimed to clarify the impact of topical administration of sesame oil on acute pain of adult outpatients with minor limb trauma. The online databases (e.g., Scopus, PubMed, Web of Science) were searched up to 31 January 2024. The RCTs were included if they compared the effect of applying standard treatments plus topical sesame oil to administering standard treatments alone or with a placebo/sham treatment. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) and the Cochrane Collaboration's risk of bias tool were applied to address the evidence quality and the study's methodological rigour, respectively. Four RCTs had the inclusion criteria, and their findings were pooled in a meta-analysis employing a random-effects approach. According to the pooled analysis, the reduction in mean change of the pain score from baseline to the second/third intervention day was significantly higher in favour of clients who received standard care plus daily massage of the trauma site with sesame oil compared to those who received a control condition (weighted mean difference: −1.10; 95% confidence interval [−1.62, −0.57]; $p < 0.001$). However, the evidence quality was moderate, and only two studies had good methodological

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rigour. Hence, more high-quality studies are needed to make a solid evidence-based conclusion about the favourable consequence of topical sesame oil on alleviating acute traumatic limb pain.

KEYWORDS

acute pain, analgesics, meta-analysis, sesame oil, wounds and injuries

Key Messages

- This review sought to synthesise available randomised controlled trials regarding the impact of external administration of sesame oil on acute pain of adult outpatients with minor limb trauma.
- Based on the pooled analysis, standard care plus daily massage of the trauma area with topical sesame oil substantially reduced the pain severity in comparison with the control condition.
- Although the topical use of sesame oil seems an intriguing choice for alleviating the severity of limb trauma pain, more high-quality investigations are required to make a solid evidence-based decision.

1 | INTRODUCTION

Trauma is identified as one of the leading causes of mortality, morbidity, and functional disability among different age groups, resulting in substantial personal and societal burdens.[1,2] Trauma-related injuries with both blunt and penetrating natures typically induce moderate to severe pain, which can remain up to months and years after the injuries.[3,4] Based on a recent study, most patients with minor traumas remain in pain up to 6 months after their trauma.[5] Also, a review reported that acute pain from extremity trauma could be converted to chronic pain in up to 86% of sufferers.[6] Short- and long-term pain following trauma is associated with an interruption in day-to-day activities, delayed return to work, poorer recovery, and psychological troubles; hence, it is not only a significant concern for victims, but it can also substantially affect their trauma care quality.[7,8] Therefore, nursing staff and physicians should manage this type of pain in an emergency by implementing an appropriate caring protocol.[9]

Opioids have historically been prescribed in the emergency department to relieve pain associated with injuries and traumas.[10] Although early prescription of opioid analgesics may relieve pain more rapidly, they might result in an increased risk of adverse consequences (e.g., nausea, vomiting, constipation, and respiratory depression) as well as opioid misuse and abuse.[7,11] The overall prevalence of prolonged opioid use following musculoskeletal trauma was 27% and 6% among high-risk and low-risk adults, respectively.[12] Thus, there is a great necessity for the timely provision of non-pharmacological methods in the emergency department to control trauma-induced pain.[11]

Traditionally, herbal remedies have been used to relieve pain and inflammation induced by traumas and injuries.[13,14] Besides, in recent decades, different herbal treatments as alternatives/adjuvants to modern medicines have received attention in attenuating acute traumatic pain due to their easy usage, low cost, and lack of adverse consequences.[15,16] Sesame oil (SO), extracted from the seeds of the sesame plant (*Sesamum indicum L.*, Pedaliaceae family), is one of the well-known herbal agents with analgesic and anti-inflammatory properties utilised in traditional medicines to treat different wounds, injuries, and pains.[17,18] In Traditional Iranian Medicine (TIM), SO is suggested for healing musculoskeletal pain and inflammation.[19,20] Besides, in the Unani system of medicine, SO is a well-known remedy for treating musculoskeletal stiffness and pain, pruritus, wounds, and headaches.[18] Also, in traditional Taiwanese medicine, SO has been utilised to relieve joint pains, toothaches, scrapes, cuts, and muscle cramps.[21] Likewise, the medicinal properties of SO have been acknowledged and incorporated into the traditional medical systems of China and India, given its benefits for treating pain, inflammation, wound, and haemorrhoid.[22,23] Meanwhile, SO has been used for massage therapy in Ayurvedic medicine, and surprisingly, it is considered a sacred oil in the Hindu religion.[24]

Recent trials suggested the analgesic properties of SO in topical administration form for various painful

conditions.[19,25] Furthermore, based on an experimental study, SO probably has an action similar to that of analgesic drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs) and opioids. It contains substantial amounts of unsaturated fatty acids (e.g., linoleic acid, oleic acid, palmitic acid, and stearic acid), which inhibit pain transmission pathways by anti-inflammatory effects on prostaglandins and leukotrienes.[26] Also, SO has lignans (e.g., sesamin, sesamolin, sesamol, and sesaminol), which are assumed responsible for this oil's analgesic, anti-swelling, and anti-inflammatory properties.[27]

Recently, randomised controlled trials (RCTs) indicated a great interest in evaluating the potential analgesic effect of SO among patients with limb trauma; nevertheless, their data are inconsistent. In a recent trial, massage of the trauma site with SO for 3 days did not have any substantial effect on reducing limb trauma pain, while it significantly decreased the usage of analgesics in the SO arm in comparison with the placebo arm (i.e., paraffin oil massage).[28] Also, gentle massage with SO compared with paraffin oil during 9 days led to more reduction in pain of victims with limb traumas on the sixth and ninth days of intervention, but no considerable between-group differences were observed in pain severity on the first and third days of interventions as well as intake of diclofenac during 9 days of intervention.[29] However, another trial observed that topical SO applied with massage for 2 days prevented skin discoloration induced by bruising and relieved pain in traumatic limbs.[30] The other study also showed that topical usage of SO for 10 days significantly reduced the pain severity and the frequency of the received NSAIDs among clients with limb traumas on most endpoints.[31]

Recent reviews of human and animal experiments on the ethnopharmacology and phytochemistry of sesame also established promising evidence of SO's pain-alleviating and anti-inflammatory properties.[27,32,33] Furthermore, recent narrative or systematic reviews suggested the potential analgesic efficacy of topical administration of SO for subjects with musculoskeletal extremity traumas.[23,34] Nevertheless, as far as we know, no systematic review with a meta-analysis approach has ever explicitly assessed the impact of SO on the pain of patients with trauma. Given the conflicting findings of recent trials and minor observed side effects of topical SO (e.g., allergic contact dermatitis),[23,35] it is challenging to consider this inexpensive complementary approach in trauma pain management guidelines for contemporary and future practice. Hence, the present study aimed to synthesise and appraise all available RCTs regarding the impact of the topical application of SO on the pain of patients with limb trauma. Besides, it sought to estimate the potential effect of intervention by data pooling in a meta-analysis.

2 | MATERIALS AND METHODS

2.1 | Study protocol

The Institutional Review Board of Abadan University of Medical Sciences, Abadan, Iran, approved the current review (Grant No. 1770; Ethical Licence No. IR.ABADANUMS.REC.1402.141). Besides, the research protocol was confirmed in the International Prospective Register of Systematic Reviews (PROSPERO, Registry No. CRD42023485594).

2.2 | Eligibility criteria

The identified records were included in the case that they (1) recruited adult outpatients who were admitted to the emergency department with single or multiple non-penetrating minor trauma to the left and/or right limb or lower and/or upper limb (e.g., superficial contusion, bruising, and erosion); (2) were conducted using parallel-group or cross-over RCTs published in peer-reviewed journals in any language; (3) investigated the impact of administrating routine care plus SO on the trauma site in the form of topical use with or without massage compared with administrating the routine care alone or with a placebo/sham treatment; and (4) measured pain severity by a validated tool.

The studies were excluded if they (1) were redundant publications, quasi-experimental trials, animal studies, theses, commentaries, conference proceedings, case reports, and reviews; (2) administered SO blended with other herbal preparations; (3) included patients with severe limb trauma pain; (4) considered limb trauma-induced pain in addition to the pain of any other aetiology; (5) recruited patients who experienced trauma in areas other than upper and lower limbs or those admitted to the emergency department more than 6 h after occurrence of their trauma; (6) conducted on patients with penetrating traumas or those with blunt traumas associated with bone fractures, dislocations, subluxations, open wounds, nerve injuries, infections, foreign body embedment, or external bleeding; and (7) recruited children or older adults.

2.3 | Data sources and search strategy

A comprehensive search was conducted on Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science (Core Collection), PubMed, Scopus, and Google Scholar. Moreover, we scanned the International Clinical Trials Registry Portal (ICTRP) to retrieve the ongoing and finished trials. Also, the reference lists of the

eligible publications and earlier reviews were scanned manually to discover more appropriate studies and ensure all related studies were included.

Two independent researchers (OR and MN) searched all data sources systematically, utilising a combination of key terms and Medical Subject Headings (MeSH), without considering any search filters (e.g., publication type, time, and language). The search syntax for each data source is presented in Supplementary Table 1. First, a search was executed in November and December 2023. Then, an email alert service was made to determine the new eligible records that might be published after the first search. Finally, a search was accomplished on 31 January 2024 to retrieve new eligible trials. The researchers' disagreements during the systematic search were settled by the principal researcher (MA) via back-and-forth discussions. The Kappa coefficient for agreement between the researchers during the final search was acceptable ($K = 0.83–0.89$).

2.4 | Study selection and data extraction

The screening and selection of studies and data extraction from the eligible studies were accomplished by two independent researchers (FY and SZ), and a consensus was achieved among them through discussion. First, all identified records were exported to Endnote software. Then, after removing duplicates, the titles and abstracts of all remaining records were scrutinised meticulously. Subsequently, full texts of the eligible trials were investigated against eligibility criteria. Finally, the required information from each included trial was extracted employing an electronic data extraction sheet. In addition to pain severity, adverse effects of treatments were documented. Changes in means and standard deviations (SDs) in each study group were extracted to estimate the pooled pain severity. If studies did not report differences in means and SDs, these data were calculated by considering the baseline and post-treatment values. In case of unclear data, the required information was obtained by emailing the corresponding authors. Also, the register entry of the included trials was inspected to get additional details when the studies contained unclear data.

2.5 | Quality of evidence and risk of bias

The criteria offered by the Grading of Recommendations Assessment, Development, and Evaluation Working Group (GRADE) were applied to evaluate the overall evidence quality.[36] Also, the quality of each trial was inspected with the revised version of Cochrane Collaboration's Risk of Bias assessment tool (RoB2).[37] The GRADE evidence profile and RoB2 were completed by three independent researchers (MoA, AS, MA), and any controversies among them were fixed by extra consultations. To this end, when the three researchers decided differently about the GRADE and RoB domains, other research team members resolved any uncertainty or dispute between them through consensus adjudication.

2.6 | Data analysis

Data were pooled through a random-effects model employing Stata (version 11.2, Stata Corp., College Station, TX, USA). The effect sizes (ESs) were reported as weighted mean difference (WMD) with a corresponding 95% confidence interval (CI), and a $p < 0.05$ was supposed to be significant. The Cochran's Q test was applied to address the heterogeneity between studies ($p < 0.05$ was considered significant). Likewise, the inconsistency was examined using the I-squared statistic ($I^2 \geq 50\%$ was defined as moderate-to-high). Subgroup analysis, meta-regression, and sensitivity analysis were also performed when necessary.[38] Besides, Egger's linear regression test was run to estimate the potential of publication bias.[39]

3 | RESULTS

3.1 | Search results

The flow diagram for the screening and selection process of studies is visualised in Figure 1. In the initial phase, 751 records were retrieved from databases. Besides, 14 further records were discovered via other sources. Out of the 621 records screened by title and abstract, 12 were sought for retrieval. Finally, four publications were eligible and were included in this review.[28–31]

3.2 | Studies characteristics

Details about the substantial features of the four included publications are outlined in Table 1. All RCTs were conducted in Iran with a two-arm parallel group design. Considering the blinding, two used a triple-blinded approach,[28,29] one had a double-blinded design,[30] and the remaining was an open-label trial.[31] All studies were conducted on individuals with moderate pain severity (i.e., obtaining a score between 3 and 7, based on a 0–10

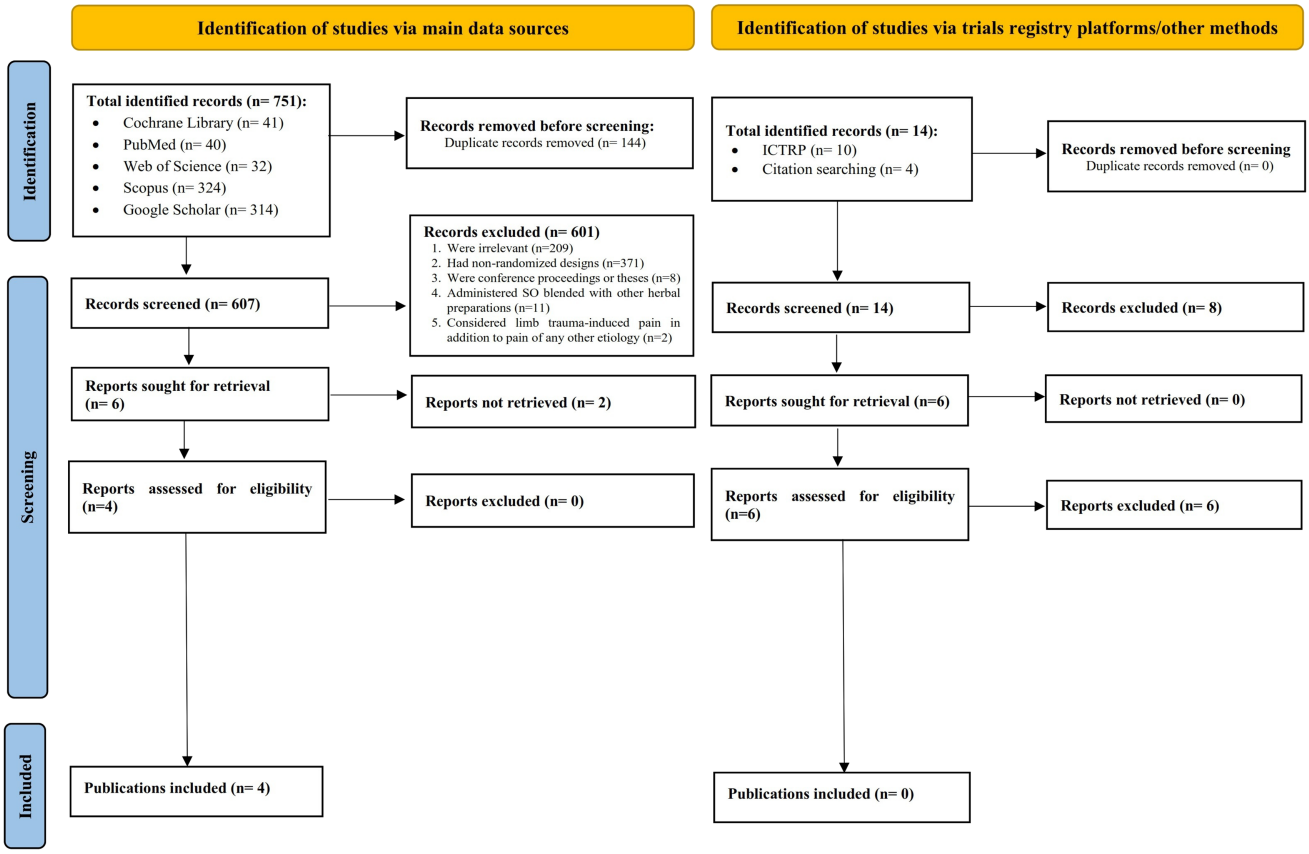


FIGURE 1 Flow diagram for the process of studies screening and selection.

scale). The sample size of the experimental and control arms ranged from 17 to 66 samples and 18 to 60 samples, respectively.

Patients received routine care in addition to massage of the trauma site with SO or a placebo in all studies, except one trial compared routine care plus SO massage to routine care plus a sham intervention (i.e., massage with no topical product).[31] In all studies, routine care included irrigation or cleansing of the affected area with a sterile normal saline solution, but details on patient safety indicators were not provided. Additionally, all studies administered analgesics to alleviate pain and applied cold compress on the affected area within the first 24 h and warm compress on the area within the following day(s). Also, all trials used 3.8 mL (10 drops) of SO/placebo based on the trauma area, and administered massage in a circular motion. The total duration of intervention ranged from 2 to 10 days. The administration duration was also 5–7 min with a frequency of once a day,[31] twice a day,[28,29] or thrice a day.[30] In two RCTs, patients did interventions at their homes after being educated on how to apply them.[28,30] In comparison, in the remaining two RCTs, the interventions were done by a trained nursing assistant at the patient's home/recruitment hospital.[29,31]

3.3 | Pain severity

All studies measured pain severity with a 0–10 scale, including a visual analogue scale ($n = 3$) and a numerical rating scale ($n = 1$). However, some trials reported changes in means and SDs from baseline to post-treatment day without reporting the raw means and SDs. Accordingly, to estimate the pooled pain severity, we compared groups regarding changes in means and SDs from baseline to post-treatment day. Yet, there were some variations in the time of post-treatment pain recording. Hence, to provide consistent data for pool analysis in the current study, data were extracted as indicated in Table 2 (baseline vs. 3rd intervention day in all studies, except one with baseline vs. 2nd intervention day[30]).

Based on the combined four ESs, the reduction in mean change of the pain score from baseline to the second/third intervention day was significantly higher in favour of clients who received routine care plus daily massage of the trauma site with SO compared to those who received routine care plus daily massage of the trauma site with a placebo/no topical product (WMD: −1.10; 95% CI [−1.62, −0.57]; $p < 0.001$) (Figure 2). After excluding each RCT from the primary meta-analysis, there were no notable dissimilarities between the pre-

TABLE 1 Characteristics of included randomised controlled trials on the effect of topical administration of sesame oil on pain severity of adult outpatients with minor limb trauma.

Study ID	Study design	Trauma site (extremities)[a]	Trauma size (cm^2: mean ± SD/ range)	Sample age (years: mean ± SD)	Groups (sample size)	Study protocol	Administration dosage, time, and duration	RoB[b]
Kafash Mohammadjani et al., 2022	Triple-blinded RCT	Upper right/left, lower right/left	T: 157.9 ± 137.8 C: 147.7 ± 122.7	T: 38.8 ± 14.2 C: 40.3 ± 14.6	T (60): SO massage + routine care C (60): Placebo massage (paraffin oil) + routine care	Products were poured on the trauma site and massaged in circular motions for 5–7 min	3.8 mL (10 drops) per 250 cm^2 of trauma area, BID, 3 d	Low
Gholami et al., 2022	Double-blinded RCT	Upper/lower	nrep.	T + C: 28.3 ± 6.8	T (49): SO massage + routine care C (41): Placebo massage (cooking oil) + routine care	Products were poured on the trauma site and massaged with light technique for 5 min	3.8 mL (10 drops, 1 mm thick) per 50 cm^2 of trauma area, TID (with 8 h interval), 2 d	High
Nasiri and Farsi, 2017	Triple-blinded RCT	Upper right/left, lower right/left	T, C: 50–200	T: 29.6 ± 8.3 C: 27.3 ± 7.3	T (17): SO massage + routine care C (18): Placebo massage (paraffin oil) + routine care	Products were poured on the trauma site and massaged with the light pressure stroking method for 5 min	3.8 mL (10 drops) per 50 cm^2 of trauma area, BID (with 12 h interval), 9 d	Low
Bigdeli Shamloo et al., 2015	Non-blinded RCT	Upper right/left, lower right/left	T, C: 50–200	T: 33.8 ± 1.3 C: 32.6 ± 9.1	T (60): SO massage + routine care C (66): massage with no topical product + routine care	Oil was poured on the trauma site and massaged in circular motions for 5–7 min	3.8 mL (10 drops, 1 mm thick) per 50 cm^2 of trauma area, QD, 10 d	High

Abbreviations: BID; Twice a day; cm^2: Square centimetre; C: Control group; min: Minutes; mL: Millilitre; mm: Millimetre; nrep.: Not reported; QD: Once a day; RCT: Randomised control trial; RoB: Risk of bias; SD: Standard deviation; SO: Sesame oil; T: Treatment group; TID: Thrice a day.

[a]Upper extremities were finger, wrist, lower arm, elbow, and upper arm, while lower extremities were toe, foot, ankle, lower leg, knee, upper leg, and lower trunk.

[b]The modified version of Cochrane Collaboration's Risk of Bias assessment tool for randomised trials (RoB 2): (1) Low: the study is believed to be at low RoB for all domains; (2) High: the study is judged to be at high RoB in at least one domain, or have some concerns for more than two domains in a way that substantially lowers confidence.

TABLE 2 Pain characteristics in included randomised controlled trials regarding the effect of topical administration of sesame oil on pain severity of adult outpatients with minor limb trauma.

		Measured times		Findings[a]	
Study ID	**Measurement**	**Included trials**	**Current review**	**Included trials**	**Current review**
Kafash Mohammadjani et al., 2022	NPRS	T0: before intervention on 1st d; T1: 30 min after 1st intervention on 1st d; T2: 30 min after 2nd intervention on 1st d; T3: 30 min after 3rd intervention on 2nd d; T4, 30 min after 4th intervention on 2nd d; T5: 30 min after 5th intervention on 3rd d; T6: 30 min after 6th intervention on 3rd d	T0 (baseline) vs. T6 (3rd d)	N/S (T0 to T6, T0 vs. T1, T0 vs. T2, T0 vs. T4, T0 vs. T5, T0 vs. T6) Sig. ↓ (T0 vs. T3)	N/S (T0 vs. T6: −3.38 ± 1.64 compared to −3.02 ± 1.63)
Gholami et al., 2022	VAS	T0: before intervention; T1: 48 h after T0	T0 (baseline) vs. T1 (2nd d)	Sig. ↓ (T0 vs. T1)	Sig. ↓ (T0 vs. T1: −1.53 ± 0.57 compared to 0.22 ± 0.52)
Nasiri and Farsi, 2017	VAS	T0: before intervention; T1: 30 min after 2nd intervention on 3rd d; T2: 30 min after 2nd intervention on 6th d; T3: 30 min after 2nd intervention on 9th d	T0 (baseline) vs. T1 (3rd d)	Sig. ↓ (T2 and T3)	Sig. ↓ (T0 vs. T1: −0.90 ± 0.83 compared to −0.20 ± 0.70)
Bigdeli Shamloo et al., 2015	VAS	T0: 1st d of intervention; T1: 3rd d of intervention; T2: 7th d of intervention; T3: 10th d of intervention)	T0 (baseline) vs. T1 (3rd d)	Sig. ↓ (T1, T2, and T3)	Sig. ↓ (T0 vs. T1: −1.95 ± 0.69 compared to −0.61 ± 0.71)

Abbreviations: d, day; h, hours; min, minutes; NPRS, numerical pain rating scale; N/S, not significant; Sig., significantly; T, timepoints; VAS, visual analogue scale; ↓, decreased.

[a]Changes in mean and standard deviation from baseline to post-treatment day in the treatment group compared to the control group.

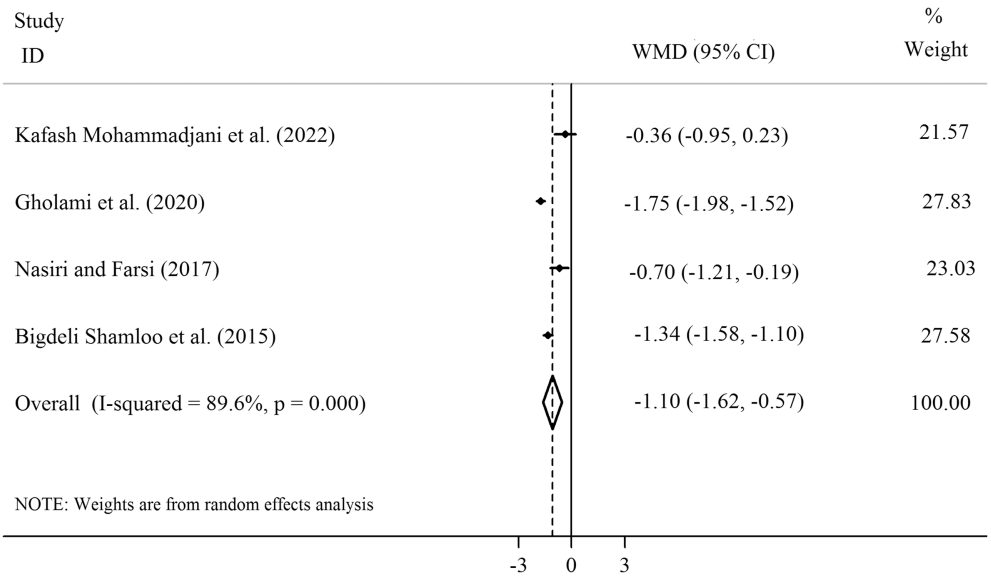


FIGURE 2 Forest plot for the effect of massage of trauma site with sesame oil on pain severity of adult outpatients with minor limb trauma (data are reported as changes from baseline to the second/third intervention day).

and post-sensitivity pooled analysis (Supplementary Figure 1). Also, after excluding the only RCT that applied intervention during 2 days,[30] the overall pooled ES for the remaining three RCTs that considered a three-day intervention was consistent with the primary finding (WMD: −0.84; 95% CI [−1.47, −0.22]; $p = 0.008$). Similarly, after excluding the only RCT that administered a sham intervention in the control arm (i.e., massage with no topical product),[31] the overall pooled ES for the remaining three RCTs that utilised placebo massage in the control group was compatible with the primary finding (WMD: −0.96; 95% CI [−1.90, −0.03]; $p = 0.04$).

The between-study statistical heterogeneity was high in the primary analysis (I^2: 89.6%, $p < 0.001$). However, according to the subgroup analysis, the frequency of intervention and the study's methodological rigour might be a heterogeneity source (Supplementary Table 2). Yet, based on the meta-regression results, none of the continuous variables was a source of heterogeneity (Supplementary Table 3). Egger's test also revealed no evidence of publication bias ($p = 0.07$).

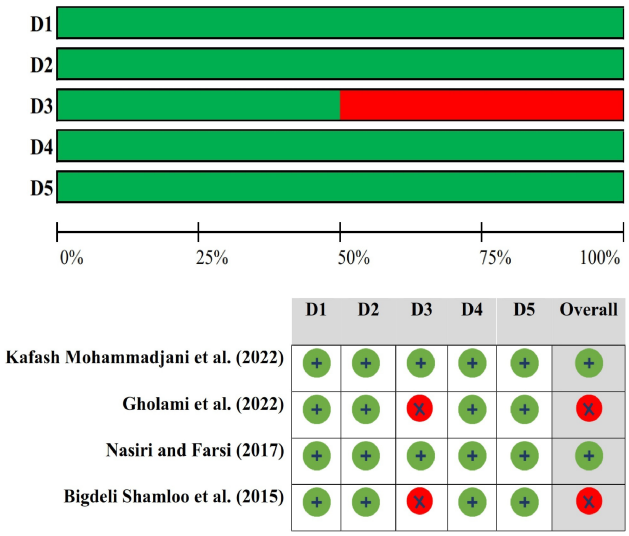
3.4 | Adverse effects

All studies recorded potential adverse effects of interventions; nevertheless, none reported any severe consequences.

3.5 | The evidence quality and risk of bias

The judgement of the authors regarding the RoB2 assessment tool is outlined in Figure 3. The details of the assessment are also documented in Supplementary Table 4. Two studies had a low RoB for all domains,[28,29] while the remaining two had a high RoB regarding bias due to missing outcome data.[30,31]

According to the GRADE, the evidence quality was moderate. The inconsistency criterion was the main reason for diminishing the evidence quality rate (Table 3).



Abbreviations: *D1*, bias arising from the randomization process; *D2*, bias due to deviations from intended interventions; *D3*, bias due to missing outcome data; *D4*, bias in measurement of the outcome; *D5*, bias in selection of the reported result.
Symbols: *red circles*, high risk of bias; *green circles*, low risk of bias.

FIGURE 3 Summary of the authors' judgements about the risk of bias domains across and within the included randomised controlled trials regarding the effect of topical administration of sesame oil on alleviating pain severity of adult outpatients with minor limb trauma.

TABLE 3 GRADE evidence profile: the effect of topical administration of sesame oil on pain severity of adult outpatients with minor limb trauma.

Outcome (number of studies)	Quality assessment					Summary of findings			
	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Number of participants		Effect (95% CI)	Quality of evidence
						Experimental group	Control group		
Pain score (4 RCTs)	No serious[a]	Serious[b]	No serious[c]	No serious[d]	Undetected[e]	192	179	WMD: 1.10 lower (1.62 lower to 0.57 lower)[f]	⊕⊕⊕⊖ Moderate[g]

Abbreviations: CI, confidence interval; RCTs, randomised controlled trials; WMD, weighted mean difference.

[a]The higher percentage of risk of bias domains across the studies was low.

[b]I-squared statistic (I^2) = 89.6%.

[c]Studies were sufficiently directed regarding population, intervention protocol, comparator, and intended outcomes.

[d]The boundaries of the confidence interval included the overall treatment effect, but the optimal information size was met.

[e]Egger's test ($p = 0.075$).

[f]Large magnitude of effect (0.80 ≤effect size <1.30).

[g]We are moderately confident in the effect estimate: The actual effect is likely to be close to the estimate of the impact, but there is a possibility that it is substantially different.

4 | DISCUSSION

The functional disability rate and psychological troubles of traumatic limb pain are incredibly high; consequently, employing an appropriate and cost-effective caring protocol is crucial to managing this type of pain.[15] Different herbal preparations have been traditionally administered for pain relief induced by musculoskeletal disorders or tissue injuries due to their low costs, ease of use, and better patient adherence.[40] SO is one of the well-known herbal remedies traditionally used to treat various conditions, including musculoskeletal pain and stiffness, inflammation, bruising, wound, and injury.[18,22,41] Recent RCTs have investigated the potential impact of administrating SO on treating the pain of limb trauma; however, their findings are controversial. Accordingly, we synthesised these conflicting findings qualitatively and quantitatively to elicit a reliable conclusion regarding the potential effect of topical SO for alleviating limb trauma pain. We found that pain changes from baseline to the second/third intervention day were significantly different between adult outpatients who received routine care plus daily massage of the trauma site with SO and those who received routine care plus daily massage of the trauma site with placebo/no topical product. Indeed, SO massage on the trauma site could better reduce acute pain severity induced by minor limb trauma.

To the authors' best knowledge, this work is the first review with a systematic and meta-analysis design that addresses the effect of topical administration of SO on alleviating pain severity. Yet, the findings could substantiate and augment the previous reviews that addressed SO as an intriguing choice for relieving traumatic pain. A recent study reviewed clinical trials on sesame benefits for pain management as a subheading of the potential health benefits of sesame. Although the mentioned review sought to investigate the impact of sesame products in relieving the pain of patients with different conditions using a synthesis matrix, it addressed the analgesic properties of SO in trauma-induced pain.[23] Also, a systematic review of non-pharmacologic approaches for ameliorating adult pain severity in the emergency department suggested the potential analgesic efficacy of SO for musculoskeletal extremity trauma.[34] Although the findings of the mentioned reviews align with the present review on the usefulness of SO in treating traumatic limb pain, caution should be taken when comparing the results. The reviews described above were conducted using a systematic or narrative design. They also combined the findings of animal and human studies in their synthesis. In contrast, we included only RCTs and pooled their data in a meta-analysis to provide more valid evidence.

This review can also guide future investigators in performing a well-designed trial on the subject. Based on the

Cochrane RoB2 assessment tool, two RCTs had excellent methodological rigour. In contrast, the remaining two had a low methodological rigour due to bias from missing outcome data. Moreover, according to the GRADE, the evidence quality was moderate due to downgrading the quality for observed inconsistency. The subgroup analysis also indicated the study's methodological rigour as a potential source of heterogeneity. Besides, this analysis showed that pain was reduced more significantly in low-quality studies. Hence, to make a trustworthy conclusion on utilising SO alone or along with routine interventions for ameliorating pain severity of limb trauma, further RCTs with improved quality and minimised RoB are required. Since the studies were performed only in Iran, related trials must be conducted in other countries to provide more reliable information about how the intervention can influence the study outcome. Moreover, since the included studies evaluated the intervention safety via a self-reported method, the adverse effects of this treatment still need to be investigated meticulously (e.g., by recording safety laboratory indices), because a significant issue regarding sesame products is their allergenicity.[23]

The other notable finding of this review was the variation of studies in administration frequency (i.e., once, twice, or thrice a day), total duration of the intervention (i.e., 2 to 10 days), and interventionist (i.e., patients or nurses), making it challenging to present a standard protocol to obtain the maximum results. In contrast, all included studies administered 3.8 mL (10 drops) of SO based on the trauma area and massaged the affected site for five to 7 min. Although studies had different endpoints, we compared the study groups regarding changes from baseline to the second/third intervention day. However, according to the subgroup analysis, the intervention was more efficacious in the studies conducted with a longer duration. Also, subgroup analyses revealed administration frequency as a source of heterogeneity. Yet, we could not find the optimal frequency due to a limited number of included trials. Moreover, subgroup analyses showed that the intervention was more efficacious when administered by a nursing assistant. Hence, further studies should compare diverse administration frequencies and intervention durations to specify the optimal frequency and duration that must be considered to observe the maximum results. Also, comparing the intervention efficiency when administered by nursing staff and patients is of merit.

4.1 | Implications for practice

Based on the meta-analysis, massage of the trauma site with SO as an adjunct to routine care had a significant and large effect on attenuating acute traumatic limb pain. Accordingly, since the included studies documented the safety of the intervention, and also due to undesirable side effects of opioids commonly utilised for alleviating acute pain associated with traumas,[7,11] it seems that SO, which is readily obtainable in most regions, could be applied topically in the trauma site to manage limb trauma pain. Since this intervention is simple, low-cost, and non-pharmacological, it is noteworthy in clinical practice, especially in complementary and alternative medicine and emergency nursing. Yet, more high-quality investigations must be performed to make a solid evidence-based decision.

4.2 | Limitations

The findings should be cautiously interpreted because of some limitations. Firstly, the evidence quality was moderate, and a high degree of heterogeneity was observed between trials, which may affect the rigour of the results and limit evidence-based conclusions. Secondly, there was a methodological heterogeneity in the type of administered analgesics, which made a pooled analysis impossible. Thirdly, given the limited pooled ESs, conducting a dose–response analysis was unattainable. Fourthly, the findings cannot be generalised to all regions because the included studies were executed in Iran.

5 | CONCLUSION

This review showed that topical SO could potentially reduce the severity of adults' acute pain induced by minor limb trauma. However, there are concerns about eliciting a trustworthy conclusion for the efficacy or safety of the intervention due to the moderate quality of evidence, significant statistical heterogeneity, and a lack of trials recording the intervention's adverse consequences employing safety laboratory parameters. Therefore, the efficacy and safety of the intervention require more investigation in forthcoming RCTs. Moreover, exploring a standard administration protocol to obtain the maximum beneficial impact of the intervention is of merit.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationships that could influence the work reported in this review.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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