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Review

Effectiveness of *Zingiber montanum* Herbal Compress Remedy for Pain Management: An Updated Systematic Review and Meta-Analysis

Kanjana Worasing [1], Bunleu Sungthong [2] and Wiraphol Phimarn [3,*]

[1] Science Program in Medicinal Plant and Natural Product, Faculty of Pharmacy, Mahasarakham University, Kantharawichai, Maha Sarakham 44150, Thailand
[2] Integrative Pharmaceuticals and Innovative of Pharmaceutical Technology Research Unit, Faculty of Pharmacy, Mahasarakham University, Kantharawichai, Maha Sarakham 44150, Thailand
[3] Social Pharmacy Research Unit, Faculty of Pharmacy, Mahasarakham University, Kantharawichai, Maha Sarakham 44150, Thailand
* Correspondence: wiraphol.p@msu.ac.th; Tel./Fax: +66-4375-4360

Abstract: The *Zingiber montanum* herbal compress remedy is a type of herbal medicine that can be used as an alternative treatment for improving pain symptoms. This study aimed to evaluate the clinical efficacy of a *Z. montanum* herbal compress remedy for pain relief. PubMed, Scopus, ScienceDirect, and Thai databases were systematically searched for relevant articles published from inception to December 2022. Only randomized clinical trials (RCTs) wherein the efficacy of the *Z. montanum* remedy was compared to that of a placebo or non-steroidal anti-inflammatory drugs (NSAIDs) were included. Six RCTs with a total of 812 patients were included in the analysis. The efficacy of the *Z. montanum* remedy had a significantly decreased pain score compared to the placebo (SMD = −0.63; 95% CI = −1.20, −0.06; I^2 = 90%), but there was no significant difference when compared to NSAIDs (SMD = −0.61; 95% CI = −1.41, 0.81; I^2 = 73%). Moreover, the efficacy of the *Z. montanum* remedy in terms of the flexibility score (SMD = 0.59; 95% CI −0.56, 1.74; I^2 = 86.0%) and quality of life (SMD = 0.34; 95% CI −0.38, 1.05; I^2 = 81.0%) was similar to that of the placebo. This meta-analysis demonstrates that the use of the *Z. montanum* herbal compress remedy significantly reduces the pain scores reported by patients.

Keywords: *Zingiber montanum*; pain; quality of life; systematic review

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1. Introduction

Pain is a discomforting experience that encompasses both sensory and emotional dimensions and may result in harm to bodily tissues. Pain perception variations among individuals can be attributed to psychological, social, personal pain thresholds, and tolerance factors [1]. Pain has been known to reduce the quality of life of patients, impair social interactions and leisure activities, and in certain cases, cause mortality [2]. As a means of alleviating pain and inflammation, non-steroidal anti-inflammatory drugs (NSAIDs) are frequently employed; however, prolonged use of these agents has been linked to the development of gastrointestinal ulcers and bleeding [3].

Herbal remedies are commonly utilized as complementary or alternative treatments for pain, inflammation, and stress. Of these remedies, Plai or Cassumunar ginger (*Zingiber cassumunar* Roxb. or *Zingiber montanum*) has been widely used for pain relief [4]. One study demonstrated that a 14% *Z. montanum* cream is effective in alleviating pain and significantly reduces muscle soreness [5]. Cheechareoan et al. found that *Z. montanum* effectively lowered the pain score in individuals with muscle strain [6]. In 2013, *Z. montanum* was officially recognized and included in the Thai National List of Essential Medicines for the treatment of muscle sprains, muscular pain, and joint discomfort [7].

Furthermore, Thai herbal compresses, specifically the *Z. montanum* herbal compress remedy, are utilized as supplementary traditional therapies and as a rehabilitation approach for pain relief. The preparation of the *Z. montanum* remedy involves combining *Z. montanum* with other herbs that have analgesic, anti-inflammatory, and muscle relaxant properties; these plants are then tightly bundled in a piece of cloth to form a herbal compress ball which is then steamed in a stacked steamer pot. When the heated compress ball is applied to targeted areas of the body, active herbal compounds (including essential oils) can penetrate the skin, leading to therapeutic effects [8].

In 2014, Chiranthanut et al. [8] conducted a randomized controlled trial (RCT) to compare the efficacy of multiple herbal compresses with that of oral NSAIDs. The results showed no significant difference between the participants in the two treatment groups. Further, another study found no significant statistical difference between the *Z. montanum* remedy and Thai massage in terms of pain relief [9]. *Z. montanum* has a favorable effect in reducing pain associated with muscular discomfort and ankle sprains [4]. Dhippayom et al. [7] evaluated the clinical outcomes of Thai herbal compresses in treating osteoarthritis and muscular discomfort and found that *Z. montanum* is one of the most frequently used herbs in Thai herbal compress remedies. Despite these findings, most studies included in this systematic review and meta-analysis were quasi-experimental.

A prior systematic review expressed the need for more robust and comprehensive research to validate the effectiveness of *Z. montanum* as a pain management therapy [7]. To address this requirement, the present study is an updated systematic review and meta-analysis of RCTs aimed at providing substantive clinical evidence for the use of *Z. montanum* in pain management.

2. Materials and Methods

This systematic review and meta-analysis adhered to the guidelines and standards set forth by the Cochrane Collaboration framework [10] and is reported in accordance with the Preferred Reporting Items for the Systematic Reviews and Meta-Analyses (PRISMA) statement updated in 2020 [11]. (Supplementary Table S1).

2.1. Search Strategies and Study Selection

A comprehensive search for original research papers was conducted using multiple repositories including PubMed, Scopus, ScienceDirect, and Thai (such as ThaiJo and TDC) databases, covering the period from the inception of the database until December 2022. The key search phrases used included Plai, phlai, *Zingiber cassumunar* roxb., *Zingiber montanum*, and pain. In addition to these databases, offline sources and reference lists of the full-text reviewed papers were also searched to identify any other relevant research that might not have been indexed in the databases used. Specialists in the field were also consulted to ensure that no relevant studies were missed.

The research publications that were considered for inclusion in the analysis had to meet certain criteria, specifically: (1) they had to be an RCT, and (2) they had to evaluate the clinical efficacy and/or safety of the *Z. montanum* remedy in the treatment of pain. The selection process involved two independent reviewers (KW and WP) who screened the titles and abstracts of the studies to determine their eligibility for inclusion in the analysis. The full-text publications of the eligible studies were then reviewed by KW and WP, and any disagreements or ambiguities regarding the eligibility of a study were resolved with the help of a third reviewer (BS), who was consulted as needed.

2.2. Data Extraction and Quality Assessment

KW and WP utilized a standardized data extraction tool to obtain the relevant information from the selected studies. This information included the author's name, year of publication, research design, sample size, participant demographics (e.g., age), intervention details, and outcome measures. The primary outcome measure used was the pain score assessed after treatment intervention. The methodological quality of the studies included in

the systematic review and meta-analysis was assessed by KW and WP using two commonly used quality assessment tools: the Cochrane risk of bias tool [10] and the Jadad score [12]. The Cochrane risk of bias tool evaluates the bias potential in intervention studies based on several key factors, such as the method used to generate the sequence of allocation, the concealment of allocation, the use of blinding, missing outcome data, selective reporting, and other sources of bias. Each study was categorized as having a low, high, or uncertain risk of bias. The Jadad score, which ranges from 0 to 5, is used to assess the quality of RCTs and scores < 3 or ≥3 are considered to have poor or good quality, respectively. Any quality assessment differences by the two reviewers were resolved through discussion and consensus.

2.3. Statistical Analysis

In the meta-analysis, data from all the trials were combined to calculate the total effect size with a 95% confidence interval (CI). The pooled effects were estimated and stratified based on the indication of the herbal compress containing *Z. montanum* and its comparators. The mean of the variable outcomes for each treatment arm was then calculated. The standard deviation of the mean was calculated using the weighted average. The mean of the outcome variables was compared between the intervention arm and the control arm by calculating the overall mean difference, which could be the standardized mean difference (SMD) for pain score, flexibility score, and quality of life (QOL), depending on how each study measured these outcomes using a different scale.

For pain reduction outcomes, an SMD value > 0 suggests that the *Z. montanum* remedy was less effective than the comparators in reducing pain or easing problems while performing activities. SMD values greater than 0 also suggest that this remedy was more successful at enhancing flexibility and QOL than the other materials. The χ^2-test and I^2 were used to measure the statistical heterogeneity between studies [13]. According to the size and direction of the effects as well as the quality of evidence of heterogeneity, the I^2 thresholds were interpreted as modest heterogeneity (0–50%) and significant heterogeneity (51–100%) [10]. The Dersimonian and Laird random-effects model was used for all studies [14], and STATA version 15 (STATA Corp, College Station, TX, USA) and RevMan version 5.4 (Cochrane Collaboration, Oxford, UK) were used for the meta-analysis. Statistical significance was set at $p < 0.05$, and publication bias was evaluated using funnel plots.

Sensitivity analysis: fixed-effects models were used for the sensitivity analysis to verify the robustness of the findings.

3. Results

3.1. Study Selection

After completing the initial search and screening process, 55 articles were considered for further examination based on their titles and abstracts. After conducting a full-text evaluation of these articles, 14 publications were found to be suitable for the study. However, five articles were excluded from the final analysis as they lacked randomization, two trials used an intervention other than the *Z. montanum* remedy, and two trials were pre-post intervention studies. Ultimately, this systematic review and meta-analysis included six RCTs with a total of 812 patients. The study flow is shown in Figure 1.

3.2. Study Characteristic

In accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines for reporting herbal medicine interventions, the information retrieved from the included studies demonstrated a sufficient level of detail and transparency in their reporting. All six RCTs were performed in Thailand and were aimed at evaluating the pain-relieving effects of the *Z. montanum* remedy compared to either a placebo or NSAIDs. The active component plant of the remedy was identified by its Latin binomial name in all the studies. The duration of the RCTs varied from 1 day to 15 weeks, encompassing a broad range of treatment periods.

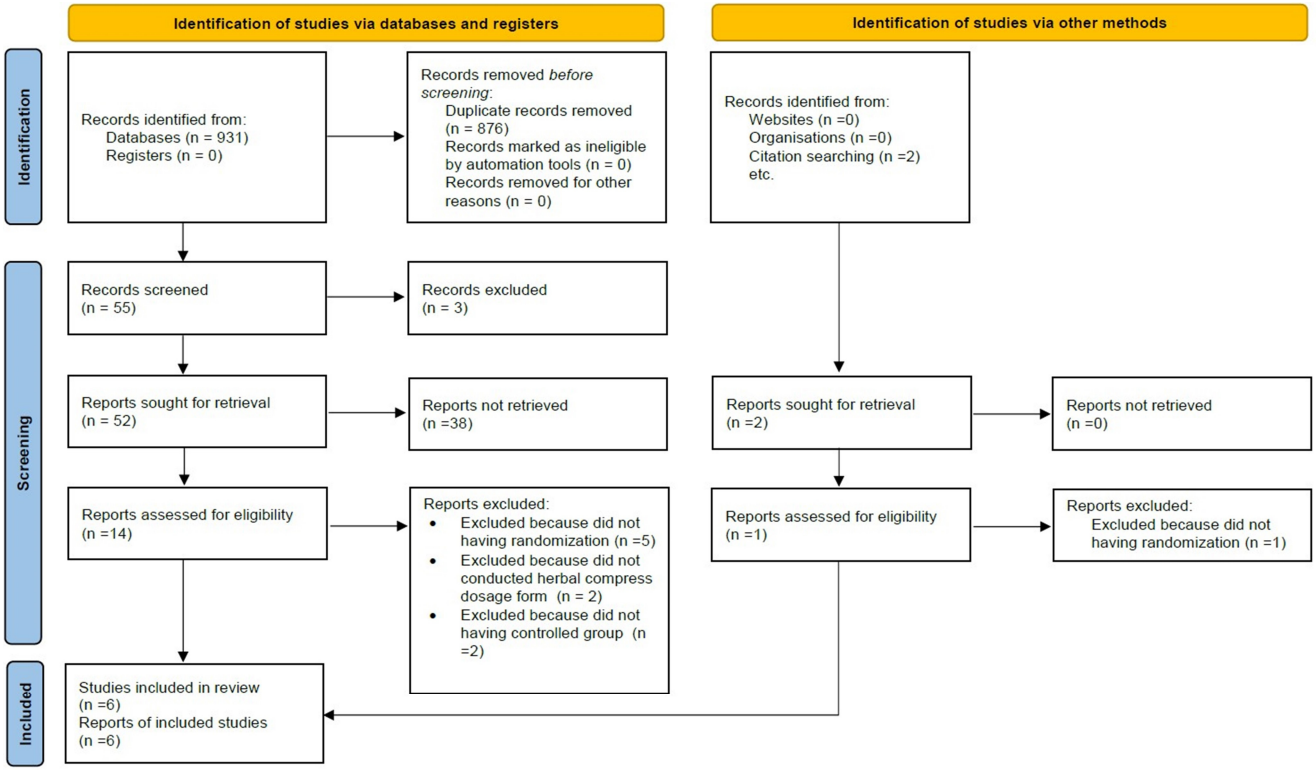

Figure 1. A PRISMA flow diagram describing the selection process for identifying studies included in the systematic review and meta-analysis.

In the included trials, patients with different pain conditions such as knee osteoarthritis (OA) [8,15], lower back pain [9], myofascial pain syndrome [16], maternal breast engorgement [17], and myogenous temporomandibular disorder [18] were diagnosed by a medical practitioner. The age range of the participants was between 18 and 65 years and the duration of discomfort reported was less than 30 days for acute pain. The other information retrieved from the studies is outlined in Table 1.

The constituents of the Thai herbal compresses utilized in the included trials were specified in each study. While there was some variation in the number of herbs used, the primary ingredients in all the trials appeared to be *Zingiber montanum*, *Curcuma longa*, and camphor. The herbal compress was typically steamed for 10–20 min before application. Only one study provided information on the proportion of *Z. montanum* in the herbal compress remedy. The majority of the trials used a placebo compress as a comparator, with two trials comparing the efficacy of a herbal compress remedy to that of NSAIDs.

Table 1. Characteristics of the included studies.

Authors	Design	Participants	Age (Year)	Intervention (n)	Comparators (n)	Duration	Outcomes	Results	Jadad Score
Chiranthanut, 2014 [8]	RCT	OA of the Knee	63.8 ± 8.44	Herbal compression (*Z casumuna* 40 %) (n = 20)	Ibuprofen 400 mg tid (n = 18) Thai massage (n = 20)	3 weeks	Pain score (VAS) Flexibility score QOL	The herbal compression, Thai massage, and ibuprofen reduced the pain score significantly.	4
Boonruab, 2018 [16]	RCT	Myofascial pain syndrome	42.14 ± 9.20	Herbal compression (n = 30)	Topical diclofenac (n = 30) Placebo compression (n = 30)	4 weeks	Pain score (VAS) Stiffness (VAS)	All the treatments significantly decreased the pain score.	3
Laosee, 2020 [9]	RCT	Acute Low Back Pain	68.65 ± 6.30	Herbal compression + Thai massage (n = 70)	Thai massage (n = 70)	15 weeks	Pain score (VAS) QOL	There was no additional benefit from the herbal compress.	3
Piwgern, 2020 [15]	RCT	OA of the Knee	40–65	Herbal compression (n = 20)	Placebo compression (n = 20)	1 week	Pain score (VAS) Flexibility score	Herbal compression reduced the pain score significantly compared to the placebo.	3
Ketsuwan, 2018 [17]	RCT	Maternal breast engorgement	27.95 ± 6.3	Herbal compression (n = 250)	Placebo compression (n = 250)	1 day	Pain score (VAS)	Herbal compression was more effective than placebo compression.	3
Chaimano, 2021 [18]	DRCT	Myogenous temporomandibular disorder	28.0 ± 10.9	Herbal compression (n = 16)	Placebo compression (n = 15)	1 day	Pain score (VAS)	Herbal compression was not more effective than placebo compression.	5

Remarks: RCT, randomized controlled trial; DRCT, double-blind randomized controlled trial; OA: osteoarthritis, VAS, visual analog scale; QOL, quality of life.

3.3. Quality of the Included Studies

In accordance with Cochrane's criterion for assessing the bias risk, the majority of the included studies were considered to have a low bias risk in terms of random sequence generation. However, one study was rated as having a high bias risk due to the lack of specification in the randomization procedure, while another two were considered high risk in terms of blinding due to the use of different dosage forms for the interventions and comparisons. None of the included studies demonstrated evidence of bias due to insufficient outcome data or selective outcome reporting (Figure 2). Furthermore, the quality of the included studies was evaluated using the Jadad score, with scores ranging from 3 to 5 out of 10, indicating good methodological quality (Table 1).

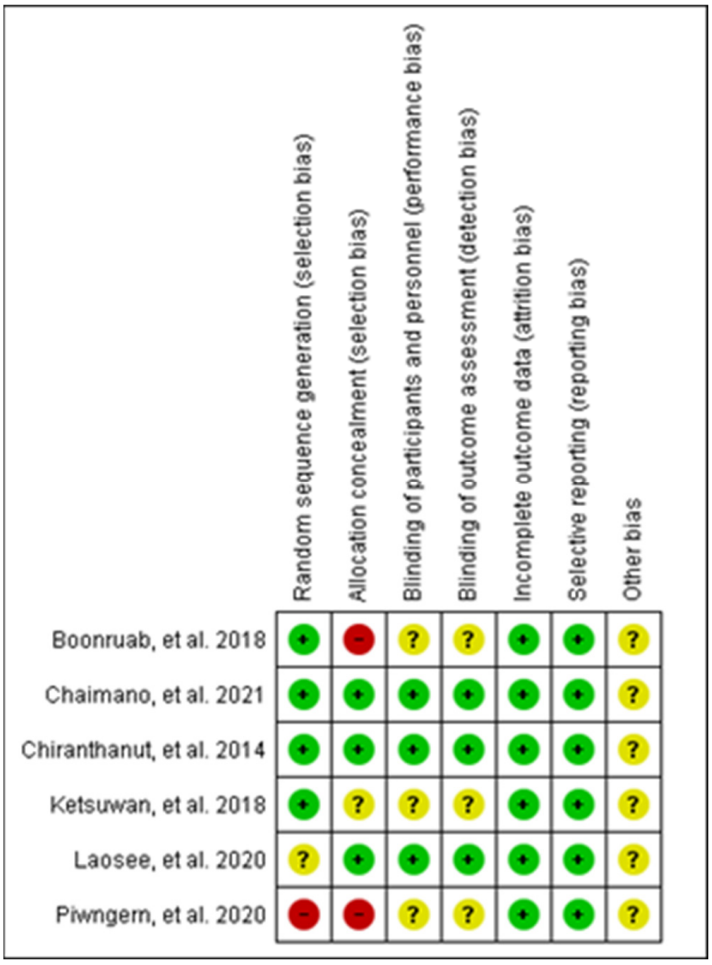

Figure 2. Methodological quality assessment of the included studies based on the Cochrane Handbook [8,9,15–18].

3.4. Clinical Effects on Pain Reduction

The six studies included RCTs [8,9,15–18] that compared the *Z. montanum* remedy efficacy for pain reduction to either a placebo or NSAIDs. A meta-analysis of the pain scores revealed that the use of the *Z. montanum* remedy resulted in significantly less pain compared to a placebo (SMD −0.63; 95% CI −1.20 to −0.06; $p = 0.03$) (Figure 3). However, there was no significant difference in pain reduction when the *Z. montanum* remedy was compared to NSAIDs (SMD −0.61; 95% CI −1.41 to 0.18; $p = 0.13$), However, these results were marked by substantial heterogeneity.

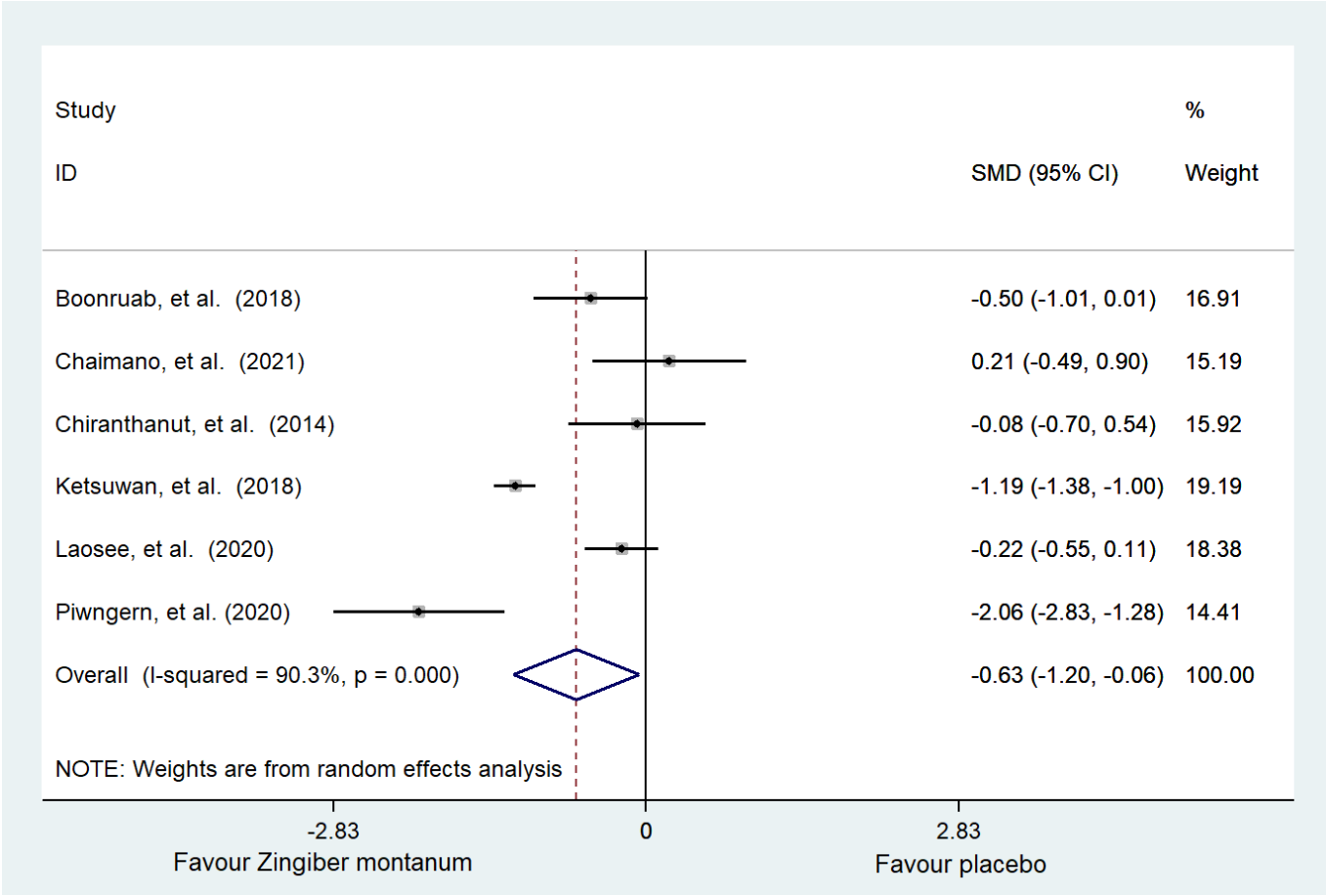

Figure 3. The effectiveness of pain reduction in the placebo and *Z. montanum* remedy-treated groups. The diamond represents the difference in the weighted mean and 95% confidence range. The size of the square is related to the study variance [8,9,15–18].

3.5. Clinical Effect on Flexibility

The results of the random-effects model applied to assess the change in flexibility score as a measure of the efficacy of the *Z. montanum* remedy showed that there was no statistically significant improvement (SMD, 0.59; 95% CI –0.55 1.50; $p = 0.31$). However, the results were marked by substantial heterogeneity ($I^2 = 86.0\%$, $p = 0.007$) (Table 2).

Table 2. Sensitivity analysis outcomes compared to the main analysis.

Outcomes	Main Analysis	Sensitivity Analysis	References
Pain score			
Plai vs. placebo	SMD = −0.63; 95% CI −1.20, −0.06; $I^2 = 90.0\%$	SMD = −0.85; 95% CI −0.99, −0.70; $I^2 = 90.0\%$	[8,9,15–18]
Plai vs. NSAIDs	SMD = −0.61; 95% CI −1.41, 0.18; $I^2 = 73.0\%$	SMD = −0.66; 95% CI −1.06, −0.25; $I^2 = 73.0\%$	[8,16]
Flexibility score	SMD = 0.59; 95% CI −0.56, 1.74; $I^2 = 86.0\%$	SMD = 0.45; 95% CI 0.04, 0.86; $I^2 = 86.0\%$	[8,15]
Quality of life	SMD = 0.34; 95% CI −0.38, 1.05; $I^2 = 81.0\%$	SMD = 0.21; 95% CI −0.07, 0.49; $I^2 = 81.0\%$	[8,9]

3.6. Quality of Life

The pooled results from the meta-analysis of the RCTs showed that there was an increase in QOL, but it was not statistically significant as evidenced by an SMD of 0.34 (95% CI = −0.38, 1.05; $p = 0.35$). However, the analysis also revealed a significant degree of heterogeneity in the QOL outcomes, as indicated by an I^2 statistic of 81% (Table 2).

3.7. Sensitivity Analysis

The results of the sensitivity analysis, performed to evaluate the robustness of the main findings, are presented in Table 2. Here, a fixed-effect model was employed to synthesize the data from the included studies. The sensitivity results indicate that the NSAIDs had substantial potency in reducing pain. Furthermore, the analysis revealed that the flexibility score, as assessed through the use of the fixed-effects model, showed a statistically significant improvement.

3.8. Publication Bias

Here, an assessment of publication bias was performed to evaluate the potential influence of missing or unpublished data on the clinical therapeutic effect of the *Z. montanum* remedy. The analysis was conducted using funnel-plot asymmetry. The results show that the funnel plots approached symmetry, which suggests that publication bias is unlikely to have impacted the findings of this study (Figure 4).

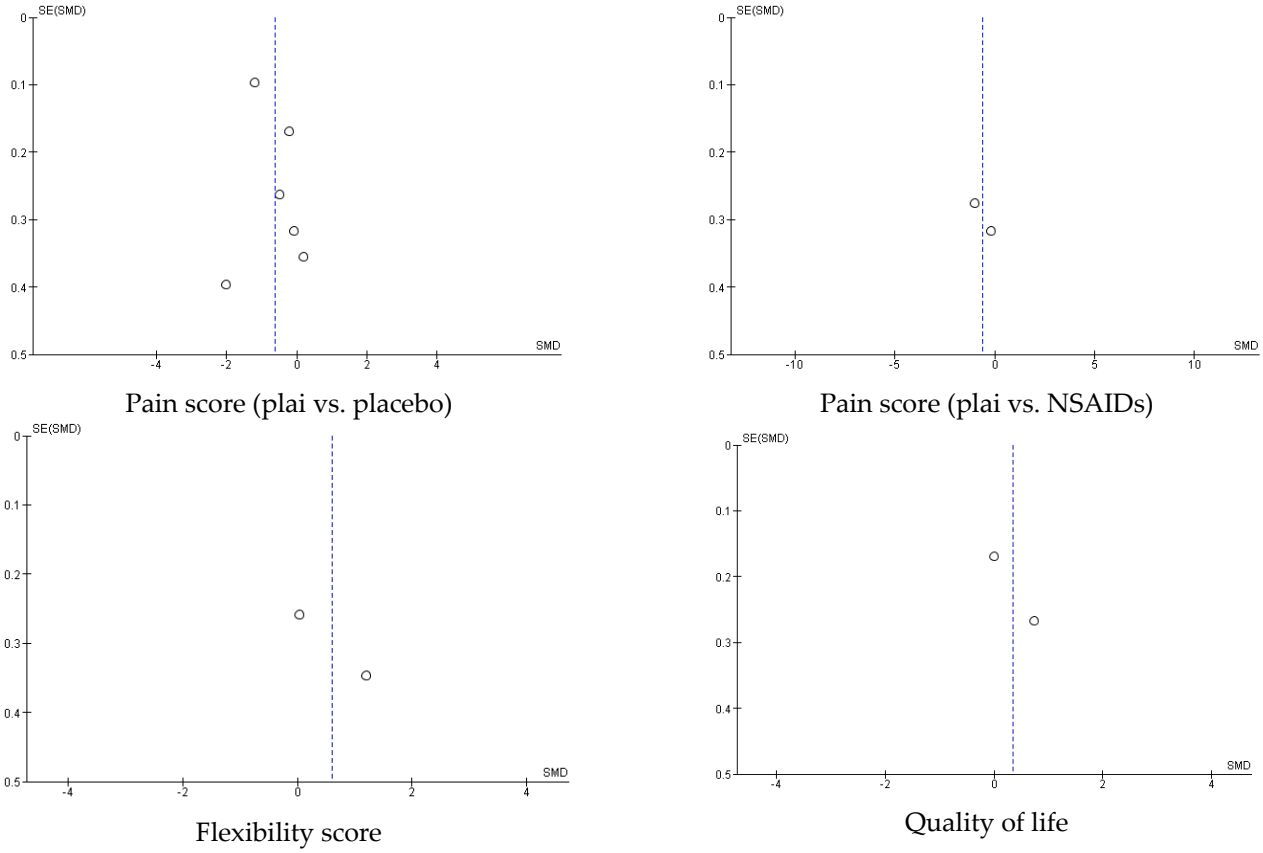

Figure 4. Publication bias.

4. Discussion

This comprehensive systematic review and meta-analysis aimed to evaluate the effectiveness of the *Z. montanum* herbal compress remedy in reducing pain among individuals with musculoskeletal disorders. Through a thorough examination of the available literature, six studies that compared the efficacy of the *Z. montanum* remedy to a placebo or NSAIDs were identified and analyzed. The meta-analysis demonstrated that the *Z. montanum* remedy was superior in reducing pain compared to a placebo and showed comparable effectiveness to NSAIDs in all patients after each trial. In Thailand, the use of the *Z. montanum* remedy is common for treating conditions such as muscle sprains and joint and muscular discomfort. It is believed that the benefits derived from herbal compresses are due to a combination of several factors, including heat conduction for improved regional

blood flow, anti-inflammatory actions of the herbal constituents, and the calming effects of the volatile aromatic oils [7].

The results of this meta-analysis provide new insights into the therapeutic potential of the *Z. montanum* remedy for pain management. Although the results showed promising evidence of the effectiveness of *Z. montanum* in reducing pain, the differences in the location and intensity of pain among the trials may have contributed to the disparities in the results. Nevertheless, our research highlights the importance of continued investigation into the use of the *Z. montanum* remedy as a complementary treatment option for individuals with musculoskeletal pain.

Pain scores are complex and multifaceted, as pain is a subjective experience that can vary greatly between individuals. The VAS- and NRS-assessed pain scores in the studies were included in our meta-analysis. However, here, we attempted to address this issue by using a standardized pain score measure that subtracts the post-intervention score from the prior score. While this method does not eliminate individual variation in pain perception and experience, it does provide a more standardized measure that can be compared across different studies. Moreover, in our meta-analysis, we used the SMD as the effect size measure to compare the efficacy of the *Z. montanum* remedy to control interventions for pain management in musculoskeletal disorders. The use of SMD as an effect size measure is appropriate for our study because it enables us to compare the magnitude of treatment effects across different outcome measures and scales.

The results of this study agree with prior studies regarding the anti-inflammatory and analgesic properties of *Z. montanum*. For instance, Dhippayom et al. [7] conducted a systematic review and meta-analysis on the clinical effects of Thai herbal compress, which demonstrated that the use of a herbal compress was comparable to nonsteroidal anti-inflammatory drugs, knee exercise, and hot compress in reducing osteoarthritis (OA) and muscle pain. Similarly, Lakhan et al. [19] investigated the analgesic effects of Zingiberaceae extracts and reported a significant pain reduction.

The action mechanism of the *Z. montanum* remedy is likely to involve anti-inflammatory pathways related to cyclooxygenase and lipoxygenase. A previous study [20] researched the anti-inflammatory properties of (E)-1-(3,4-dimethoxyphenyl) butadiene (DMPBD), a phenylbutanoid that is the active component of *Z. montanum*. This study utilized both in vitro and in vivo models and found that DMPBD dose-dependently inhibited ear inflammation in rats induced by ethyl phenylpropiolate, arachidonic acid, and 12-o-tetradecanoylphorbol 13-acetate.

Another study [21] investigated the impact of seven phenylbutanoids derived from *Z. montanum* and similarly found evidence for their anti-inflammatory effects, found to be mediated by the cyclooxygenase-2 pathway. These findings support the decision of the Thai NLEM committee to include *Z. montanum* as a therapeutic option for muscular and skeletal pain treatment. The anti-inflammatory mechanisms identified in these studies provide a scientific basis for the use of *Z. montanum* in the management of pain [4].

One of the potential mechanisms through which *Z. montanum* may exert its effects is via the modulation of the gut microbiota. However, it is also important to consider the potential effects of this herbal remedy on skin permeability and skin microbiota. The skin serves as a protective barrier against various environmental stressors and pathogens. The skin microbiota, similar to the gut microbiota, is a complex community of microorganisms that play an important role in maintaining the skin's barrier function and immune responses. Any alterations in the skin microbiota or skin barrier function can lead to various skin conditions such as atopic dermatitis, psoriasis, and acne [22].

There is some evidence to suggest that the application of herbal remedies, including *Z. montanum*, on the skin can enhance skin permeability and facilitate the absorption of functional compounds. For instance, a study by Priprem et al. [23] reported that the application of *Z. montanum* extracts on the skin of mice resulted in enhanced permeability and bioavailability of the functional compounds. Some studies have reported that the application of herbal remedies can alter the composition of the skin microbiota [24]. Overall,

while the potential effects of *Z. montanum* on the skin microbiota are important to consider, it is also necessary to investigate its effects on skin permeability and the skin microbiota. However, the effects of herbal remedies on the skin microbiota are not yet fully understood. Further research is needed to elucidate the potential benefits and risks of using this herbal remedy for pain management and other ailments.

While the role of microbiota in enhancing the bioavailability of herbal remedies is an important and emerging area of research, to the best of our knowledge, no studies have been conducted to investigate the specific interactions between the microbiota and *Z. montanum* compounds. For example, a study by Zhang et al. [25] examined the effects of gut microbiota on the bioavailability of ginsenosides, which are active compounds in Panax ginseng. However, it is currently limited to a few specific herbs and their active compounds. Therefore, we believe that further studies are necessary to investigate the potential interactions between the microbiota and *Z. montanum*, which could enhance its bioavailability and therapeutic efficacy.

A prior systematic review highlighted heat as a non-pharmacologic intervention for OA [26], implying that heat from herbal compresses may play a role in treating pain. The use of the *Z. montanum* remedy was found to be combined with massage therapy, a well-known method for alleviating pain through relaxation and release of tension from the body [27,28]. Additionally, massage helps improve blood flow and the lymphatic system [29]. However, the results of this review indicate no significant difference between the use of the *Z. montanum* remedy and placebo herbal compresses.

The strengths of this meta-analysis study are as follows: (1) this study is an updated meta-analysis, most of which were of high quality and had low ROB; (2) this MA performed a systematic search through three international databases and a Thai data-base, along with a manual search for unpublished trials.

In most of the literature reviewed, the use of the *Z. montanum* remedy has been shown to have beneficial effects in reducing pain and increasing flexibility; however, the number of studies conducted to date is limited. Furthermore, the age distribution of study participants has been quite broad, rendering it difficult to generalize the findings to specific age groups or populations. Therefore, future studies should focus on the following points: (1) obtaining larger sample sizes to provide more robust and reliable estimates of treatment effects; (2) providing a focus on specific age groups or populations to better understand the potential benefits of this herbal remedy for pain management in these groups; (3) making use of longer follow-up periods: many of the studies included in our meta-analysis had relatively short follow-up periods; and (4) employing the standardization of treatment protocols to better understand the optimal dosing and administration of this herbal remedy: there is significant variability in the preparation and application of the *Z. montanum* remedy across studies. Moreover, there is a lack of standardization in the preparation of this herbal remedy, which raises concerns about its clinical effectiveness and safety. Variables such as the location of harvest and time of year may impact the effectiveness of the product [30]. Despite the widespread perception among Thai patients that herbal medicines are safe due to their natural origin, the absence of a safety profile for *Z. montanum* remains a concern [31].

5. Conclusions

This comprehensive systematic review supports the therapeutic benefits of using the *Z. montanum* herbal compress remedy for the treatment of musculoskeletal pain, but its efficacy for treating other types of pain remains unclear. Despite the available evidence, the number of investigations conducted is limited and requires further large-scale studies for validation. Therefore, the use of a Thai herbal compress containing *Z. montanum* as adjunctive therapy in a randomized controlled study design may provide further insight into its efficacy and clinical applications. Healthcare practitioners may consider incorporating this herbal compress remedy into their treatment plans for individuals with musculoskeletal pain.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/scipharm91020024/s1, Table S1: PRISMA checklist.

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