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Herbal medicine for low-back pain (Review)

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[Intervention Review]

Herbal medicine for low-back pain

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ABSTRACT

Background

Low-back pain (LBP) is a common condition and imposes a substantial economic burden upon people living in industrialized societies. A large proportion of people with chronic LBP use complementary and alternative medicine (CAM), visit CAM practitioners, or both. Several herbal medicines have been purported for use in treating people with LBP. This is an update of a Cochrane Review first published in 2006.

Objectives

To determine the effectiveness of herbal medicine for non-specific LBP.

Search methods

We searched the following electronic databases up to September 2014: MEDLINE, EMBASE, CENTRAL, CINAHL, Clinical Trials.gov, World Health Organization International Clinical Trials Registry Portal and PubMed; checked reference lists in review articles, guidelines and retrieved trials; and personally contacted individuals with expertise in this area.

Selection criteria

We included randomized controlled trials (RCTs) examining adults (over 18 years of age) suffering from acute, sub-acute, or chronic non-specific LBP. The interventions were herbal medicines which we defined as plants used for medicinal purposes in any form. Primary outcome measures were pain and function.

Data collection and analysis

A library scientist with the Cochrane Back Review Group conducted the database searches. One review author contacted content experts and acquired relevant citations. We downloaded full references and abstracts of the identified studies and retrieved a hard copy of each study for final inclusion decisions. Two review authors assessed risk of bias, GRADE criteria (GRADE 2004), and CONSORT compliance and a random subset were compared to assessments by a third individual. Two review authors assessed clinical relevance and resolved any disagreements by consensus.

Main results

We included 14 RCTs (2050 participants) in this review. One trial on *Solidago chilensis M.* (Brazilian arnica) (20 participants) found very low quality evidence of reduction in perception of pain and improved flexibility with application of Brazilian arnica-containing gel twice daily as compared to placebo gel. *Capsicum frutescens* cream or plaster probably produces more favourable results than placebo in people with chronic LBP (three trials, 755 participants, *moderate quality evidence*). Based on current evidence, it is not clear whether topical capsicum cream is more beneficial for treating people with acute LBP compared to placebo (one trial, 40 participants, *low quality evidence*). Another trial found equivalence of *C. frutescens* cream to a homeopathic ointment (one trial, 161 participants, *very low quality evidence*). Daily doses of *Harpagophytum procumbens* (devil's claw), standardized to 50 mg or 100 mg harpagoside, may be better than placebo for short-term improvements in pain and may reduce use of rescue medication (two trials, 315 participants, *low quality evidence*). Another *H. procumbens* trial demonstrated relative equivalence to 12.5 mg per day of rofecoxib (Vioxx®) but was of very low quality (one trial, 88 participants, *very low quality*). Daily doses of *Salix alba* (white willow bark), standardized to 120 mg or 240 mg salicin, are probably better than placebo for short-term improvements in pain and rescue medication (two trials, 261 participants, *moderate quality evidence*). An additional trial demonstrated relative equivalence to 12.5 mg per day of rofecoxib (one trial, 228 participants) but was graded as very low quality evidence. *S. alba* minimally affected platelet thrombosis versus a cardioprotective dose of acetylsalicylate (one trial, 51 participants). One trial (120 participants) examining *Symphytum officinale L.* (comfrey root extract) found low quality evidence that a Kytta-Salbe comfrey extract ointment is better than placebo ointment for short-term improvements in pain as assessed by VAS. Aromatic lavender essential oil applied by acupressure may reduce subjective pain intensity and improve lateral spine flexion and walking time compared to untreated participants (one trial, 61 participants,*very low quality evidence*). No significant adverse events were noted within the included trials.

Authors' conclusions

C. frutescens (Cayenne) reduces pain more than placebo. Although *H. procumbens*, *S. alba*, *S. officinale L.*, *S. chilensis*, and lavender essential oil also seem to reduce pain more than placebo, evidence for these substances was of moderate quality at best. Additional well-designed large trials are needed to test these herbal medicines against standard treatments. In general, the completeness of reporting in these trials was poor. Trialists should refer to the CONSORT statement extension for reporting trials of herbal medicine interventions.

PLAIN LANGUAGE SUMMARY

Herbal medicine for low-back pain

Review question

We examined the evidence regarding the effect of herbal medicine on pain in people with non-specific low-back pain (LBP).

Background

Back pain is common and up to 35% of the population can be affected in a given month. Non-specific LBP is defined as pain between the lowest rib and the bottom of the buttocks that is not caused by serious, underlying problems such as rheumatoid arthritis, infection, fracture, cancer, or sciatica due to a ruptured disc or other pressure on nerves. Herbal medicines taken orally or applied to the skin are being used to treat many conditions including back pain.

Study characteristics

Researchers from the Cochrane Collaboration examined the evidence available up to August 5, 2013. Fourteen studies tested six herbal medications and included 2050 adults with non-specific acute or chronic LBP. Two oral herbal medications, *Harpagophytum procumbens* (devil's claw) and *Salix alba* (white willow bark), were compared to placebo (fake or sham pills) or to rofecoxib (Vioxx®). Three topical creams, plasters, or gels, *Capsicum frutescens* (cayenne), *Symphytum officinale* L. (comfrey), and *Solidago chilensis* (Brazilian arnica), were compared to placebo creams or plasters and a homeopathic gel. One essential oil, lavender, was compared to no treatment. The average age of people included in the trials was 52 years and studies usually lasted three weeks.

Key results

Devil's claw, in a standardized daily dose of 50 mg or 100 mg harpagoside, may reduce pain more than placebo; a standardized daily dose of 60 mg reduced pain about the same as a daily dose of 12.5 mg of Vioxx®. While willow bark, in a standardized daily dose of 120 mg and 240 mg of salicin reduced pain more than placebo; a standardized daily dose of 240 mg reduced pain about the same as

a daily dose of 12.5 mg of Vioxx® (a non-steroidal, anti-inflammatory drug). Cayenne was tested in several forms: in plaster form, it reduced pain more than placebo and about the same as the homeopathic gel Spiroflor SLR. Two other ointment-based medications, *S. officinale* and *S. chilensis* appeared to reduce perception of pain more than placebo creams. Lavender essential oil applied by acupressure appeared effective in reducing pain and improving flexibility compared to conventional treatment. Adverse effects were reported, but appeared to be primarily confined to mild, transient gastrointestinal complaints or skin irritations.

Quality of the evidence

Most included trials were at low risk of bias and the quality of the evidence was mainly very low to moderate. A moderate grade of evidence was only found for *C. frutescens*. Trials only tested the effects of short term use (up to six weeks). Authors of eight of the included trials had a potential conflict of interest and four other authors did not disclose conflicts of interest. Vioxx® has been withdrawn from the market because of adverse effects, so all three substances should be compared to readily-available pain medications, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen, for relative effectiveness and safety.

Conclusion

Low to moderate quality evidence shows that four herbal medicines may reduce pain in acute and chronic LBP in the short-term and have few side effects. There is no evidence yet that any of these substances are safe or efficacious for long-term use. Large, well-designed trials are needed to further test the efficacy of these interventions.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Brazilian arnica extract compared to placebo for patients with non-specific chronic back pain or soft tissue pain

Patient or population: patients with back pain
Settings: outpatient clinic
Intervention: extract of Brazilian arnica
Comparison: placebo

Outcomes	No of participants (trials)	Quality of the evidence (GRADE)	Comments
Pain reduction based on Pain VAS instrument 0-100 scale	20 (one trial)	⊕◯◯◯ **very low**[1]	Very small sample size only N = 10 in the treatment group. This trial found that topical application of Brazilian arnica reduced the perception of pain and increased flexibility in the treated group compared to baseline values in that group. Unknown if acute or chronic LBP

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Selection bias was high to unclear, performance bias was low risk to unclear risk, with other attributes being low risk.

BACKGROUND

Low-back pain (LBP) and its related disability are major public health problems across industrialized nations. As a result, research efforts have intensified to identify effective treatment and management strategies for people with LBP (Mounce 2002). Point prevalence estimates of LBP vary widely depending on the methodology used, but range from 12% to 40% of the population (Friedley 2010). Additionally, several studies indicate that LBP prevalence is increasing over time (Friedley 2010). Data from a United States. national survey from 2002 reported a three-month prevalence of 26.4%, with higher prevalence among American Indians and Alaskan Natives (35.0%), and lower prevalence among Asian Americans (19.0%) (Deyo 2006). LBP prevalence peaks between the ages of 45 to 64 years and is more common among lower socioeconomic status groups, as defined by income and education (Deyo 2006). Lifetime prevalence of LBP is estimated at 67% (Deyo 2006).

In the United States, back pain accounts for 19 million physician visits, 250 million workdays lost, and $14 billion (USD) in direct expenditures (Grabois 2005). Indirect costs, excluding short- and long-term disability, are estimated at up to $100 billion (USD) per year (Eisenberg 2012). LBP-related disorders caused 2.63 million annual emergency department (ED) visits, or 2.3% of all visits to EDs in the United States (Friedman 2010). This amounts to substantial societal productivity losses and an economic burden for health-care systems in many industrialized countries (Mounce 2002).

Wide variations in the medical and surgical management of LBP reflect widespread professional uncertainty about optimal care of people with LBP (Eisenberg 2012). Over 1000 randomized

controlled trials (RCTs) have been published evaluating all types of conservative, complementary, or surgical treatments for LBP that are commonly used in primary and secondary care (Koes 2006). A special focus issue of *The Spine Journal* reviewed 25 categories of treatment presented for the management of chronic LBP (Haldeman 2008). Several interventions are included in clinical practice guidelines on LBP, including: back schools, non-steroidal anti-inflammatory drugs (NSAIDs), the McKenzie method, needle acupuncture, spinal manipulation, trigger point injections, and watchful waiting (Haldeman 2008). A summary of European clinical guidelines for chronic LBP includes cognitive behavior therapy, supervised exercise therapy, educational interventions, biopsychosocial treatment, and short-term use of NSAIDs and weak opioids (Koes 2006).

Although systematic reviews suggest that few of these interventions have sufficient evidence to suggest benefit, it does appear that acute LBP can usually be effectively managed by encouraging activity, reassurance, and short-term symptom control (analgesics or NSAIDs) (Koes 2006). Treatments that demonstrate some effectiveness for the management of chronic LBP include exercise therapy, behavioural treatment, and multidisciplinary treatment programs, as well as short-term use of analgesics or NSAIDs (Koes 2006).

Research in complementary and alternative medicine (CAM) has increased over the past 15 years. Rigorous literature is growing steadily and is subsequently clarifying the validity of these techniques (e.g., Vickers 2000) . Specifically, the number of randomized trials of complementary treatments has doubled approximately every five years (Vickers 2000) and currently, the Cochrane Complementary Medicine Field Trials Registry contains over 43,000 records. In addition, CAM teaching institutions are now beginning to teach principles of evidence-based medicine and clinical epidemiology (Mills 2002; Sierpina 2002). These initiatives are well placed, given the large number of visits to CAM practitioners (Metcalfe 2010; Frass 2012). A recent population survey in Canada found that 12.4% of Canadians visited a CAM practitioner in the year they were surveyed, between 2001-2005 (Metcalfe 2010). A review article on the international acceptance and use of CAM found prevalence rates between 5.0% to 74.8%, with an overall average prevalence of 32.2% (Frass 2012). Follow-up studies indicate that there has been a steady increase in CAM use (Frass 2012). More CAM users are women, middle-aged, educated, and experiencing chronic disease (Metcalfe 2010; Frass 2012). Back pain or back problems are one of the five most common medical conditions for which CAM has most often been used (Frass 2012). Among people reporting back problems, between 16.8% to 57.2% seek CAM treatments (Frass 2012).

Several herbal medicines are reported treatments for various types of pain. These include *Cammiphora molmol* (myrrh) , *Capsicum frutescens* (capsicum), *Salix alba* (white willow bark), *Melaleuca alternifolia* (tea tree) , *Angelica sinensis* (don quai) , *Aloe vera* (aloe), *Thymus officinalis* (Thyme), *Menthe peperita* (peppermint), *Arnica montana* (Arnica), *Curcuma longa* (curcumin), *Tanacetum parthenium* (feverfew), *Harpagophytum procumbens (devil's claw)* , and *Zingiber officinale (ginger)* (Blumenthal 1998). Many have been the subject of extensive biochemical research, resulting in the delineation of their pharmacological and physiological effects (Mills 2000). For example, the mechanism of *C. frutescens* is partially related to its ability to deplete substance P, a neurotransmitter for pain perception (Keitel 2001). *S. alba* is a platelet inhibitor and analgesic, and *H. procumbens* has analgesic and anti-inflammatory properties (Chrubasik 1996). In addition, some of these herbal species have been clinically tested for the relief of symptoms of LBP (Krivoy 2000; Laudahn 2001a; Mills 2000; Stam 2001).

Given the large public health and economic burden LBP causes and the large number of people with LBP who regularly visit CAM practitioners, a systematic review of these herbal medicines was warranted.

OBJECTIVES

To determine the effectiveness of herbal medicine compared to placebo, no intervention, or other interventions in the treatment of non-specific LBP.

METHODS

Criteria for considering studies for this review

Types of studies

RCTs.

Types of participants

Adults aged over 18 years, suffering from acute (lasting up to six weeks), sub-acute (six to 12 weeks) or chronic (longer than 12 weeks) non-specific LBP.

We defined LBP as pain localized to the area between the costal margin or the 12th rib to the inferior gluteal fold. Non-specific LBP indicated that no specific cause was detectable, such as infection, neoplasm, metastasis, osteoporosis, rheumatoid arthritis, fracture, inflammatory process, or radicular syndrome (Waddell 1996).

Types of interventions

For the purpose of this Cochrane Review, we defined a herbal medicine as all or part of a plant used for medicinal purposes, administered orally (ingestion) or applied topically. This definition

did not include plant substances smoked (e.g. *Cannabis sativa*), individual chemicals derived from plants, or synthetic chemicals that were based on constituents of plants. However, we considered *C. sativa* and other plants that can be smoked as herbal medicines in this Cochrane Review if they were ingested. Various forms of oral herbal medicine include: standardized extracts (encapsulated or tablet form), tinctures (alcohol, glycerine, etc.), dried herb (encapsulated or tablet form), raw whole herb infusion (e.g. tea) and decoction (e.g. boiled-down tea). Topical herbal applications include ointments, essential oils, creams (petroleum or glycerine-based), powders, plasters, and poultices. We excluded opioids as they bridge the definitions of herbal medicine and analgesic.

Types of outcome measures

1. Pain intensity (e.g. visual analogue scale (VAS), numerical rating scale (NRS)) and proportion of pain-free patients (use of analgesic medications);
2. Back pain specific functional status measured by validated instruments (e.g. Roland Disability Questionnaire (RDQ), Owestry Disability index (ODI), modified Aberdeen LBP Scale);
3. Overall improvement (% reporting subjective improvement, NRS);
4. Return to Work or Work Status (% of population, number of days of absenteeism);
5. Lumbar flexibility (measured by Schober method, fingertip-to-ground distance).

Search methods for identification of studies

We used the search strategy recommended by the Cochrane Back Review Group (CBRG) (Bombardier 2011; Furlan 2009). The search stratgies for the identification of RCTs recommended by Robinson 2002 was also used in some of the strategies in this update.

Electronic searches

We searched the following electronic databases up to September 11, 2014:

1. MEDLINE (OvidSP, 1946 to September Week 1 2014) and MEDLINE In-Process & Other Non-Indexed Citations (OvidSP, September 10, 2014)
2. EMBASE (Ovid SP, 1980 to 2014 Week 36)
3. Cochrane Central Registry of Controlled Trials (CENTRAL, The Cochrane Library; Issue 8 of 12, August 2014)
4. Cumulative Index to Nursing and Allied Health Literature (CINAHL; EBSCO, 1981 to 2014)
5. ClinicalTrials.gov
6. World Health Organization International Clinical Trials Registry Portal (WHO ICTRP)
7. PubMed

Searches have been conducted annually since 2009. CENTRAL (which contains the Complementary Medicine Field trials register) and CINAHL were added to the strategy in 2009, the trials registries ClinicalTrials.gov and WHO ICTRP were added in 2012, and Medline In-Process & Other non-Indexed Citaitons was added in 2013. A supplemental search of PubMed was added in 2014 to capture items not indexed in Medline using the strategy recommended by Duffy 2014. The 2014 search strategies for all databases are included in Appendix 1; Appendix 2 contains the 2009 strategies and highlights updates to these strategies to 2013.

Searching other resources

We reviewed reference lists in review articles, guidelines, and in the retrieved trials. Also we contacted individuals with expertise in herbal medicine and LBP to identify additional trials. We translated non-English articles and JJG and MvT discussed these articles following the same procedures described below.

Data collection and analysis

Selection of studies

A library scientist with the CBRG conducted the electronic searches. Two review authors (HNO and JJG) independently selected studies based on title, abstract, and keywords. We included studies that met the inclusion criteria. If it was unclear from the title and abstract if a study fulfilled the inclusion criteria, we retrieved the full-text article for final selection. We used a consensus method to resolve any disagreements.

Data extraction and management

Two review authors (HNO and JJG) independently extracted the data from each trial using a standardized form. We extracted the following data from each trial: recruitment, characteristics of the trial population (age, gender), setting (e.g. year, country of origin), duration of LBP (acute, subacute, or chronic), previous treatment for LBP, number of participants initially recruited, number of participants randomized, number of drop-outs or withdrawals, duration of intervention, type of herbal medicine used (plant name and form of delivery and dosage), standardization information (e.g. percentage of active constituent per delivery unit), characteristics of the control intervention (type and duration), types of outcome measures, summary statistics, timing of outcome assessments, compliance, adverse effects due to intervention, and authors' conclusions as to the intervention's effectiveness.

Reporting quality

One review author (HNO) assessed the reporting quality of each included trial using the CONSORT statement (Moher 2012) and the CONSORT statement for herbal interventions (Gagnier 2006c). HNO scored each criterion as 'yes' (Y), 'no' (N) or 'don't know' (DK). 'Yes' indicated that the criterion was met. 'No' reflected the lack of fulfilment of that criterion. 'Don't know' reflected the fact that there was insufficient information to determine if this criterion was fulfilled or not. We considered a trial to have high reporting quality if it contained at least 50% of the CONSORT checklist items or at least 50% of the CONSORT for herbal interventions items.

Assessment of risk of bias in included studies

Two review authors (HNO and JJG) independently assessed methodological quality using the method recommended by Furlan 2009. Given JJG's familiarity with the literature, trials were not blinded for authors, institution or journal. We used the 12 items in the methodological quality assessment reflecting internal validity, together with operational definitions, recommended by the CBRG in their updated method guidelines for systematic reviews to assess methodological quality (Furlan 2009). We scored each criterion as high, low, or unclear. 'High' indicated that the criterion was not met. 'Low' reflected the fulfilment of that criterion. 'Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not. We considered a trial to have low risk of bias if the trial met over 50% (6/12) of internal validity items and we found no other serious flaws.

Data synthesis

We planned to analyse dichotomous outcomes by calculating the relative risk values (RR). For continuous outcomes, we planned to calculate the mean difference (MD) when the same instrument was used to measure outcomes or the standardized mean difference (SMD) when different instruments were used to measure the outcomes. We planned to use 95% confidence intervals (95% CI) to express the uncertainty of the findings. However, we were unable to combine the trials through meta-analysis because of insufficient data and clinical heterogeneity. Therefore we conducted a qualitative analysis of trial findings.

Two review authors (HNO and JJG) independently assessed the overall quality of the evidence for each outcome using the GRADE approach (GRADE 2004), as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) and adapted in the updated CBRG method guidelines (Furlan 2009). Domains that decreased the quality of the evidence include: study design and risk of bias, inconsistency of results, indirectness, imprecision (sparse data) and other factors (e.g. reporting bias).

We determined the overall quality of evidence for each outcome by combining the assessments on all domains. The five levels of evidence include:

- **High quality evidence:** there are consistent findings among at least 75% of RCTs with low risk of bias, consistent, direct and precise data and no known or suspected publication biases. Further research is unlikely to change either the estimate or our confidence in the results.
- **Moderate quality evidence:** one of the domains is not met. Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- **Low quality evidence:** two of the domains are not met. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- **Very low quality evidence:** three of the domains are not met. We are very uncertain about the results.
- **No evidence:** no RCTs were identified that addressed this outcome

Clinical relevance

One review author (JJG) assessed the clinical relevance of each trial using these five questions:

1. Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practice?
2. Are the interventions and treatment settings described well enough so that you can provide the same for your patients?
3. Were all clinically relevant outcomes measured and reported?
4. Is the size of the effect clinically important?
5. Are the likely treatment benefits worth the potential harms?

RESULTS

Description of studies

We identified 775 references in total and excluded 725 references after reviewing titles and abstracts. Fifty papers were retrieved in full, 34 of which were excluded. We have listed the reasons for exclusion in the Characteristics of excluded studies section. We excluded a further six articles, for a total of 40 excluded articles, because they were notes or comments on a previous study or repeated articles. Threfore, in the original search we included 10 articles(Chrubasik 1996; Chrubasik 1999; Chrubasik 2000; Chrubasik 2001a; Chrubasik 2003; Frerick 2003; Ginsberg 1987; Krivoy 2001; Keitel 2001; Stam 2001). In this search update (July 2005 to August 5, 2013), we identified a total of four citations that met the inclusion criteria (Chrubasik 2010; da Silva 2010; Giannetti 2010; Yip 2004), which we included with the 10 articles (Chrubasik 1996; Chrubasik 1999; Chrubasik 2000; Chrubasik 2001a; Chrubasik 2003; Frerick 2003; Ginsberg 1987;

Krivoy 2001; Keitel 2001; Stam 2001) identified in earlier literature searches. In a search update, through September 2014, we identified 5 citations with none meeting the inclusion criteria.

Three trials used an oral form of the herbal species *H. procumbens* (devil's claw; Chrubasik 1996; Chrubasik 1999; Chrubasik 2003), three trials used oral *S. alba* (white willow bark; Chrubasik 2000; Chrubasik 2001a; Krivoy 2001), five trials used topical *C. frutescens* (cayenne; Chrubasik 2010; Frerick 2003; Ginsberg 1987; Keitel 2001; Stam 2001), one used lavender essential oil applied by acupressure (Yip 2004), one used topical *S. chilensis* (Brazilian arnica; da Silva 2010), and one used topical *Symphytum officinale L.* (comfrey; Giannetti 2010).

Four trials compared various oral herbal medicines with placebo (Chrubasik 1996; Chrubasik 1999; Chrubasik 2000; Krivoy 2001). Two trials compared oral herbal medicines to standard pain medications (Chrubasik 2001a; Chrubasik 2003). Six trials compared topical herbal medicines to placebo (Chrubasik 2010; da Silva 2010; Frerick 2003; Giannetti 2010; Ginsberg 1987; Keitel 2001). One trial compared a topical herbal medicine to a topical homeopathic medicine (Stam 2001) and one trial compared a topical herbal medicine to no treatment (Yip 2004).

The three *H. procumbens* trials included participants with acute exacerbations of chronic non-specific LBP (Chrubasik 1996; Chrubasik 1999; Chrubasik 2003). Similarly, the three trials of *S. alba* preparations included homogeneous populations with acute episodes of chronic non-specific LBP (Chrubasik 2000; Chrubasik 2001a; Krivoy 2001). One trial using a topical *C. frutescens* ointment included patients with acute mechanical LBP (Ginsberg 1987). Two trials using a Capsicum pain plaster included participants with chronic non-specific LBP (Frerick 2003; Keitel 2001). One trial using Capsicum cream included patients with chronic pain of the soft tissues of the musculoskeletal apparatus, with a subgroup of back pain patients (Chrubasik 2010). A second trial using a topical Capsicum ointment included a sample of patients with either newly occurring acute LBP or acute episodes of chronic LBP (Stam 2001). The lavender essential oil trial included patients with non-specific sub-acute LBP (Yip 2004). The trial assessing *S. chilensis* included patients seeking treatment for a diagnosis of lumbago (da Silva 2010). Finally, the *S. officinale* trial included patients with acute non-specific upper or lower back pain (Giannetti 2010).

Three trials (Chrubasik 1996; Chrubasik 1999; Frerick 2003) used a relatively unknown LBP scale, the Arhus Index, which was designed to monitor outcomes of clinical trials of LBP. The Arhus Index is a back-pain specific index that includes physical impairment, pain, and disability scores, which are summed into a total score (Manniche 1994). The pain scale is rated by the patient and includes back pain and leg pain, with a score that ranges from 0 to 60. The disability scale consists of a questionnaire that asks about 15 daily tasks, with a score that ranges from 0 to 30. The physical impairment score is obtained by scoring on a deep knee bend, a modified Schober's test, a low-back strength test and a measure of analgesic use, with a total combined score ranging from 0 to 40. The higher the scores, the more physical impairment, pain and disability. This test takes approximately 15 minutes to complete. It has been shown to be a valid and reliable measure of LBP (Manniche 1994).

In the *H. procumbens* trials, Chrubasik 1996 used a standardized dosage of 50 mg harpagoside per day or 2400 mg of the crude extract; Chrubasik 1999 used daily dosages of the proprietary extract WS 1531 at 600 and 1200 mg of the crude herb, which was the equivalent of 50 and 100 mg harpagoside; and Chrubasik 2003 used a proprietary extract of Doloteffin, containing a daily dose of 60 mg harpagoside, or 12.5 mg rofecoxib (Vioxx®).

In the white willow bark extract trials, Chrubasik 2000 utilized an extract containing 0.153 mg salicin per mg and made comparisons between daily dose of 120 mg salicin, 240 mg of salicin and a matched placebo; Chrubasik 2001a used *S. alba* containing a daily dose of 240 mg salicin and compared it to 12.5 mg rofecoxib; and Krivoy 2001 used a daily dose of *S. alba* containing 240 mg salicin compared to placebo and 100 mg acetylsalicyliate.

The five trials of topical *C. frutescens* preparations used: a topical plaster application containing 11 mg of capsaicinoids per plaster (Keitel 2001); a plaster containing an ethonolic extract of cayenne pepper standardized to 22 $\mu g/cm^2$ of capsaicinoids (Frerick 2003); a gel called Cremor Capsici Compositus FNA (CCC), which contains 100 mg of Capsicum Oleoresin (BPC), 10 g of glycol salicylate, 1 g of methylnictinate, and a combined 1 g of histamine hydrochloride, sorbitol, methylprahydroxybenzoate, triethanolamine, lanette wax, stearic acid, and purified water (Stam 2001); a gel called Rado-Sailil, containing 17.64 mg acetylsalicylate, 26.47 mg methylsalicylate, 8.82 mg glycosalicylate, 8.82 mg salicylic acid, 4.41 mg camphor, 55.14 mg menthol and 15.44 mg Capsicum Oleoresin per gram (Ginsberg 1987); and a cream called Finalgon CPD Warmecreme, containing 2.2 to 2.6 g soft extract of capsici fructus acer corresponding to 53 mg capsaicin (0.05%) (Chrubasik 2010).

In the trial using *Symphytom officinale*, Giannetti 2010 used an ointment called Kytta-Salbe containing 35 g 99% reduced *Rad symphyti* fluid extract per 100 g.

The *S. chilensis* trial used a gel containing plant extract diluted in propylene glycol and added at a proportion of 5% to carbomer gel, corresponding to active substances in 5 g of dry raw material (da Silva 2010).

The trial that applied lavender oil using acupressure used 3% *Lavandula angustifolia* essential oil in grape seed oil.

Twelve of the 14 included studies reported information regarding adverse events associated with the study medication. We have reported details of the included trials in the Characteristics of included studies.

We assessed the included trials for any potential conflicts of interest by looking at funding sources (public vs. private) and whether a trial author was employed by a private pharmaceutical, nutraceutical, or herbal medicine manufacturer. Three trials reported no con-

flict of interest (Chrubasik 1999; Giannetti 2010; Ginsberg 1987). However, we deemed a conflict of interest possible in Giannetti 2010, as several trial authors were employed by pharmaceutical companies. The authors of eight trials had potential conflicts of interest (Chrubasik 1996; Chrubasik 2000; Chrubasik 2003; Chrubasik 2010; Frerick 2003; Giannetti 2010; Keitel 2001; Stam 2001). In five trials, an author was employed by a pharmaceutical company (Chrubasik 2010; Frerick 2003; Giannetti 2010; Keitel 2001; Stam 2001), one trial was funded by a professional academy (Chrubasik 2000), one trial was funded by a pharmaceutical company (Chrubasik 2003), and for one trial, the experimental herbal medicine was supplied by a company (Chrubasik 1996). The remaining trial was funded by an oil company; we could not determine whether this was a conflict of interest (da Silva 2010). In the final three trials (Chrubasik 2001a; Krivoy 2001; Yip 2004), we considered conflicts of interest unlikely.

Risk of bias in included studies

Two review authors (HNO and JG) assessed the methodological quality criteria in full of all included papers. Agreement between the review authors was over 98%. The mean score for methodological quality assessment criteria (Furlan 2009) of all included studies was 7.2, with a median score of 7.5 and a range of four to ten. Using a cut-off point of six fulfilled criteria out of 12, 11 trials (79%) were at low risk of bias (Chrubasik 1996; Chrubasik 1999; Chrubasik 2000; Chrubasik 2001a; Chrubasik 2003; Chrubasik 2010; Frerick 2003; Giannetti 2010; Keitel 2001; Krivoy 2001; Stam 2001). The main methodological shortcomings of the *H. procumbens* trials included a lack of reporting of allocation concealment, compliance rates, controls for co-interventions and acceptability of withdrawal or drop-out rates during the follow-up period. Of the included *S. alba* trials, one was an open-label trial and the additional two did not report allocation concealment, compliance rates, controls for co-interventions, or the acceptability of withdrawal or drop-out rates during the follow-up period. Stam 2001's capsicum trial was at low risk of bias. The additional capsicum trials (Frerick 2003; Keitel 2001; Ginsberg 1987; Chrubasik 2010) failed to report the type of randomization, allocation concealment, similarity of baselines, outcome assessor, investigator and participant blinding, comparability of co-interventions, and acceptability of compliance. The lavender Yip 2004 and Brazilian arnica da Silva 2010 trials were at high risk of bias, meeting less than half of the criteria. The comfrey trial failed to report randomization and treatment allocation, blinding of the outcome assessor, and similarity of the groups at baseline. The risk of bias assessment of each included trial is given in Figure 1.

Figure 1. Summary of risk of bias for each of the included trials.

GRADE

We applied the GRADE criteria to the included trials as recommended in Higgins 2011. Four treatments (Capsicum cream, Capsicum plaster, *S. alba*, and devil's claw) had several RCTs investigating their use, and we subsequently assessed them on all GRADE criteria. We assessed the remaining six treatments as having moderate to very low quality of evidence, as there was only one included RCT for each treatment.

We downgraded the evidence from three trials to low quality evidence due to limitations in study design (da Silva 2010; Ginsberg 1987; Yip 2004,). For two of these treatments (lavender and Brazilian arnica) there was evidence from only one RCT, therefore we downgraded the evidence to very low quality due to insufficient data and having less than 400 included participants. Giannetti 2010 had no other downgrades aside from being a singular study and having less than 400 included participants, resulting in a grade of low quality**.** The trials comparing Capsicum cream or plaster to placebo for chronic LBP (Chrubasik 2010; Frerick 2003; Keitel 2001) were analyzed together and determined to provide moderate quality evidence for this treatment. Ginsberg 1987 compared capsicum to placebo in acute LBP and was downgraded for study limitations and a small sample size. Stam 2001 was the only article examining Capsicum cream compared to a homeopathic gel; therefore we graded this evidence as very low quality due to a small sample size and low patient compliance. We downgraded the evidence from the trials comparing *H. procumbens* to placebo (Chrubasik 1996; Chrubasik 1999) for imprecise data and a sample size of less than 400, resulting in an overall grade of low quality. Chrubasik 2003 compared *H. procumbens* to rofecoxib was the only article to examine this comparison, and thus we downgraded the evidence due to study limitations (problems with allocation concealment and compliance) and a small sample size. Two trials assessed *S. alba* compared to placebo (Chrubasik 2000; Krivoy 2001); we rated this evidence as moderate quality due to a small sample size, potential selection bias, and differences in baseline characteristics. Finally, we rated the evidence from the single trial comparing *S. alba* to rofecoxib (Chrubasik 2001a) as very low quality due to indirectness, imprecision and a small sample size.

Clinical relevance

Four trials met all five clinical relevance criteria (Chrubasik 1996; Chrubasik 2000; Ginsberg 1987; Yip 2004). Of the trials testing *H. procumbens*, two trials did not meet items four and five (Chrubasik 1999; Chrubasik 2003). Of the *S. alba* trials, one did not meet item one (Krivoy 2001), one did not meet items four and five (Chrubasik 2001a) and it was not possible to tell if one trial fulfilled items four and five or not (Krivoy 2001). Of the *C. frutescens* trials, three did not meet item one (Chrubasik 2010; Ginsberg 1987; Keitel 2001), one did not meet item three (Chrubasik 2010), two did not meet items four and five (Frerick 2003; Stam 2001), and for Keitel 2001, it was not possible to tell if items four and five were met or not. Giannetti 2010 did not meet items 1 to 3, while da Silva 2010 did not meet item three and it was not possible to tell if it met item 5.

Reporting (CONSORT)

We assessed reporting in the published articles using the CONSORT statement and the CONSORT statement for herbal interventions. On average, the included trials had information on 45.3% of the CONSORT items, with a range from 19.4% (Ginsberg 1987) to 59.5% (Chrubasik 2000; Stam 2001). Items missing in over half of the included trials included a description of trial design, any changes to methods or outcomes after trial commencement, how sample size was determined, explanation of interim analyses and stopping guidelines, type of randomization, method used to implement the random allocation sequence (including who generated it), methods for subgroup or adjusted analyses, dates defining periods of recruitment and follow-up, why the trial was stopped, trial limitations and sources of bias, generalizability, registration number and name of trial registry, where the full protocol can be accessed, and sources of funding and support. Using the arbitrary cut-off of 50% of items, the average reporting in these trials was poor. However, eight trials had good completeness of reporting (Chrubasik 1999; Chrubasik 2000; Chrubasik 2001a; Chrubasik 2003; Chrubasik 2010; Giannetti 2010; Stam 2001; Yip 2004).

Also, we assessed reporting using the CONSORT statement for herbal interventions. Using these guidelines, the average trial included information on 45.4% of the checklist items, with a range from 27.3% (Ginsberg 1987) to 58.2% (Giannetti 2010). Information that was reported in under half of the trials included the Latin binomial for the herbal medicine product, the part of the plant used, the authority and family name of all herbal ingredients, the name of the manufacturer of the product, the type and concentration of extraction solvent used, the drug to extract ratio, the method of authentication of raw material, whether a voucher specimen was retained and where it is stored, how the duration of drug administration was determined, weight amount of all known herbal product constituents, qualitative testing of product, a description of the practitioners, concomitant herbal medicine use, and discussion of results in relation to other available products. Using the arbitrary cut-off of 50% of items, the average reporting in these studies was poor. However, five trials had good completeness of reporting (Chrubasik 1996; Chrubasik 2000; Chrubasik 2003; Chrubasik 2010; Giannetti 2010).

Effects of interventions

See: **Summary of findings for the main comparison** Summary of findings table 1: Brazilian arnica extract compared to placebo for patients with non-specific chronic back pain or soft tissue pain; **Summary of findings 2** Summary of findings table 2: Topical capsaicin cream or plaster compared to placebo for patients with non-specific chronic back pain or soft tissue pain; **Summary of findings 3** Summary of findings table 3: Topical capsaicin cream compared with placebo for patients with acute non-specific LBP; **Summary of findings 4** Summary of findings table 4: *H. procumbens* compared to placebo for non-specific chronic back pain; **Summary of findings 5** Summary of findings table 5: *H. procumbens* extract compared to Vioxx® for non-specific chronic LBP; **Summary of findings 6** Summary of findings table 6: Willow bark extract compared to placebo for non-specific chronic LBP; **Summary of findings 7** Summary of findings table 7: Willow bark extract compared to rofecoxib for non-specific chronic LBP; **Summary of findings 8** Summary of findings table 8: Comfrey root extract compared to placebo for acute lower and upper back non-specific pain; **Summary of findings 9** Summary of findings table 9: Lavender oil acupressure massage and acupoint stimulation compared to usual treatment for acute non-specific LBP; **Summary of findings 10** Summary of findings table 10: Spiroflor SRL compared to CCC for chronic non-specific LBP

1a) H. procumbens (devil's claw) verses placebo

The included two trials testing *H. procumbens* enrolled participants suffering from acute exacerbations of chronic LBP lasting longer than six months (Summary of findings 4).

Chronic LBP

50 mg Harpagoside dose

Two four-week trials, which included 315 participants, tested extracts of *H. procumbens* standardized to 50 mg harpagoside (H) per day versus placebo (Chrubasik 1996; Chrubasik 1999). Both trials found a significant increase in the number of pain-free patients in the 50 mg H group (9% to 17%) versus placebo (2% to 5%). One trial found that for participants taking 50 mg H, the percentage with no pain or mild LBP increased over the four week period (from 2% in week 1, to 24% in week 4), whereas the percentage with unbearable or severe pain decreased over the four weeks (from 59% in week 1 to 35% in week 4, (Chrubasik 1999). Tramadol consumption decreased more in both trials in the group that received 50 mg H than in the group that received placebo. However, this decrease did not reach statistical significance in Chrubasik 1999 and Chrubasik 1996 did not perform a statistical test on this measure. Both trials used the Arhus Index. The overall Arhus score improved by 21% in both the 50 mg H group and the placebo group, with no significant difference between groups. The pain subscale was significantly improved in favour of the 50 mg H group in both trials (median change for those with current LBP of 43%, Chrubasik 1999; median change of 34%, Chrubasik 1996), which was a greater improvement than that of the group that received an additional 100 mg H in one trial (median change for those with current LBP of 37%, Chrubasik 1999).

Based on this low quality evidence, a daily dose of 50 mg harpagoside in an aqueous extract of *H. procumbens* may reduce pain more than placebo in the short-term, in patients with acute episodes of chronic non-specific LBP. Long-term treatment data are not yet available.

100 mg Harpagoside dose

Chrubasik 1999, a four-week trial which included 197 participants, tested *H. procumbens* standardized to 100 mg harpagoside (H) per day versus placebo. The number of patients who were pain-free for at least five days in the fourth week of treatment was significantly higher (N = 10) than in either the placebo (N = 3) or lower dose (50 mg H) groups (N = 6). Half of the pain-free patients in the 100 mg H group had a neurological deficit at the start of the trial. The changes from baseline in the overall Arhus Index, the pain index, invalid index and physical impairment index did not differ between the three groups. The percentage of patients with no or mild LBP increased over the four-week period, whereas the percentage with unbearable or severe pain decreased.

Therefore, there is low quality evidence that a daily dose of 100 mg harpagoside in an aqueous extract of *H. procumbens* may lead to a greater number of patients who are pain-free for at least five days, in the fourth week of treatment of acute episodes of chronic non-specific LBP. Superiority of the higher dose has not been shown.

1b) S. alba versus placebo

We included two trials which enrolled participants suffering from acute exacerbations of chronic LBP lasting longer than six months (Summary of findings 6).

Chronic LBP

120 mg salicin dose

A four-week trial, including 210 participants, tested two doses of *S. alba*, standardized to either 120 mg or 240 mg salicin (S) per day, against placebo (N = 70 for each group; Chrubasik 2000). The number of patients who were pain-free for at least five days in the fourth week of treatment increased from baseline in the placebo (N = 4), 120 mg salicin group (N = 15) and the 240 mg salicin group (N = 27), with the trend for dose being significant. The number of patients requiring relief medication (Tramadol) during

each week decreased to 33 during week four for the placebo group, 10 for the 120 mg salicin group and three for the 240 mg salicin group; with the trend for dose being significant. The total Arhus Index, pain index, invalid index, and physical impairment index did not change from baseline for the placebo group but improved in the groups receiving either 120 mg or 240 mg salicin. The trend for dose was significant, with the group receiving 240 mg salicin showing more improvement in the total Arhus Index score and the pain index than the group receiving 120 mg salicin group.
There is moderate quality evidence that a daily dose of 120 mg salicin from an extract of *S. alba* results in more pain-free patients in the short-term for individuals with acute episodes of chronic non-specific LBP.

240 mg salicin dose

Two trials included 261 patients tested 240 mg salicin (Chrubasik 2000; Krivoy 2001). Results for the Chrubasik 2000 trial are reported above. In summary, for the 240 mg salicin per day, there were more participants who were pain-free for five days during the fourth week of treatment, and fewer patients required relief medication. There was a trend of greater improvements with higher dose for all outcomes and significant differences between the groups receiving 120 mg and 240 mg salicin for the total Arhus Index score and the pain index. The additional trial by Krivoy 2001, which was designed to test platelet aggregation of *S. alba* extract, did not measure clinically relevant outcomes. Although the trial authors stated that fewer patients in the group receiving 240 mg salicin required rescue medication (i.e. Tramadol) than in the placebo group, they did not provide any data.
Based on moderate quality evidence a daily dose of 240 mg salicin from an extract of *S. alba* probably reduces pain more than either placebo or a daily dose of 120 mg of salicin in the short term for individuals with acute episodes of chronic non-specific LBP.

1c) C. frutescens versus placebo

We included four trials: one that enrolled participants with acute LBP (Ginsberg 1987), though the actual duration of LBP was not described; two trials with participants with chronic LBP that had lasted longer than three months (Frerick 2003; Keitel 2001); and one trial which included participants with chronic soft tissue pain (with a subset of patients experiencing chronic back pain) and did not describe duration of pain (Chrubasik 2010; Summary of findings 2; Summary of findings 3).

Acute LBP

Cream

Ginsberg 1987 gave 40 participants with acute mechanical LBP either a cream called Rado-Salil, containing salicylate and capsicum (N = 20) or a placebo cream containing bergamot and lavender (N = 20) for 14 days. At day three, there was an improvement in pain score in the Rado-Salil group of almost 2 cm on the VAS, which was significantly better than the placebo group. By day 14, the improvement increased to 3.79 cm, which was also significantly greater than the placebo group. In addition, both patients and physicians rated the effect of Rado-Salil more favourably than the placebo group rated the effect of their cream.

Chronic LBP

Cream

Chrubasik 2010 included 281 participants suffering from chronic non-specific soft-tissue pain who were randomly allocated to either a placebo cream group (N = 141) or a Capsicum cream group (N = 140) for 21 days. A reduction in pain by at least 30% was achieved in 75.0% of the Capsicum group and 40.9% of the placebo group. A reduction in pain by at least 50% was achieved in 50.0% of the Capsicum group and 28.8% of the placebo group. The median relative pain sum score improvement was 48.9% in the Capsicum group and 22.5% in the placebo group. The capsicum treatment was rated as either "excellent" or "good" by patients in 59.3% of cases compared to 21.9% for the placebo group. The absolute number of days where patients reported an analgesic effect were > 70% among the Capsicum group and below 30% in the placebo group. For the majority of patients, the maximum effect was reached within two hours after application, and in 50% of patients the effect persisted for two to four hours.

Plaster

Keitel 2001 included 154 participants with acute episodes of chronic non-specific LBP, who were randomly allocated to either a placebo plaster group (N = 77) or a Capsicum plaster group (n = 77) for three weeks. A reduction in pain by at least 30% was achieved in 60.9% of the Capsicum group and 42.1% of the placebo group. A reduction in pain by at least 50% was reported in 35.1% of the Capsicum group and 17.1% of the placebo group. The total Arhus score improved significantly more in the group using Capsicum (38.5%) than in the group using placebo (28%). Physician global ratings of efficacy were considered "excellent" or "good" in 75.7% of those using Capsicum and 47.4% of those using the placebo. After treatment, 13.5% of participants using Capsicum and 6.6% using placebo were symptom-free. Compliance was 90.6% in the group using Capsicum and 88.1% in the group using placebo.
Frerick 2003 enrolled 320 participants suffering from chronic non-specific LBP, who were randomly allocated to either a placebo plaster group (N = 180) or a Capsicum plaster group (N = 180) for 21 days. The total Arhus Index score decreased significantly

more in the group using Capsicum (33%) than in the group using placebo (22%). The Arhus compound pain score decreased significantly more in the group using Capsicum (42%) than in those using placebo (31%). A reduction in pain by at least 30% was achieved in 67% of those using Capsicum and 49% in those using placebo, and a reduction in pain by at least 50% was seen in 45% and 24%, respectively. The Arhus subscale for physical impairment also decreased significantly more in the Capsicum group (21%) than in the placebo group (10%). Similar results were found for the disability subscale (35% vs. 22%, respectively). The capsicum treatment was rated as either "excellent" or "good" by investigators in 74% of cases compared to 36% for the placebo group. Compliance was reported as being "very good" or "good" in both groups (91% and 93%, respectively).

Therefore, there is moderate quality of evidence that a plaster and moderate quality evidence that a cream of *C. frutescens* reduces pain and improves function more than placebo in the short-term for individuals with chronic non-specific LBP. There is very low GRADE of evidence that a cream of *C. frutescens* may reduce pain more than placebo in the short-term for individuals with acute non-specific LBP.

1d) S. officinale versus placebo

Acute LBP

Giannetti 2010 included 120 participants with acute non-specific upper or lower back pain, and randomized participants to either-comfrey ointment treatment (N = 60) or placebo ointment (N = 60) for five days, with three applications per day. Over the course of the treatment, pain intensity by VAS decreased 95.2% in the comfrey group, a significant difference from the placebo group (37.8%). Reported back pain at rest decreased 97.4% in the comfrey group compared to 39.6% in the placebo group. Pressure algometry values in the trigger point increased 125% in the comfrey group and 71.8% in the placebo group. Global assessment of efficacy by patients and investigators were all superior in the comfrey group (good or excellent for 80%) compared to the placebo group (good or excellent for 18.4%) (Summary of findings 8).

There is low quality evidence that a cream of *S. officinale* reduces pain more than placebo in the short-term for individuals with acute episodes of upper or lower back pain.

1e) S. chilensis versus placebo

da Silva 2010 randomized 20 patients seeking treatment for lumbago to either treatment with *S. chilensis* gel (N = 10) or placebo gel (N = 10) for 15 days. Each gel was applied twice per day. The *S. chilensis* treatment group reported a significant change in pain, as assessed by VAS at the end of the treatment period compared to baseline values. Also they experienced a significant increase in lumbar flexibility. Participants treated with placebo did not experience significant changes in perception of pain or lumbar flexibility over the course of treatment. The placebo and treatment groups were not statistically compared to one another.

Therefore, based on low quality evidence, *S. chilensis* gel may reduce pain and improve lumbar flexibility in the short term for people with lumbago (Summary of findings for the main comparison).

2a) H. procumbens versus rofecoxib

Chronic LBP

Chrubasik 2003 included 88 patients with acute episodes of chronic non-specific LBP in a six-week trial, and tested *H. procumbens* standardized to 60 mg harpagoside per day (N = 44) versus 12.5 mg rofecoxib per day (N = 44). There were no significant differences in the number of patients who were pain-free for at least five days in the sixth week of treatment in the 60 mg *H. procumbens* group (10/44) than in the rofecoxib group (5/44). The number of patients with improvements in pain scores did not differ between the two groups. This trial may lack power due to its small sample size. The number of patients using rescue medication (Tramadol) decreased from baseline in both groups, but did not differ between groups at week six. At the end of six weeks, there were no differences between groups for current LBP, scores on the Arhus pain index, invalid index, functional index, or the total score for the Arhus Index. The health assessment questionnaire (HAQ) improved in both groups during the six-week period, with no differences between groups.

Therefore, based on current evidence, it is unclear whether a daily dose of 60 mg harpagoside in an aqueous extract of *H. procumbens* differs in effectiveness compared to a daily dose of 12.5 mg rofecoxib in the short-term for individuals with acute episodes of chronic non-specific LBP (*very low quality evidence*; Summary of findings 5).

2b) S. alba versus rofecoxib

Chronic LBP

Chrubasik 2001a included 228 participants with acute episodes of chronic non-specific LBP in a four-week trial, and tested *S. alba* standardized to provide a daily dose of 240 mg salicin against 12.5 mg per day of rofecoxib. Both the rofecoxib and the 240 mg salicin groups improved by 44% on the pain scale, the Arhus invalid index, pain index, and physical impairment index. The percentage of patients requiring NSAIDs, Tramadol, or both was 10% for the *S. alba* group and 13% for the rofecoxib group. Approximately 90% of physicians and patients rated either treatment as effective and close to 100% rated either treatment as acceptable.

It is unclear, based on current evidence whether a daily dose of 240 mg salicin (of an extract of *S. alba*) is more effective than a daily dose of 12.5 mg rofecoxib in the short term for people with acute episodes of chronic non-specific LBP in the short-term (*very low quality evidence*; Summary of findings 7).

3) C. frutescens versus homeopathic treatment

Acute and chronic LBP

Stam 2001 included 161 participants, who were a mixed group of patients with new acute LBP and acute episodes of chronic LBP. Participants were randomly allocated to either a Spiroflor SLR homeopathic gel (SLR) group (N = 83) or the CCC, the Capsici Oleoresin gel, group (N = 78) for a period of seven days. Each of the gels was applied at 3 g/day. Both groups showed a significant reduction in pain on the VAS scale, with a decrease of 38.2 mm in the SLR group and 36.6 mm in the CCC group. In the SLR group, 50% of participants reported that treatment was 80% effective and 18% reported total (100%) effectiveness. In the CCC group, this was 55% and 15%, respectively. There were also no differences in the proportion of participants using paracetamol, the proportion of participants still unable to work at the end of the study, and overall efficacy.

Based on current evidence, it is unclear whether Spiroflor SLR homeopathic gel and CCC gel differ in efficacy (*very low quality evidence*;Summary of findings 10).

4) Lavender versus conventional treatment

Acute LBP

Yip 2004 included 61 participants with non-specific sub-acute LBP for most days in the previous four weeks. The trial used lavender essential oil, applied by acupressure eight times over a three-week period, to treat 32 participants. "Conventional treatment", which is not described in the text, was used to treat the remaining 29 participants. One week after the end of the study, the intervention group reported significantly lower pain ratings (39% reduction) than the control group (no change). Both groups reported similar decreases in pain duration. Improvements were also seen in the lavender group in walking time and fingertip-to-floor distance, but these changes were functionally insignificant (9% and 4% changes, respectively). Acceptance of the intervention was rated as "satisfied" or "strongly satisfied" by 93% in the lavender-treatment group. Trial authors did not report acceptance of the control group.

Therefore, based on current evidence it is unclear whether lavender essential oil applied via acupressure treatments significantly reduces perception of pain among people reporting non-specific sub-acute LBP (*very low quality evidence*; Summary of findings 9).

ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Topical capsaicin cream or plaster compared to placebo for patients with non-specific chronic back pain or soft tissue pain

Patient or population: patients with chronic LBP or soft tissue pain
Settings: Outpatient clinic
Intervention: topical capsicum cream or plaster
Comparison: placebo

Outcomes	No of participants (trials)	Quality of the evidence (GRADE)	Comments
Pain perception according to the Pain VAS scale 0-10	755 (three trials)	⊕⊕⊕◯ **moderate**[1]	All three trials found a statistically significant difference between the capsaicin intervention vs. placebo. In three trials minor adverse effects were noted in the treatment groups requiring no specific follow-up treatments

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] All three trials exhibited low to unclear risk in selection bias, performance bias and attrition bias. One trial was at high risk for selective reporting.

Topical capsaicin cream compared with placebo for patients with acute non-specific LBP

Patient or population: patients with acute mechanical LBP
Settings: outpatient clinic
Intervention: Rado-Salil ointment
Comparison: placebo

Outcomes	No of participants (trials)	Quality of the evidence (GRADE)	Comments
Pain evaluation on a 10 cm linear scale	40 (one trial)	⊕◯◯◯ **very low**[1,2]	Pain improvements were significantly greater in the capsicum cream group up to day 14. Adverse events: Pruritis, one in placebo, one in Rado-Salil group. Local erythema and burning, three in the Rado-Salil group

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Exhibited unclear risk for selection bias as well unclear baseline similarities. Performance bias was low risk as was attrition bias but it was high risk for incomplete outcome data.
[2]As under 400 participants were included, evidence was downgraded to very low from low.

H. procumbens compared to placebo for non-specific chronic back pain

Patient or population: patients with chronic back pain
Settings: outpatient clinic
Intervention: *H. procumbens* extract
Comparison: placebo

Outcomes	No of participants (trials)	Quality of the evidence (GRADE)	Comments
Arhus pain index scale 0-130	315 (two trials)	⊕⊕◯◯ **low**[1,2]	In one trial a 50mg dose of *H. procumbens* was used, and in the second trial a 50 mg and 100 mg dose was used with both trialss showing a significantly improved pain score over placebo.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Both included trials exhibited low risk of bias regarding selection bias with one trial at unclear risk of bias. Performance bias was at low risk of bias, as was attrition bias with one trial at high risk of bias for incomplete outcome data.
*2*Two trials included under 400 participants and we downgraded the evidence to low from moderate.

H. procumbens extract compared to Vioxx®for non-specific chronic LBP

Patient or population: patients with chronic LBP
Settings: outpatient clinic
Intervention: *H. procumbens* extract
Comparison: Vioxx®

Outcomes	No of participants (trials)	Quality of the evidence (GRADE)	Comments
Modified Arhus Index Scale 0-120	88 (one trial)	⊕◯◯◯ **very low**[1,2]	*H. procumbens* was compared to Vioxx® and while both groups showed similar pain reduction scores there were no demonstrable difference among groups. There were adverse effects noted in both groups.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]This trial was at low risk of bias for all risk of bias factors, with the exception of allocation concealment and compliance which were at unclear risk of bias.
[2]Downgraded to very low versus low as under 400 participants were included.

Willow bark extract compared to placebo for non-specific chronic LBP

Patient or population: patients with chronic LBP
Settings: outpatient clinic and public advertisement
Intervention: willow bark extract
Comparison: placebo

Outcomes	No of participants (trials)	Quality of the evidence (GRADE)	Comments
Pain VAS Scale 0-10	261 (two trials)	⊕⊕⊕◯ **moderate**[1,2]	The high dose (240 mg) treatment group showed a significant reduction in pain scores versus the low dose (120 mg) group and the placebo group. There was

		one severe allergic reaction related to the extract noted. One trial (N = 51) also examined the effect of the extract on platelet aggregation.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Both trials were at low to unclear risk for selection bias, low risk for performance bias with one trial exhibiting high risk in baseline characteristics similarity. Both trials were rated as an overall low risk of bias since they met our predetermined cut-point of 50% of the criteria on which the trial methods were assessed.
[2]Downgraded from high to moderate as under 400 participants were included between both trials.

Willow bark extract compared to rofecoxib for non-specific chronic LBP

Patient or population: patients with chronic LBP
Settings: outpatient clinic
Intervention: willow bark extract
Comparison: rofecoxib

Outcomes	No of participants (one trial)	Quality of the evidence (GRADE)	Comments
Arhus Index Scale 0-130 Pain VAS Scale 0-10	228 (one trial)	⊕◯◯◯ **very low**[1,2]	There was no significant difference in the effectiveness and adverse events between the extract and rofecoxib.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Low risk for selection bias, high risk for performance bias, and high and low risk for attrition bias.
[2]Downgraded from low to very low due as under 400 participants were included.

Comfrey root extract compared to placebo for acute lower and upper back non-specific pain

Patient or population: patients with acute lower and upper back pain
Settings: outpatient setting
Intervention: comfrey root extract
Comparison: placebo

Outcomes	No of participants (studies)	Quality of the evidence (GRADE)	Comments
Pain VAS sum (decrease) on active standardized movement (mm)	120 (one trial)	⊕⊕◯◯ **low**[1,2]	The root extract showed a statistically and clinically relevant reduction in acute back pain versus placebo.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Unclear risk for selection bias, low risk for both performance and attrition bias.
[2]Downgraded from moderate to low as under 400 participants were included.

Lavender oil acupressure massage and acupoint stimulation compared to usual treatment for acute non-specific LBP

Patient or population: patients with acute LBP
Settings: old aged home and community centre
Intervention: lavender oil massage
Comparison: usual therapy

Outcomes	No of participants (trials)	Quality of the evidence (GRADE)	Comments
Pain VAS 0-10 scale	61 (one trial)	⊕◯◯◯ **very low**[1]	One week post-study the treatment group showed a significant (P = 0.0001) reduction in VAS pain as well as improved walking time and lateral spine flexion range.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Sequence generation was at low risk of bias but allocation concealment was at high risk. Performance bias was at high and unclear risk. Co-interventions and timing outcome assessment factors were at high risk of bias.

Spiroflor SRL compared to CCC for chronic non-specific LBP

Patient or population: patients with acute and chronic LBP
Settings: outpatient clinic
Intervention: Spiroflor SRL
Comparison: CCC

Outcomes	No of participants (trials)	Quality of the evidence (GRADE)	Comments
Pain VAS 0-100 scale	161 (one trial)	⊕◯◯◯ **very low**[1]	Spiroflor SRL and CCC were equally effective in treating acute LBP but the CCC group experienced greater adverse events and adverse drug reactions.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

CCC = Cremor Capsici Compositus FNA; SRL = Homeopathic combination of *Symphytum officinale, Rhus toxicodendron* and *Ledum palustre*
[1]All risk of bias factors were at low risk of bias, except patient compliance which was at high risk.
[2]Downgraded from low to very low as under 400 participants were included.

Quality of the evidence

We included 14 RCTs in this review. Three trials examined *H.*

DISCUSSION

procumbens (devil's claw), three trials examined *S. alba* (white willow bark), five assessed *C. frutescens* (cayenne), one examined *S. officinale* (comfrey), one *Lavandula angustifolia* (lavender), and one *S. chilensis* (Brazilian arnica). Although reporting quality in the included trials was poor, risk of bias is not directly related to reporting quality (Huwiler-Muntener 2002). Therefore, the risk of bias of poorly reported trials remains unclear. We attempted to contact all trial authors to clarify aspects of trials that were inadequately reported in the published manuscripts but did not receive replies from several corresponding trial authors.

Efficacy

The results of the included trials suggest that specific herbal medicines may be effective for short-term (four to six weeks) improvement in pain and functional status for individuals with acute episodes of chronic non-specific LBP. Ten trials were placebo-controlled while four trials were comparative. There is insufficient evidence to make definitive conclusions regarding those trials comparing herbal medicine interventions to standard drugs. Two of the comparative trials used Vioxx® as a comparator (Chrubasik 2001a; Chrubasik 2003), another used a homeopathic topical preparation (Stam 2001), and the last compared to "conventional treatment" (Yip 2004). Given the severe adverse effects of Vioxx® and its subsequent removal from the retail market, additional trials testing these herbal medicines against standard drugs (acetaminophen, NSAIDs) are needed.

Although the majority of these trials were considered to have homogenous LBP populations, we were unable to pool and analyse trial data due to lack of reporting of sufficient raw data. Therefore, we could not provide quantitative evidence of efficacy of the six individual herbal medicines used in these trials. Instead, we used the GRADE criteria to synthesize the data. The included trials did not assess long term efficacy (e.g. return to work, recurrence) and therefore remains to be determined.

Given the overwhelming evidence that conflicts of interest may bias trial results, we assessed the potential for conflict of interest in these trials. We determined that a conflict of interest was a possibility in eight included trials. It is not possible to determine the specific influence of these potential conflicts on results of this Cochrane Review.

This review highlights research that, when combined, indicates that there are at least four herbal medicines that have low to moderate quality of evidence for the short-term treatment of acute episodes of non-specific LBP. These interventions are reported to have very few side effects, but more research is required to extensively explore the safety of these herbals. The adverse effects appear to be primarily confined to mild, transient gastrointestinal complaints and skin irritations. Large observational studies are needed to explore the relative safety of these herbals to standard medications such as acetaminophen and NSAIDs.

This review has several strengths, including the comprehensive search strategy, the inclusion of only the highest quality trial design and use of suggested methods for systematic reviews of interventions for LBP (Furlan 2009). One drawback of this review is that many included trials were authored by the same trialists (Chrubasik and colleagues). It is possible that the results may be systematically biased in some way. It is imperative that trials of these herbal medicines be repeated by other research groups and in different settings.

The qualitative analysis used here may be regarded as a strength and drawback. That is, though it would have been incorrect to statistically combine data from heterogeneous trials, the qualitative method used does not provide information on the size of the treatment effect. Without this quantitative data it is hard to determine whether these herbal interventions cause clinically significant effects on patients suffering from non-specific LBP. Quantitative analyses were precluded by incomplete reporting of data in these trials. Evidence suggests that reporting of clinical trials, irrespective of the intervention, is poor (e.g. Moher 2001). Specifically, RCTs of herbal interventions report less than half of the required information as outlined by the CONSORT statement (Gagnier 2006a). An extension of the CONSORT statement for the reporting of RCTs of herbal medicine interventions has been developed and should be referred to when reporting such trials (Gagnier 2006b). These guidelines will aid trialists in planning, implementing, and reporting controlled clinical trials.

Another point of note is from the known heterogeneity of herbal medicine products. That is, herbal medicines often vary in the type of preparation (liquid, VS dried, VS topical) and thus in the amount of chemical constituents per dose. These variations influence the pharmacokinetics and therefore the relative efficacy of these products.

Summary of main results

We included 14 trials (2050 participants) in this Cochrane Review. Daily doses of *H. procumbens* (Devil's Claw) standardized to 50 mg or 100 mg harpagoside may be better than placebo for short-term improvements in pain and reduced use of rescue medication (two trials, 315 participants, *low quality evidence*). Another *H. procumbens* trial demonstrated relative equivalence to 12.5 mg per day of rofecoxib (Vioxx®) (one trial, 88 participants, very *low quality evidence*). Daily doses of *S. alba* (White Willow Bark) standardized to 120 mg or 240 mg salicin are probably better than placebo for short-term improvements in pain and rescue medication (two trials, 261 participants, *moderate quality evidence*). An additional trial demonstrated relative equivalence to 12.5 mg per day of rofecoxib (one trial, 228 participants, *very low quality evidence*). *S. alba* minimally affected platelet thrombosis versus a cardioprotective dose of acetylsalicylate (one trial, 51 patients). *C. frutescens* cream produced more favourable results than placebo and *C. frutescens* plaster produced more favourable results than placebo in people

with chronic LBP (three trials, 755 participants, *moderate quality evidence*). Also, *C. frutescens* cream was preferable to placebo in people with acute LBP (one trial, 40 patients, *very low quality evidence*). Another trial found equivalence of *C. frutescens* cream to a homeopathic ointment (one trial, 161 participants, *very low quality evidence*). *S. officinale L.* (comfrey root extract) applied three times daily may be better than placebo ointment for short-term improvements in pain (one trial, 120 participants, *low quality evidence*). *S. chilensis M.* (Brazilian arnica) found very low quality evidence of reduction in perception of pain and improved flexibility with application of Brazilian arnica-containing gel twice daily as compared to placebo gel (one trial, 20 participants, *very low quality evidence*). Aromatic lavender essential oil applied by acupressure reduced subjective pain intensity and improved lateral spine flexion and walking time compared with participants who were not offered treatment (one trial, 61 participants, *very low quality evidence*). There were no significant adverse events noted within the trials included in this Cochrane Review.

Implications for practice

A topically applied plaster or cream of *C. frutescens*, and a cream of *S. officinale* appear to reduce pain more than placebo. These herbal medicines could be considered as a treatment option for acute (*S. officinale*) and of chronic LBP (*C. frutescens*).

Implications for research

Additional large RCTs at low risk of bias and completely reported must be done to determine if the herbal medicines discussed above are effective in the treatment of acute and chronic LBP. In particular, more trials are needed that include people with acute and subacute LBP. Also, additional trials testing these herbal medicines against standard treatments (acetaminophen, NSAIDs) will clarify their equivalence in terms of efficacy and effectiveness. The quality of reporting in these trials was generally poor and thus trialists should refer to the CONSORT and related statements in designing and reporting clinical trials of herbal medicines.

AUTHORS' CONCLUSIONS

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Chrubasik 1996

Methods	RCT with two groups. Patients were placed in groups by random number allocation. Period: Four weeks
Participants	118 participants were allocated to a *H. procumbens* (H) group (N = 59) and a placebo (P) group (N = 59)and 109 participants completed the trial (H; N = 54; P; N = 55). Inclusion criteria: participants were between 18 to 75 years of age, had at least six months of LBP not attributable to identifiable causes, were suffering from acute increases in pain, and were expected to require at least four weeks of symptomatic treatment. Exclusion criteria: participation in other clinical studies or had done so within the past 30 days, pregnancy, lactation, insufficient contraception, difficulties with language or cooperation, known allergy to proposed trial medication, history of drug or alcohol abuse, requirement of psychotherapeutic agents, or a serious organic illness affecting any of the organ systems
Interventions	Oral form of *H. procumbens* (devil's claw) standardized to a dosage of 50 mg harpagoside per day or 2400 mg of the crude extract. Matched placebo.
Outcomes	Primary: cumulative requirement for Tramadol (an oral opiate-based analgesic) over the last three weeks of the study period. Secondary: number of pain free patients based on a five-point visual rating scale and the Arhus LBP index
Notes	Total Quality Score: 7/12 Adverse events: four adverse effects occurred in the *H. procumbens* group with only two potentially due to the treatment (i.e. repeated coughs and tachycardia). A total of 10 adverse events occurred in the P group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were placed in groups by random number allocation
Allocation concealment (selection bias)	Unclear risk	Further description beyond randomized allocation is not included
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	Treatment group assignment blinded to participants.
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	Treatment group assignment blinded to providers.

Chrubasik 1996 (*Continued*)

Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	Blinding done and unlikely the blinding was broken.
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	Only nine participants were lost to attrition, with the remaining 109 participants completing all outcome measures. Missing data not related to outcomes
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	High risk	Treatment group had four participants not complete the final examination and one suffered tachycardia; the control group had four participants not complete the final examination, but participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Low risk	No significant difference within baseline characteristics between groups
Co-interventions avoided or similar?	Unclear risk	Unclear from text.
Compliance acceptable?	Unclear risk	Unclear from text.
Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	Low risk	All prespecified outcomes were reported.

Chrubasik 1999

Methods	RCT with three groups. Period: four weeks
Participants	One hundred and ninety-seven participants allocated to *H. procumbens* at 600 mg (N = 65), or 1200 mg (N = 66) or matched placebo (N = 66) Inclusion criteria: 18 to 75 years of age, six months of non-specific LBP, a current exacerbation of their complaint that was effecting both rest and movement, which was giving rise to pain greater than five on a 1-10 VAS and was expected to require at least four weeks of symptomatic treatment. Exclusion criteria: current or recent participation in any other clinical study, serious organic illness effecting any organ system, a history of drug or alcohol abuse or requirement for psychotherapeutic agents, pregnancy (actual or possible), or lactation, known allergy to any the proposed trial medications, difficulties with language or anticipated co-operation
Interventions	*H. procumbens* extract WS 1531 600 mg (50 mg harpagoside), 1200 mg (100 mg harpagoside)

Chrubasik 1999 (*Continued*)

Outcomes	Primary outcome: proportion of pain-free participants without Tramadol for at least five days during the last week of treatment. Secondary outcomes: Arhus index, percentage requiring Tramadol, verbal pain ratings
Notes	Total Quality Score: 8/12 Adverse effects included: nine participants with gastrointestinal upset (four in each active group and one in the placebo group)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization was conducted via stratified random allocation based on informed consent sequence
Allocation concealment (selection bias)	Unclear risk	No additional information provided beyond randomization method
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	Treatment allocation blinded to participants.
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	Treatment allocation blinded to providers.
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	Treatment allocation blinded to both participants and providers and not likely broken. Treatment and placebo medications identical in appearance
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	All participants completed the study.
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Low risk	Groups were well matched for age, height, weight, and gender and of 120 matched indicators only four would have reached statistical significance in single isolated comparisons
Co-interventions avoided or similar?	Unclear risk	Unclear from text.
Compliance acceptable?	Unclear risk	Unclear from text.

Chrubasik 1999 (*Continued*)

Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	Low risk	All prespecified outcomes were reported.

Chrubasik 2000

Methods	RCT with three groups. No report of randomization method. Period: four weeks
Participants	Participants were recruited from the Haifa area in Israel between May and November. Two hundred and ten participants were randomized into three groups (N = 70 in each group) and 191 completed the trial (P; N = 59; 120; N = 67; 240; N = 65). Inclusion criteria: Between 18 and 75 years of age, at least six months of intermittent LBP that was not attributable to identifiable causes, a current exacerbation of their complaint at rest and with movement that caused pain of at least five out of 10 on a VAS, and that was expected to require at least four weeks of treatment. Exclusion criteria: participation in other clinical studies or had done so in past 30 days, pregnancy, lactation, insufficient contraception, difficulties with language or cooperation, known allergy to proposed trial medication, history of drug or alcohol abuse, requirement of psychotherapeutic agents
Interventions	Extract of dry willow bark (*S. alba*): 120 mg salicin, 240 mg salicin. Matched placebo.
Outcomes	Primary outcome: the proportion of participants who responded to treatment by being pain free without Tramadol for at least five days during the last week of treatment. Secondary outcome: The Arhus LBP Index scores
Notes	Total quality score: 7/12 Adverse events: one adverse reaction (exanthem, swollen eyes, pruritis) could be attributed to the 120 mg willow bark extract group. A total of two participants in the 240 mg group reported short lasting adverse events (dizziness attributed to Tramadol, dizziness and fatigue). These patients dropped-out for seemingly unrelated reasons. Six adverse events were reported in the placebo group including three attributable to Tramadol (dizziness or headache; dizziness, vomiting ordiarrhoea; dry mouth) and the three others reported mild abdominal pain, two of whom dropped out on the first day of the trial

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Three group randomized double-blind study with randomization conducted by "computerized list" but no further details provided
Allocation concealment (selection bias)	Unclear risk	Unclear from text.

Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	Participants were given identical coded tables.
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	Investigators were blinded from the medication coding scheme
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	Treatment allocation blinded to both participants and providers and not likely broken. Treatment and placebo medications identical in appearance
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	191 participants out of 210 completed baseline and final outcome measures. Analysis was conducted with and without drop-out data
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	High risk	Baseline characteristics were similar across all three groups only differing on six reported factors out of 110
Co-interventions avoided or similar?	Unclear risk	Unclear from text.
Compliance acceptable?	Unclear risk	Unclear from text.
Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	Low risk	All prespecified outcomes data and analyses was available.

Chrubasik 2001a

Methods	Open RCT with two groups comparing an herbal medicine (*S. alba*) to a synthetic antirheumatic (rofecoxib). Period: four weeks.
Participants	228 participants divided equally in to two groups (N = 114 per group). Inclusion criteria: age 18 to 80, at least six months non-specific LBP. Exclusion criteria: recent trauma, a history of cancer or risk factors for spinal infection, unexplained weight loss or recent fever or chills, pain exacerbated by being supine or severe nocturnal pain, perineal anaesthesia, recent onset of bladder dysfunction or severe progressive neurological deficit in the lower extremity, recent participation in other clinical trial, serious organic illness affecting any organ system, a history of drug or alcohol abuse or requirement for psychotherapeutic drugs, pregnancy or lactation, known allergy

Chrubasik 2001a (*Continued*)

	to salicylates, difficulties with language or expected corporation
Interventions	A proprietary extract of *S. alba* called Assalix at four capsules per day providing a total of 240 mg of salicin per day, or a single 12.5 mg tablet of rofecoxib per day
Outcomes	Pain on a VAS, modified Arhus index, its pain component and the total pain index, physician and patient-rated success and the acceptability of the treatment on a verbal scale (very good, good, moderate, poor)
Notes	Total quality score: 6/12 Adverse events: 23 in the *S. alba* group (13 of gastrointestinal (GI) origin, five cutaneous allergy, remaining undefined), and 27 in the rofecoxib group (17 GI effects, one asthma, the remainder undefined). Trial authors judged GI adverse events as more severe and caused more withdrawals in the rofecoxib group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization completed by pre-determined computer-generated random sequence
Allocation concealment (selection bias)	Low risk	Group allocation concealed prior to the start of the trial.
Blinding (performance bias and detection bias) All outcomes - patients?	High risk	Participants only blinded to group allocation until after enrolment were non-blinded at study start
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	Providers not blinded to group allocation.
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	The only blinded provider was an independent reviewer for adverse outcomes
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	Forty-five participants were disenrolled prior to the trial conclusion, leaving 183 participants which allows adequate number of participants per group. The PAID group lost 21 participants (five due to non-compliance, one for severe LBP, and 12 due to adverse events), the NSAID group lost 24 participants (six for non-compliance, three for severe LBP, three for other pain reasons, and 14 to adverse events)

Chrubasik 2001a (*Continued*)

Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	High risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Low risk	Similarity between groups at baseline was adequate.
Co-interventions avoided or similar?	Low risk	Participants were allowed to continue with current medications, or current alternative treatments and therapies, or both
Compliance acceptable?	Unclear risk	Unclear from text.
Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	Low risk	All prespecified outcomes were reported.

Chrubasik 2003

Methods	RCT with two groups. Period: six weeks
Participants	88 participants allocated to *H. procubens* (N = 44) group or rofecoxib (N = 44). Inclusion criteria: age 45 to 75, at least six months of non-specific LBP, current exacerbation of complaints for eight weeks that was affecting both rest and movement, was causing pain of at least five out of 10 on a VAS and judged to require symptomatic treatment for six weeks. Exclusion criteria: red flags for LBP, participation in any other clinical study within the last 30 days, serious organic illness affecting any organ system, a history of drug or alcohol abuse or requirement of psychotherapeutic drugs, pregnancy or lactation, known allergies to trial medication, and anticipated difficulties with language or corporation
Interventions	*H. procumbens* in a proprietary aqueous extract called Doloteffin (standardized to contain 60 mg harpagoside) or 12.5 mg rofecoxib per day
Outcomes	Primary outcome: proportion of participants who recorded "no pain" without using Tramadol for at least five days in the final week or treatment. Secondary and other outcomes: proportion of patients in whom the averaged daily pain scores in the 6th week had decreased by 20 to 50% of the average in the first week; the percentage change from baseline of a modified Arhus LBP index; the percentage change from baseline on the Health Assessment Questionnaire; Tramadol requirement
Notes	Total Quality Score: 8/12 Adverse effects: 14 participants in each group. GI: eight in the devil's claw group, nine in the Vioxx® group which tended to be more severe. Two serious adverse events occurred in the devil's claw group but were judged unrelated to the trial medication. Circulatory and laboratory variables were not affected by either treatment

Risk of bias

Chrubasik 2003 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Prospective, randomized, double-blind, double-dummy study with randomization via assigned random number. No further description of the randomization process
Allocation concealment (selection bias)	Unclear risk	Not enough information in the text.
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	The trial is described as a double blind double-dummy RCT. However, there is very little description of the blinding in the manuscript
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	The trial is described as a double blind double-dummy RCT. However, there is very little description of the blinding in the manuscript
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	It is unclear if participants were blinded to the intervention medication or just the accompanying placebo. However if the study medication is unblinded it should not incur unacceptable bias into the outcomes
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	Of the 88 participants who enrolled, nine participants dropped out. This should not significantly impact the outcome data
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Low risk	Baseline characteristics of participants between groups was similar with no significant differences noted
Co-interventions avoided or similar?	Low risk	Participants were allowed to supplement the trial medications with Tramadol liquid. However, this was used as an additional outcome measure
Compliance acceptable?	Unclear risk	Unclear from text.
Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	Low risk	All prespecified outcomes were reported.

Chrubasik 2010

Methods	RCT with two groups. Participants were placed in groups by computerized randomization list. Period: three weeks
Participants	Two hundred and eighty-two participants were allocated to Finalgon® CPD Warmecreme (a capsicum-containing cream) (N = 140), or matched placebo (N = 141) . Inclusion criteria: aged between 18 and 65 years, Caucasian, chronic pain of the soft tissues of the musculoskeletal apparatus, subjective pain at enrolment ≥ 5 (VAS 0-10; 0, no pain; 10, intolerable pain), ability and expressed willingness of the patient to follow the investigator's instructions, i.e. meeting the prerequisites of the study, applying study medication according to the dosage regimen and filling in the questionnaires at the control visits, and granting of written informed consent Exclusion criteria: severe co-morbidity, addiction to alcohol or other drugs, pregnancy and lactation, insufficient contraceptive protection, participation in another clinical trial within the past four weeks, concomitant psychiatric disorders, a surgical procedure required in the immediate future, inability of the patient to understand the nature, importance and consequences of the study, muscle rupture, vertebral disk prolapse, spondylolisthesis, spinal canal stenosis, known or clinically proven instability of the spine, spinal fractures, tumours, infections, inflammatory joint conditions, seronegative spondyloarthropathies, osteoporosis as the cause of pain, chronic skin diseases, known hypersensitivity to capsaicin or other ingredients of the cream, anxiety or depressive conditions, ≥ 11 points of anxiety or depression scores (Hamilton Anxiety Depression Scale)
Interventions	'Finalgon® CPD Wärmecreme', of which 100 g contain 2.2 to 2.6 g soft extract of *Capsici fructus acer* corresponding to 53 mg capsaicin (0.05%), applied as a thin layer thrice daily over a three week period
Outcomes	Primary outcome: treatment response, defined as pain sum score reduction ≥ 30%. Secondary outcomes: median relative pain sum score improvement, average pain in the last 24 hours, worst pain in the past three days, average pain in the past three days, pain intensity at the moment of maximum pain relief, the delay between the application of cream and the onset of maximum effect, the duration of analgesia, efficacy as determined by the investigator (excellent, good, adequate, unsatisfactory) and patient (free of complaints, symptoms improved, unchanged, worsened)
Notes	Total quality score: 7/12 Adverse effects: three patients in the treatment group experienced adverse effects and none in the placebo group. In the treatment group, these included unpleasant local heat sensation in two participants and pruritus in one participant

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization completed by computerized randomization list.
Allocation concealment (selection bias)	Unclear risk	Unclear from text.

Chrubasik 2010 (*Continued*)

Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	Participants were randomized to treatment groups with intervention and placebo medications identical in appearance
Blinding (performance bias and detection bias) All outcomes - providers?	Unclear risk	Unclear from text.
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	Outcome assessment unblinded but unlikely to influence outcomes
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	There were seven participants who withdrew during the course of the study, six from the treatment group (three due to symptom abatement, two for insufficient pain relief and one for refusal to continue) and one from the placebo group due to symptom abatement
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	High risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Low risk	Baseline characteristics of participants between groups was similar with no significant differences noted
Co-interventions avoided or similar?	Low risk	No co-interventions noted.
Compliance acceptable?	Unclear risk	Unclear from text.
Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	Low risk	All prespecified outcomes were reported.

da Silva 2010

Methods	RCT with two groups. Period: 15 days
Participants	Twenty participants allocated to Brazilian arnica gel (N = 10) or placebo gel (N = 10) . Inclusion criteria: No specific criteria listed. Patient recruitment was based on spontaneous demand for treating lumbago within the academic community at UVV/ES and was accompanied by the physiotherapy clinic. All participants went through a screening process coordinated by the physiotherapist responsible for the orthopaedics, traumatology, and rheumatology sector of the clinic. After screening, participants were submitted to medical evaluations to diagnose the nature of their lumbago before being allowed to participate in the research program. Exclusion criteria: volunteers under 18 were not permitted to participate in the program, unless they had their parent's or legal guardian's

	permission, people who were not in otherwise good physical and/or mental condition, who did not pass the screening process, who were eliminated as a result of diagnoses made by the physiotherapy sector, or pregnant women
Interventions	5% concentrated plant extract from aerial vegetative and reproductive parts of *S. chilensis* Meyen, diluted in propylene glycol and added at a proportion of 5% (w/v) in carbomer gel, corresponding to active substances in 5 g of dry raw material. 10 g of the placebo or arnica gels was manually and uniformly applied on the area of the lesion twice daily
Outcomes	Primary outcome: Change in perception of pain by VAS. Secondary outcome: lumbar flexibility, as determined by the modified Schober method
Notes	Total quality score: 5/12 Adverse effects: nothing reported.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	No method of randomization described.
Allocation concealment (selection bias)	Unclear risk	Unclear from text.
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	Participants were blinded to treatment group and were unaware of which compound was being applied
Blinding (performance bias and detection bias) All outcomes - providers?	Unclear risk	Providers were blinded to treatment group and were unaware of which compound was being applied
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Unclear risk	Unclear from text.
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	No loss to follow-up noted.
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Low risk	There were no significant differences noted in baseline comparisons between the placebo and intervention group
Co-interventions avoided or similar?	Unclear risk	Unclear from text.

da Silva 2010 (*Continued*)

Compliance acceptable?	Low risk	No issued noted with compliance.
Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	Low risk	Outcome measures were straightforward with pre-specified outcomes being reported

Frerick 2003

Methods	RCT with two groups. Period: three weeks
Participants	Three hundred and twenty participants with chronic non-specific LBP divided equally between capsicum plaster group and placebo group
Interventions	Topical plaster containing an ethonolic extract of cayenne pepper standardized to 22 µg/cm^2 of capsaicinoinds or placebo plaster
Outcomes	Outcomes: Arhus LBP Rating Scale, global assessment of efficacy by patient and investigator, global assessment of safety by patient and investigator
Notes	Total Quality Score: 6/12 Adverse effects: 14 participants in each group. GI: 8 in the devil's claw group, 9 in the Vioxx® group which tended to be more severe. Two serious adverse events occurred in the devil's claw group but were judged unrelated to the trial medication. Circulatory and laboratory variables were not affected by either treatment

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization was computer generated.
Allocation concealment (selection bias)	Low risk	Allocation was done by external personnel not involved in the trial
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	Participants were blinded to study group, and study medication and placebo were identical in appearance
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	Providers were blinded to study group and study medication and placebo were identical in appearance
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Unclear risk	Unclear from text.

Frerick 2003 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	There were seventy withdrawals in the course of the trial, which resulted in a reduction of 319 participants to 249 participants. Despite the withdrawals, the study groups remained balanced
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Low risk	With the exception of slightly more female participants in the placebo group, the groups were comparable
Co-interventions avoided or similar?	Low risk	No co-interventions noted.
Compliance acceptable?	Low risk	No issues regarding compliance.
Timing outcome assessments similar?	Unclear risk	Unclear from text.
Selective Reporting	Low risk	All pre-specified outcomes were reported.

Giannetti 2010

Methods	RCT with two groups. Period: five days
Participants	120 patients allocated to Kytta-Salbe (a cream containing Comfrey root extract) (N = 60) or a matched placebo cream (N = 60). Inclusion criteria: Age range 18 to 60 years, good general condition, written informed consent, acute back pain (either upper or lower back pain) not in combination, sensitivity to algometric pressure on the site contralateral to the painful trigger point at least 2.5 N/cm^2, basic value of the pressure algometry on the trigger point shall not exceed 50% of the respective value of the site contralateral to the painful trigger point Exclusion criteria: upper or lower back pain that is attributable to any identifiable cause, any recent trauma, any recent strains of the back muscles documented by clinical evaluation and anamnesis, chronic back pain, diabetes mellitus, risk factors for spinal infection, recent onset of bladder dysfunction or severe or progressive neurological deficit in the low extremity (as a possible indication of prolapsed disc), concomitant use of any anti-inflammatory drugs, heparinoids or analgesics, including herbal preparations (glucocorticosteroids, NSAID, etc) for the same indication or other indications (e.g. rheumatoid arthritis), analgesics or NSAID applied by any route of administration within 10 days of study entry or corticoid drugs applied by any route of administration within 60 days of study entry, any other concomitant treatment or medication that interferes with the conduct of the trial, known intolerance or hypersensitivity (allergy) to the trial treatments, including known toxic reactions, local skin infections that do not allow the application of the test ointment, participation in a clinical trial within the previous 30 days before enrolment in the trial, participation in this study before or simultaneous participation in another clinical trial, pregnancy or lactation period, women with childbearing poten-

	tial without an effective contraceptive method, abuse of alcohol, medicaments or illicit drugs, any patient in the investigator's opinion not considered suitable for enrolment, legal incapacity or limited legal capacity to give informed consent
Interventions	Kytta-Salbe f. 100 g contains 35 g 99% PA reduced Rad symphyti fluid extract. Four grams were applied topically, administered three times a day at intervals of approximately eight hours and continued for five days
Outcomes	Primary outcome: Area under the curve (AUC) of the VAS values on active standardized movement. Secondary outcomes: AUC of back pain at rest by VAS, AUC over five days of pressure algometry values, global assessment of efficacy by the patients, global assessment of efficacy by the investigators
Notes	Total quality score: 8/12 Adverse effects: four participants in the treatment group and three participants in the placebo group experienced adverse effects. In the treatment group, two participants experienced headaches and one participant experienced pruritus. In the control group, participants experienced eczema, cold, nausea, and rhinitis

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Unclear from text.
Allocation concealment (selection bias)	Unclear risk	Unclear from text.
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	The trial medication and placebo ointments were similar in appearance
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	The clinicians were blinded to treatment group. However, there is little description of care taken to disguise the intervention or placebo ointment
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Unclear risk	Unclear from text.
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	All participants completed baseline to end of study measures
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated

Giannetti 2010 (*Continued*)

Similarity of baseline characteristics?	Low risk	Groups were well balanced at baseline, with slightly more female participants than males
Co-interventions avoided or similar?	Low risk	No co-interventions noted.
Compliance acceptable?	Low risk	No issues regarding compliance.
Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	Low risk	All pre-specified outcomes were reported.

Ginsberg 1987

Methods	RCT with 40 patients assigned to one of twp groups for period of 14 days
Participants	Forty participants with acute mechanical LBP were assigned to either the Rado-Salil (a capsicum-containing cream) group (N = 20) or a placebo group (N = 20). Each patient was also given 45 paracetamol 250 mg tablets. No other analgesic, anti-inflammatory drug or physical treatment was allowed during the 12-week period. Method of participants selection: clinical examination, standard radiological examination of the lumber spine, routine laboratory tests
Interventions	Rado-Salil ointment (containing 17.64 mg ethysalicylate, 26.47 mg methylsalicylate, 8. 82 mg glycosalicylate, 8.82 mg salicylic acid, 4.41 mg camphor, 55.14 mg menthol, and 15.44 mg Capsicum Oleoresin per 1 g) in the form of a 40 g stick applied as needed or a placebo (containing only the excipient with three times the amount of lavendula and bergamot essences) matched for appearance
Outcomes	Outcomes: pain evaluation on a 10 cm linear scale, duration of confinement to bed, muscular reflex contracture evaluation by the physician on a scale of 0 to 4, and spine mobility by determination of Schober's index, the finger to floor distance, the degree of lumbar extension, global appreciation of treatment by patient and physician
Notes	Total Quality Score: 5/12 Adverse events: pruritis, one in placebo, one in Rado-Salil group. Local erythema and burning, three in the Rado-Salil group

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The exact method used for randomization was not described.
Allocation concealment (selection bias)	Unclear risk	Unclear from text.

Ginsberg 1987 (*Continued*)

Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	Participants were given either a treatment ointment or a placebo that are identical in appearance
Blinding (performance bias and detection bias) All outcomes - providers?	Unclear risk	Unclear from text.
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	Outcome assessments unblinded but unlikely to influence outcomes
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	No withdrawals noted in the trial.
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Unclear risk	Unclear from text.
Co-interventions avoided or similar?	Low risk	Participants were given paracetamol tablets in addition to study medication or placebo. No other medication or physical treatment was allowed
Compliance acceptable?	Unclear risk	Unclear from text.
Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	High risk	No comparison of groups noted and certain baseline measures were not reported in the final results

Keitel 2001

Methods	RCT with two groups. No report of randomization method. Period: one plaster per day at maximum pain site for four to 12 hours for three weeks
Participants	One hundred and fifty-four participants were randomly allocated to a placebo plaster group (N = 77) and a capsicum plaster group (N = 77). A total of 132 participants completed the study, with data available for the intention to treat (ITT) analysis on 150 participants (P = 0.002). A total 22 participants were excluded due to premature discontinuation of the treatment (N = 19) failure to meet the inclusion criteria (N = 2) or unauthorized concurrent treatment (N = 1). Inclusion criteria: subjective back pain rating of five or more on an 11 grade VAS, as well as a duration of back pain for a minimum of three months at enrolment. Exclusion criteria: alcohol abuse, drug dependence, forms of specific back pain, concomitant systemic inflammatory rheumatic condition, no concurrent therapy for back pain

Keitel 2001 (*Continued*)

Interventions	Topical plaster type application of *C. frutescens* (cayenne) containing 12 mg of capsaicinoids per plaster. Matched placebo plaster
Outcomes	Primary outcome measure: Arhus Low Back Rating Scale. Secondary outcome measures: global assessment of efficacy and tolerance by physician and patient
Notes	Total quality score: 6/12 Adverse events: a total of 24 adverse events were reported (C = 15; P = 9). Most of these were warmth and itching locally. The C group had five cases of severe adverse events (inflammatory contact eczema, urticaria, minute haemorrhagic spots, and vesiculation or dermatitis) and the P group had two such cases (vesiculation or allergic dermatosis). A total of 16 participants withdrew because of adverse events (C = 10; P = 9). Also, 95.9% of the C group and 48.7% of the P group experienced sensations of warmth locally. Pruritis was mentioned in 45.9% of the C group and 31.6% of the P group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No report of randomization method.
Allocation concealment (selection bias)	Unclear risk	Unclear from text.
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	Study medication and placebo were identical in appearance.
Blinding (performance bias and detection bias) All outcomes - providers?	Unclear risk	Unclear from text.
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Unclear risk	Unclear from text.
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	Out of 154 participants, 22 were excluded due to premature discontinuation of treatment (N = 19, failure to meet exclusion criteria (N = 2), and unauthorized outside treatment (N = 1). Of the remaining 132 participants the groups maintained adequately balanced
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated

Keitel 2001 (*Continued*)

Similarity of baseline characteristics?	Low risk	Apart from a slightly higher BMI in the placebo group the groups were comparable
Co-interventions avoided or similar?	Low risk	No co-intervention noted.
Compliance acceptable?	Low risk	No issues with compliance noted.
Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	Low risk	All pre-specified outcomes were reported.

Krivoy 2001

Methods	Thirty-five participants randomized to two groups and a further 16 participants acted as controls. Period: four weeks
Participants	Fifty-one participants with 19 in the *Salix alba* group, 16 in a placebo group, and 16 in an acetylsalicylate group. Inclusion criteria: acute exacerbations of chronic LBP, stable ischemic heart disease. Exclusion criteria: NSAID use
Interventions	786.48 mg twice per day of an ethanol extract of the bark of *Salix daphnoides* (240 mg salicin content per day), matched placebo, or 100 mg acetylsalicylate
Outcomes	Primary outcome: platelet aggregation
Notes	Total quality score: 5/12 Adverse events: none reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization process not defined.
Allocation concealment (selection bias)	Unclear risk	Unclear from text.
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	Participants were blinded from treatment group allocation, and study medication and placebo were identical
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	Providers were blinded from treatment group allocation.

Krivoy 2001 (*Continued*)

Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	Outcome assessors were unblinded. However knowing the outcome of interest, platelet aggregation, is unlikely to effect outcomes
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	There were no withdrawals noted.
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Low risk	The groups were similar in baseline measures except gender; there were more female participants in the placebo group (P = 0. 01)
Co-interventions avoided or similar?	Low risk	Participants were disallowed the use of anti-inflammatory drugs within the trial period. Tramadol was allowed as an emergency medication
Compliance acceptable?	Unclear risk	Unclear from text.
Timing outcome assessments similar?	Unclear risk	Unclear from text.
Selective Reporting	Low risk	All pre-specified measures were reported.

Stam 2001

Methods	RCT with two groups (no placebo). Randomization was performed using RCODE software (Version 3.4) in blocks of four. Period: seven days
Participants	One hundred and sixty-one participants were randomly allocated to either group. A total of six participants were lost to follow-up (SLR = 2; CCC = 4). Twenty-one participants met all per protocol criteria. Inclusion criteria: between the ages of 18 and 65, acute attack of LBP within previous 72 hours, free from back pain during the previous three months, at least moderately painful limitation of movement on physical examination. Exclusion criteria: radicular symptoms, pain above T12, rheumatoid arthritis, ankylosing spondylitis, known hypersensitivity to treatment compounds, use of analgesics other than paracetamol during the treatment period, use of NSAIDs during the treatment period, receiving other treatment for acute LBP, pregnancy, over 96 hours elapsed since onset of pain, including washout for analgesic or NSAIDs or both
Interventions	Spiroflor SLR homeopathic gel (SLR) group (N = 83) or CCC group (N = 78). Each gel was applied at 3 g per day

Stam 2001 (*Continued*)

Outcomes	Primary outcome: reduction in VAS scores for pain (100 mm scale) and the proportion of treatment success (a VAS reduction of at least 80%). Secondary outcome measures: proportion of participants using paracetamol, number of nights with disturbed sleep, duration of absence from work and an overall assessments of treatment efficacy or usefulness by the general practitioners (GP) and the patients
Notes	Total quality score: 9/12. Adverse Events: Approximately 12% of SLR and 26% of the CCC group experienced an adverse event. Adverse drug reactions were reported by 4% of the SLR group and 24% of the CCC group. A total of four adverse drug reactions in the CCC group and none in the SLR group were considered "severe". A total of eight participants in the CCC group and 0 participants in the SLR group withdrew due to adverse drug reactions

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization was performed using RCODE software (version 3.4) in blocks of four
Allocation concealment (selection bias)	Low risk	Allocation concealment was adequate, providers were not influential in group selection
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	Participants were blinded to treatment group and although trial medications were not identical, they were packed in identical containers
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	Providers were blinded to group allocation and were only able to access treatment group allocation if there was an adverse event which required unblinding. The trial medications were not available to the providers in the trial country at the time and all stakeholders assumed both medications held active ingredients
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	This was a double-blinded trial. While there were reservations with the blinding due to non-similar medications, there was no evidence that unblinding occurred
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	One hundred and fifty-four out of 161 participants were able to provide evaluable results from baseline to seven days

Stam 2001 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Low risk	Group comparison was similar with no significant differences noted between groups at baseline
Co-interventions avoided or similar?	Low risk	Anti-inflammatory drugs were disallowed during the trial phase with paracetamol used as an emergency medication
Compliance acceptable?	High risk	Poor compliance was noted among participants. Rapid improvement and three applications per day may have influenced non-compliance. Compliance was equal across groups
Timing outcome assessments similar?	Low risk	No differences noted in timing.
Selective Reporting	Low risk	All pre-specified outcomes reported.

Yip 2004

Methods	Unblinded RCT with two groups. Period: three weeks
Participants	Sixty-one patients were allocated to acupressure with lavender oil (N = 32) or conventional treatment (N = 29). Inclusion criteria: aged 18 or above with non-specific sub-acute LBP for most days in the past four weeks; who had not received acupuncture, physiotherapy, or manipulative therapy in the past week; who could understand the explanation of the study, complete the interview and comprehend the instructions. Non-specific sub-acute LBP was defined as pain on most days in the past four weeks, in the area between the lower coastal margins and the gluteal folds without known specific cause, such as a spinal deformity. Exclusion criteria: LBP caused by specific entities, such as infection, metastases, neoplasm osteoporosis, fractures, spine deformity, or prolapsed intervertebral disc; had undergone surgery or had dislocation, fracture, neurological deficits, spinal disease, varicose vein, blood dyscrasia, cancer or systemic disorders; were pregnant; were allergic to natural lavender aromatic oil; had a wound at any of the acupoints at the back or on the lower limb; or had had a surgical intervention within the last three months
Interventions	Acupoint stimulation with a digital Electronic Muscle Stimulator for 10 minutes, followed by acupressure massage, consisting of the application of a light to medium finger press with 3% aromatic natural lavender oil with grape seed oil as the base on eight fixed acupoints for two minutes each. Treatment lasted 35 to 40 minutes and occurred eight times over a three-week period

Yip 2004 (*Continued*)

Outcomes	Primary outcome: Pain intensity rating on VAS. Secondary outcomes: range of motion of lateral spine flexion, quantified by lateral fingertip-to-ground distance, walking time for 15 meters, interference with daily activities measured by the modified Aberdeen LBP scale
Notes	Total quality score: 4/12 Adverse effects: Reported no adverse effects.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were allocated by the research team consulting a random numbers table
Allocation concealment (selection bias)	High risk	Patients and clinicians were aware of group allocation.
Blinding (performance bias and detection bias) All outcomes - patients?	High risk	Intervention treatment and control treatment were dissimilar with no blinding
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	Providers were aware and involved in the treatment allocation process
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Unclear risk	Unclear from text
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	Of the 61 original participants, 10 participants dropped out but there was no difference in dropout rate between groups. Reasons for withdrawal by participants were not related to study procedures and should have little effect on outcomes
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	Participants appeared to be analysed in the groups to which they were allocated
Similarity of baseline characteristics?	Low risk	No significant differences between study groups noted.
Co-interventions avoided or similar?	High risk	No discussion or controlling for medication or additional treatment modalities noted
Compliance acceptable?	Unclear risk	Unclear from text

Yip 2004 (*Continued*)

Timing outcome assessments similar?	High risk	There was no description of the control group's therapy beyond being a conventional therapy
Selective Reporting	Low risk	All pre-specified outcomes were reported.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Blank 1970	Not a RCT.
Buttermann 2012	Did not study non-specific LBP.
Carragee 2011	Note on another article.
Chrubasik 2001b	Not a RCT.
Chrubasik 2002a	Not a RCT.
Chrubasik 2002b	Not a RCT.
Chrubasik 2002c	Not a RCT.
Chrubasik 2002d	Not a RCT.
Chrubasik 2004	Comment on another study.
Chrubasik 2005	Not a RCT.
Chrubasik 2006	Abstract from a symposium.
Chrubasik 2007	Not a RCT.
Chrubasik 2008	Not a RCT.
Corrigan 2005	Not a RCT
Gensthaler 2000	Not a RCT.
Gobel 2001	Not a RCT.
Hansen 2007	Did not study LBP.
Harden 2000	Not a RCT.

(*Continued*)

Hemmilä 1997	Not a herbal medicine.
Hogeboom 2001	Not a RCT, not a herbal medicine.
Jiang 1986	Not a herbal medicine.
Kong 2012	Not a herbal medicine.
Kucera 2005	Did not study LBP.
Laudahn 2001a	Not a RCT.
Lee 2012	Conference abstract only, unknown participants type, unknown if a herbal medicine
Liu 2013	Abstract or full text not available.
März 2002	Not a RCT.
NASSBD 2003	Comment on another article.
Pabst 2013	Mixed low back and upper back pain with no subgroup analyses
Pach 2011	Herbal medicine given by injection
Reme 2011	Not a herbal medicine.
Schmidt 2005	Not a RCT.
Sherman 2001a	Not a RCT, not a herbal medicine.
Sherman 2001b	Not a RCT, not a herbal medicine.
Takabayashi 1990	Not LBP.
Tant 2005	Did not use herbal medicine.
Uehleke 2013	Not a RCT.
Ukhalkar 2013	Not an oral or topical route of administration.
Wimmer 1997	Not LBP, not a herbal medicine.
Xu 1993	Not a RCT.
Yuan 2013	Not LBP.

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. Current search strategy

MEDLINE

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. Randomized Controlled Trials/
4. Random Allocation/
5. Double-Blind Method/
6. Single-Blind Method/
7. or/1-6
8. Animals/ not Human/
9. 7 not 8
10. clinical trial.pt.
11. exp Clinical Trial/
12. (clin$ adj25 trial$).tw.
13. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).tw.
14. Placebos/
15. placebo$.tw.
16. random$.tw.
17. Research Design/
18. (latin adj square).tw.
19. or/10-18
20. 19 not 18
21. 20 not 9
22. Comparative Study/
23. exp Evaluation Studies/
24. Follow-Up Studies/
25. Prospective Studies/
26. (control$ or prospective$ or Volunteer$).tw.
27. Cross-Over Studies/
28. or/22-27
29. 28 not 8
30. 29 not (9 or 21)
31. 9 or 21 or 30
32. dorsalgia.ti,ab.
33. exp Back Pain/
34. backache.ti,ab.
35. (lumbar adj pain).ti,ab.
36. coccyx.ti,ab.
37. coccydynia.ti,ab.
38. sciatica.ti,ab.

39. sciatic neuropathy/
40. spondylosis.ti,ab.
41. lumbago.ti,ab.
42. or/32-41
43. 31 and 42
44. Drugs, Chinese Herbal/
45. herbal.mp.
46. Plants, Medicinal/
47. phytomedicine.mp.
48. herb$.mp.
49. weed.mp.
50. algae.mp.
51. cryptophyta/ or haptophyta/ or exp glaucophyta/ or exp rhodophyta/ or exp viridiplantae/ or exp chlorophyta/ or exp streptophyta/ or exp stramenopiles/
52. exp Fungi/
53. exp Medicine, Traditional/
54. exp Phytotherapy/
55. exp Pharmacognosy/
56. (oriental adj traditional).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
57. (Camphora adj molmol).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
58. Capsicum/
59. exp Salicaceae/
60. (Maleluca adj alternifolia).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
61. Angelica sinensis/
62. Aloe/
63. (Thymus adj officinalis).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
64. Menthe piperita.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
65. Arnica Montana.mp. or Arnica/
66. Curcuma longa.mp. or Curcuma/
67. Tanacetum parthenium.mp. or Tanacetum parthenium/
68. feverfew.mp.
69. Harpagophytum procumbens.mp. or exp Harpagophytum/
70. Zingiber officii.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
71. plant preparations/ or plant extracts/ or plant oils/
72. or/44-71
73. 43 and 72
74. 31 and 42 and 72
75. limit 74 to yr=2013-Current
76. limit 74 to ed=20130806-20140911
77. 75 or 76

EMBASE

From the 2013 strategy, line 31 was changed from 14 and 30 to 14 or 30

1. Clinical Article/
2. exp Clinical Study/
3. Clinical Trial/

4. Controlled Study/
5. Randomized Controlled Trial/
6. Major Clinical Study/
7. Double Blind Procedure/
8. Multicenter Study/
9. Single Blind Procedure/
10. Phase 3 Clinical Trial/
11. Phase 4 Clinical Trial/
12. crossover procedure/
13. placebo/
14. or/1-13
15. allocat$.mp.
16. assign$.mp.
17. blind$.mp.
18. (clinic$ adj25 (study or trial)).mp.
19. compar$.mp.
20. control$.mp.
21. cross?over.mp.
22. factorial$.mp.
23. follow?up.mp.
24. placebo$.mp.
25. prospectiv$.mp.
26. random$.mp.
27. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).mp.
28. trial.mp.
29. (versus or vs).mp.
30. or/15-29
31. 14 or 30
32. exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
33. human/ or normal human/ or human cell/
34. 32 and 33
35. 32 not 34
36. 31 not 35
37. dorsalgia.mp.
38. back pain.mp.
39. exp BACKACHE/
40. (lumbar adj pain).mp.
41. coccyx.mp.
42. coccydynia.mp.
43. sciatica.mp.
44. exp ISCHIALGIA/
45. spondylosis.mp.
46. lumbago.mp.
47. exp Low back pain/
48. or/37-47
49. exp herbaceous agent/
50. herbal.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
51. exp medicinal plant/
52. exp phytotherapy/
53. exp herbal medicine/
54. phytomedicine.mp.
55. exp plant extract/

56. herb*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
57. weed.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
58. exp alga/
59. exp fungus/
60. exp traditional medicine/
61. exp pharmacognosy/
62. (oriental adj traditional).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
63. exp Chinese medicine/
64. exp pepper/
65. capsicum.mp.
66. exp willow/
67. salix.mp.
68. exp Angelica sinensis/
69. exp Aloe/
70. exp Arnica montana/
71. exp Curcuma longa/
72. tanacetum/ or exp tanacetum parthenium/
73. exp harpagophytum/ or exp harpagophytum extract/ or exp harpagophytum procumbens extract/
74. or/49-73
75. 36 and 48 and 74
76. limit 75 to yr="2013-Current"
77. limit 75 to em=201331-201436
78. 76 or 77

CENTRAL

#1 MeSH descriptor: [Low Back Pain] this term only
#2 MeSH descriptor: [Back Pain] this term only
#3 backache
#4 lumbago
#5 #1 or #2 or #3 or #4
#6 MeSH descriptor: [Drugs, Chinese Herbal] explode all trees
#7 MeSH descriptor: [Plants, Medicinal] explode all trees
#8 herbal
#9 phytomedicine
#10 herb*
#11 weed
#12 MeSH descriptor: [Algae] explode all trees
#13 MeSH descriptor: [Fungi] explode all trees
#14 MeSH descriptor: [Medicine, Traditional] explode all trees
#15 MeSH descriptor: [Phytotherapy] this term only
#16 MeSH descriptor: [Pharmacognosy] explode all trees
#17 Oriental next traditional
#18 MeSH descriptor: [Medicine, Chinese Traditional] this term only
#19 Camphora next molmo
#20 MeSH descriptor: [Capsicum] this term only
#21 MeSH descriptor: [Salix] this term only
#22 Maleluca next alternifolia
#23 MeSH descriptor: [Angelica sinensis] this term only
#24 MeSH descriptor: [Aloe] this term only

#25 Thymus next officinalis
#26 Menthe next piperita
#27 MeSH descriptor: [Arnica] this term only
#28 Arnica next Montana
#29 Curcuma next longa
#30 MeSH descriptor: [Curcuma] this term only
#31 MeSH descriptor: [Tanacetum parthenium] this term only
#32 MeSH descriptor: [Harpagophytum] this term only
#33 Harpagophytum next procumbens
#34 Zingiber next officii
#35 MeSH descriptor: [Plant Preparations] this term only
#36 MeSH descriptor: [Plant Oils] explode all trees
#37 MeSH descriptor: [Plant Extracts] explode all trees
#38 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37
#39 #5 and #38
#40 #39 Publication Year from 2013 to 2014, in Trials

CINAHL

S75 S73 OR S74
S74 S73 and EM 20130806-20140911
S73 S49 and S71 Limiters - Published Date: 20130801-20140931
S72 S49 and S71
S71 S50 or S51 or S52 or S53 or S54 or S55 or S56 or S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70
S70 (MH "Devil's Claw")
S69 (MH "Feverfew")
S68 Curcuma longa
S67 (MH "Arnica")
S66 (MH "Aloe")
S65 (MH "Dong Quai")
S64 (MH "Willow Bark")
S63 ("Capsicum") or (MH "Cayenne Pepper")
S62 Camphora W1 molmol
S61 (MH "Medicine, Traditional")
S60 oriental W1 traditional
S59 Pharmacognosy
S58 ("Phytotherapy") or (MH "Medicine, Herbal")
S57 (MH "Medicine, Chinese Traditional")
S56 (MH "Fungi+")
S55 (MH "Algae+")
S54 "weed"
S53 herb*
S52 phytomedicine
S51 (MH "Plants, Medicinal+")
S50 (MH "Drugs, Chinese Herbal")
S49 S28 and S48
S48 S35 or S43 or S47
S47 S44 or S45 or S46
S46 "lumbago"
S45 (MH "Spondylolisthesis") OR (MH "Spondylolysis")
S44 (MH "Thoracic Vertebrae")

S43 S36 or S37 or S38 or S39 or S40 or S41 or S42
S42 lumbar N2 vertebra
S41 (MH "Lumbar Vertebrae")
S40 "coccydynia"
S39 "coccyx"
S38 "sciatica"
S37 (MH "Sciatica")
S36 (MH "Coccyx")
S35 S29 or S30 or S31 or S32 or S33 or S34
S34 lumbar N5 pain
S33 lumbar W1 pain
S32 "backache"
S31 (MH "Low Back Pain")
S30 (MH "Back Pain+")
S29 "dorsalgia"
S28 S26 NOT S27
S27 (MH "Animals")
S26 S7 or S12 or S19 or S25
S25 S20 or S21 or S22 or S23 or S24
S24 volunteer*
S23 prospectiv*
S22 control*
S21 followup stud*
S20 follow-up stud*
S19 S13 or S14 or S15 or S16 or S17 or S18
S18 (MH "Prospective Studies+")
S17 (MH "Evaluation Research+")
S16 (MH "Comparative Studies")
S15 latin square
S14 (MH "Study Design+")
S13 (MH "Random Sample")
S12 S8 or S9 or S10 or S11
S11 random*
S10 placebo*
S9 (MH "Placebos")
S8 (MH "Placebo Effect")
S7 S1 or S2 or S3 or S4 or S5 or S6
S6 triple-blind
S5 single-blind
S4 double-blind
S3 clinical W3 trial
S2 "randomi?ed controlled trial*"
S1 (MH "Clinical Trials+")

ClinicalTrials.gov

Condition: back pain
AND Intervention: herbal OR botanical
Received on or after 08/06/2013

WHO ICTRP

Condition: back pain

AND Intervention: herbal OR botanical
Date of registration between 06/08/2013-(no date limit)

PubMed

((((herbal or botanical))) AND back pain) AND ((pubstatusaheadofprint OR publisher[sb] or pubmednotmedline[sb]))

Appendix 2. Previous search strategies

August 2013

Embase

The animal study filter was updated from 2010

1. Clinical Article/
2. exp Clinical Study/
3. Clinical Trial/
4. Controlled Study/
5. Randomized Controlled Trial/
6. Major Clinical Study/
7. Double Blind Procedure/
8. Multicenter Study/
9. Single Blind Procedure/
10. Phase 3 Clinical Trial/
11. Phase 4 Clinical Trial/
12. crossover procedure/
13. placebo/
14. or/1-13
15. allocat$.mp.
16. assign$.mp.
17. blind$.mp.
18. (clinic$ adj25 (study or trial)).mp.
19. compar$.mp.
20. control$.mp.
21. cross?over.mp.
22. factorial$.mp.
23. follow?up.mp.
24. placebo$.mp.
25. prospectiv$.mp.
26. random$.mp.
27. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).mp.
28. trial.mp.
29. (versus or vs).mp.
30. or/15-29
31. 14 and 30
32. exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
33. human/ or normal human/ or human cell/
34. 32 and 33
35. 32 not 34
36. 31 not 35

January 2011

Medline

Back terms and herbal medicine terms were updated from 2009

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. Randomized Controlled Trials/
4. Random Allocation/
5. Double-Blind Method/
6. Single-Blind Method/
7. or/1-6
8. Animals/ not Human/
9. 7 not 8
10. clinical trial.pt.
11. exp Clinical Trials/
12. (clin$ adj25 trial$).tw.
13. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).tw.
14. Placebos/
15. placebo$.tw.
16. random$.tw.
17. Research Design/
18. (latin adj square).tw.
19. or/10-18
20. 19 not 18
21. 20 not 9
22. Comparative Study/
23. exp Evaluation Studies/
24. Follow-Up Studies/
25. Prospective Studies/
26. (control$ or prospective$ or Volunteer$).tw.
27. Cross-Over Studies/
28. or/22-27
29. 28 not 8
30. 29 not (9 or 21)
31. 9 or 21 or 30
32. dorsalgia.ti,ab.
33. exp Back Pain/
34. backache.ti,ab.
35. (lumbar adj pain).ti,ab.
36. coccyx.ti,ab.
37. coccydynia.ti,ab.
38. sciatica.ti,ab.
39. sciatic neuropathy/
40. spondylosis.ti,ab.
41. lumbago.ti,ab.
42. or/32-41
43. 31 and 42
44. Drugs, Chinese Herbal/
45. herbal.mp.
46. Plants, Medicinal/
47. phytomedicine.mp.
48. herb$.mp.
49. weed.mp.

50. algae.mp.
51. cryptophyta/ or haptophyta/ or exp glaucophyta/ or exp rhodophyta/ or exp viridiplantae/ or exp chlorophyta/ or exp streptophyta/ or exp stramenopiles/
52. exp Fungi/
53. exp Medicine, Traditional/
54. exp Phytotherapy/
55. exp Pharmacognosy/
56. (oriental adj traditional).mp.
57. (Camphora adj molmol).mp.
58. Capsicum/
59. exp Salicaceae/
60. (Maleluca adj alternifolia).mp.
61. Angelica sinensis/
62. Aloe/
63. (Thymus adj officinalis).mp.
64. Menthe piperita.mp.
65. Arnica Montana.mp. or Arnica/
66. Curcuma longa.mp. or Curcuma/
67. Tanacetum parthenium.mp. or Tanacetum parthenium/
68. feverfew.mp.
69. Harpagophytum procumbens.mp. or exp Harpagophytum/
70. Zingiber officii.mp.
71. plant preparations/ or plant extracts/ or plant oils/
72. or/44-71
73. 43 and 72
74. limit 73 to yr="2003 - 2011"

CINAHL

The strategy was updated from 2009
S73 S49 and S71 Limiters - Published Date from: 20030101-20111231
S72 S49 and S71
S71 S50 or S51 or S52 or S53 or S54 or S55 or S56 or S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70
S70 (MH "Devil's Claw")
S69 (MH "Feverfew")
S68 Curcuma longa
S67 (MH "Arnica")
S66 (MH "Aloe")
S65 (MH "Dong Quai")
S64 (MH "Willow Bark")
S63 ("Capsicum") or (MH "Cayenne Pepper")
S62 Camphora W1 molmol
S61 (MH "Medicine, Traditional")
S60 oriental W1 traditional
S59 Pharmacognosy
S58 ("Phytotherapy") or (MH "Medicine, Herbal")
S57 (MH "Medicine, Chinese Traditional")
S56 (MH "Fungi+")
S55 (MH "Algae+")
S54 "weed"
S53 herb*
S52 phytomedicine
S51 (MH "Plants, Medicinal+")
S50 (MH "Drugs, Chinese Herbal")

S49 S28 and S48
S48 S35 or S43 or S47
S47 S44 or S45 or S46
S46 “lumbago”
S45 (MH “Spondylolisthesis”) OR (MH “Spondylolysis”)
S44 (MH “Thoracic Vertebrae”)
S43 S36 or S37 or S38 or S39 or S40 or S41 or S42
S42 lumbar N2 vertebra
S41 (MH “Lumbar Vertebrae”)
S40 “coccydynia”
S39 “coccyx”
S38 “sciatica”
S37 (MH “Sciatica”)
S36 (MH “Coccyx”)
S35 S29 or S30 or S31 or S32 or S33 or S34
S34 lumbar N5 pain
S33 lumbar W1 pain
S32 “backache”
S31 (MH “Low Back Pain”)
S30 (MH “Back Pain+”)
S29 “dorsalgia”
S28 S26 NOT S27
S27 (MH “Animals”)
S26 S7 or S12 or S19 or S25
S25 S20 or S21 or S22 or S23 or S24
S24 volunteer*
S23 prospectiv*
S22 control*
S21 followup stud*
S20 follow-up stud*
S19 S13 or S14 or S15 or S16 or S17 or S18
S18 (MH “Prospective Studies+”)
S17 (MH “Evaluation Research+”)
S16 (MH “Comparative Studies”)
S15 latin square
S14 (MH “Study Design+”)
S13 (MH “Random Sample”)
S12 S8 or S9 or S10 or S11
S11 random*
S10 placebo*
S9 (MH “Placebos”)
S8 (MH “Placebo Effect”)
S7 S1 or S2 or S3 or S4 or S5 or S6
S6 triple-blind
S5 single-blind
S4 double-blind
S3 clinical W3 trial
S2 “randomi?ed controlled trial*”
S1 (MH “Clinical Trials+”)

CENTRAL

New intervention terms were added from 2009
#1 MeSH descriptor Low Back Pain, this term only
#2 MeSH descriptor Back Pain, this term only

#3 backache
#4 lumbago
#5 (#1 OR #2 OR #3 OR #4)
#6 MeSH descriptor Drugs, Chinese Herbal explode all trees
#7 MeSH descriptor Plants, Medicinal explode all trees
#8 herbal
#9 phytomedicine
#10 herb*
#11 weed
#12 MeSH descriptor Algae explode all trees
#13 MeSH descriptor Fungi explode all trees
#14 MeSH descriptor Medicine, Traditional explode all trees
#15 MeSH descriptor Phytotherapy, this term only
#16 MeSH descriptor Pharmacognosy explode all trees
#17 Oriental NEXT traditional
#18 MeSH descriptor Medicine, Chinese Traditional, this term only
#19 Camphora NEXT molmo
#20 MeSH descriptor Capsicum, this term only
#21 MeSH descriptor Salix, this term only
#22 Maleluca NEXT alternifolia
#23 MeSH descriptor Angelica sinensis, this term only
#24 MeSH descriptor Aloe, this term only
#25 Thymus NEXT officinalis
#26 Menthe NEXT piperita
#27 MeSH descriptor Arnica, this term only
#28 Arnica NEXT Montana
#29 Curcuma NEXT longa
#30 MeSH descriptor Curcuma, this term only
#31 MeSH descriptor Tanacetum parthenium, this term only
#32 MeSH descriptor Harpagophytum, this term only
#33 Harpagophytum NEXT procumbens
#34 Zingiber NEXT officii
#35 MeSH descriptor Plant Preparations, this term only
#36 MeSH descriptor Plant Oils explode all trees
#37 MeSH descriptor Plant Extracts explode all trees
#38 (#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37)
#39 (#5 AND #38), from 2003 to 2011

April 2010

EMBASE

The strategy was updated from 2009

1. Clinical Article/
2. exp Clinical Study/
3. Clinical Trial/
4. Controlled Study/
5. Randomized Controlled Trial/
6. Major Clinical Study/
7. Double Blind Procedure/
8. Multicenter Study/
9. Single Blind Procedure/

10. Phase 3 Clinical Trial/
11. Phase 4 Clinical Trial/
12. crossover procedure/
13. placebo/
14. or/1-13
15. allocat$.mp.
16. assign$.mp.
17. blind$.mp.
18. (clinic$ adj25 (study or trial)).mp.
19. compar$.mp.
20. control$.mp.
21. cross?over.mp.
22. factorial$.mp.
23. follow?up.mp.
24. placebo$.mp.
25. prospectiv$.mp.
26. random$.mp.
27. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).mp.
28. trial.mp.
29. (versus or vs).mp.
30. or/15-29
31. 14 and 30
32. human/
33. Nonhuman/
34. exp ANIMAL/
35. Animal Experiment/
36. 33 or 34 or 35
37. 32 not 36
38. 31 not 36
39. 37 and 38
40. 38 or 39
41. dorsalgia.mp.
42. back pain.mp.
43. exp BACKACHE/
44. (lumbar adj pain).mp.
45. coccyx.mp.
46. coccydynia.mp.
47. sciatica.mp.
48. exp ISCHIALGIA/
49. spondylosis.mp.
50. lumbago.mp.
51. exp Low back pain/
52. or/41-51
53. exp herbaceous agent/
54. herbal.mp.
55. exp medicinal plant/
56. exp phytotherapy/
57. exp herbal medicine/
58. phytomedicine.mp.
59. exp plant extract/
60. herb*.mp.
61. weed.mp.
62. exp alga/

63. exp fungus/
64. exp traditional medicine/
65. exp pharmacognosy/
66. (oriental adj traditional).mp.
67. exp Chinese medicine/
68. exp pepper/
69. capsicum.mp.
70. exp willow/
71. salix.mp.
72. exp Angelica sinensis/
73. exp Aloe/
74. exp Arnica montana/
75. exp Curcuma longa/
76. tanacetum/ or exp tanacetum parthenium/
77. exp harpagophytum/ or exp harpagophytum extract/ or exp harpagophytum procumbens extract/
78. or/53-77
79. 40 and 52 and 78

October-November 2009

Medline

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. Randomized Controlled Trials/
4. Random Allocation/
5. Double-Blind Method/
6. Single-Blind Method/
7. or/1-6
8. Animal/ not Human/
9. 7 not 8
10. clinical trial.pt.
11. exp Clinical Trial/
12. (clinic$ adj trial$).tw.
13. ((single$ or double$ or treble$ or triple$) adj (mask$ or blind$)).tw.
14. Placebos/
15. placebo$.tw.
16. random$.tw.
17. Research Design/
18. (Latin adj square).tw.
19. or/10-18
20. 19 not 8
21. 20 not 9
22. Comparative Study/
23. exp Evaluation Studies/
24. Follow-Up Studies/
25. Prospective Studies/
26. (control$ or prospective$ or volunteer$).tw.
27. Cross-Over Studies/
28. or/22-27
29. 28 not 8
30. 29 not (9 or 21)
31. 9 or 21 or 30
32. low back pain/

33. low back pain.tw.
34. backache.mp.
35. lumbago.mp.
36. or/32-35
37. exp Drugs, Chinese Herbal/
38. herbal.tw.
39. exp Plants, Medicinal/
40. phytomedicine.tw.
41. herb$.tw.
42. weed.tw.
43. exp Algae/
44. exp Fungi/
45. Medicine, Traditional/
46. exp Phytotherapy/
47. exp Pharmacognosy/
48. (oriental adj traditional).tw.
49. exp Medicine, Chinese Traditional/
50. (Camphora adj molmol).tw.
51. Capsicum/
52. Salix/
53. (Maleluca adj alternifolia).tw.
54. exp Angelica sinensis/
55. Aloe/
56. (Thymus adj officinalis).tw.
57. Menthe piperita.tw.
58. Arnica Montana.mp. or exp Arnica/
59. Curcuma longa.mp. or exp Curcuma/
60. exp Tanacetum parthenium/
61. Harpagophytum procumbens.mp. or exp Harpagophytum/
62. Zingiber officii.tw.
63. or/37-62
64. 31 and 36 and 63
65. limit 64 to yr="2005 -Current"

Embase

1. Randomized Controlled Trials/
2. Random Allocation/
3. Double-Blind Method/
4. Single-Blind Method/
5. 4 or 1 or 3 or 2
6. Animal/ not Human/
7. 5 not 6
8. exp clinical trial/
9. (clinic$ adj trial$).tw.
10. ((single$ or double$ or treble$ or triple$) adj (mask$ or blind$)).tw.
11. Placebos/
12. placebo$.tw.
13. random$.tw.
14. Research Design/
15. (Latin adj square).tw.
16. or/8-15
17. 16 not 6
18. 17 not 7
19. Comparative Study/

20. exp Evaluation Studies/
21. Follow-Up Studies/
22. Prospective Studies/
23. (control$ or prospective$ or volunteer$).tw.
24. Cross-Over Studies/
25. or/19-24
26. 25 not 6
27. 26 not (7 or 18)
28. 7 or 18 or 27
29. low back pain/
30. low back pain.tw.
31. backache.mp. or exp backache/
32. lumbago.mp.
33. /29-32
34. exp Drugs, Chinese Herbal/
35. herbal.tw.
36. exp Plants, Medicinal/
37. phytomedicine.tw.
38. herb$.tw.
39. weed.tw.
40. exp Algae/
41. exp Fungi/
42. Medicine, Traditional/
43. exp Phytotherapy/
44. exp Pharmacognosy/
45. (oriental adj traditional).tw.
46. exp Medicine, Chinese Traditional/
47. (Camphora adj molmol).tw.
48. Capsicum/
49. Salix/
50. (Maleluca adj alternifolia).tw.
51. exp Angelica sinensis/
52. Aloe/
53. (Thymus adj officinalis).tw.
54. Menthe piperita.tw.
55. Arnica Montana.mp. or exp Arnica/
56. Curcuma longa.mp. or exp Curcuma/
57. exp Tanacetum parthenium/
58. Harpagophytum procumbens.mp. or exp Harpagophytum/
59. Zingiber officii.tw.
60. or/34-59
61. 28 and 33 and 60
62. limit 61 to yr="2005 -Current"

CENTRAL

#1 MeSH descriptor Low Back Pain, this term only
#2 MeSH descriptor Back Pain, this term only
#3 backache
#4 lumbago
#5 (#1 OR #2 OR #3 OR #4)
#6 MeSH descriptor Drugs, Chinese Herbal explode all trees
#7 MeSH descriptor Plants, Medicinal explode all trees
#8 herbal
#9 phytomedicine

#10 herb*
#11 weed
#12 MeSH descriptor Algae explode all trees
#13 MeSH descriptor Fungi explode all trees
#14 MeSH descriptor Medicine, Traditional explode all trees
#15 MeSH descriptor Phytotherapy, this term only
#16 MeSH descriptor Pharmacognosy explode all trees
#17 Oriental NEXT traditional
#18 MeSH descriptor Medicine, Chinese Traditional, this term only
#19 Camphora NEXT molmo
#20 MeSH descriptor Capsicum, this term only
#21 MeSH descriptor Salix, this term only
#22 Maleluca NEXT alternifolia
#23 MeSH descriptor Angelica sinensis, this term only
#24 MeSH descriptor Aloe, this term only
#25 Thymus NEXT officinalis
#26 Menthe NEXT piperita
#27 MeSH descriptor Arnica, this term only
#28 Arnica NEXT Montana
#29 Curcuma NEXT longa
#30 MeSH descriptor Curcuma, this term only
#31 MeSH descriptor Tanacetum parthenium, this term only
#32 MeSH descriptor Harpagophytum, this term only
#33 Harpagophytum NEXT procumbens
#34 Zingiber NEXT officii
#35 (#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34)
#36 (#5 AND #35)
#37 (#36), from 2005 to 2009 (Searched with limiter Clinical Trials)

CINAHL

S55 S54 and S28 and S32
S54 S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51 or S52 or S53
S53 (MH “Devil’s Claw”)
S52 (MH “Feverfew”)
S51 Curcuma longa
S50 (MH “Arnica”)
S49 (MH “Aloe”)
S48 (MH “Dong Quai”)
S47 (MH “Willow Bark”)
S46 (“Capsicum”) or (MH “Cayenne Pepper”)
S45 Camphora W1 molmol
S44 (MH “Medicine, Traditional”)
S43 oriental W1 traditional
S42 Pharmacognosy
S41 (“Phytotherapy”) or (MH “Medicine, Herbal”)
S40 (MH “Medicine, Chinese Traditional”)
S39 (MH “Fungi+”)
S38 (MH “Algae+”)
S37 “weed”
S36 herb*
S35 phytomedicine
S34 (MH “Plants, Medicinal+”)

S33 (MH "Drugs, Chinese Herbal")
S32 S29 or S30 or S31
S31 "lumbago"
S30 "backache"
S29 ("low back pain") or (MH "Low Back Pain")
S28 S8 or S18 or S27
S27 S26 not (S18 or S8)
S26 S25 not S7
S25 S19 or S20 or S21 or S22 or S23 or S24
S24 (MH "Crossover Design")
S23 "Follow-up Studies"
S22 control* or prospective* or volunteer*
S21 (MH "Prospective Studies")
S20 (MH "Evaluation Research+")
S19 (MH "Comparative Studies")
S18 S17 not S8
S17 S16 not S7
S16 S9 or S10 or S11 or S12 or S13 or S14 or S15
S15 Latin W1 Square
S14 (MH "Study Design")
S13 random*
S12 placebo*
S11 (MH "Placebos")
S10 clinic* W2 trial*
S9 "clinical trial"
S8 S6 not S7
S7 (MH "Animals") not ("Human")
S6 S1 or S2 or S3 or S4 or S5
S5 "Single-Blind Method"
S4 "randomized controlled trial"
S3 "Double-Blind Method"
S2 (MH "Random Assignment")
S1 (MH "Clinical Trials+")

Appendix 3. Criteria for assessing risk of bias for internal validity

Random sequence generation (selection bias)

Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence

There is a low risk of selection bias if the investigators describe a random component in the sequence generation process such as: referring to a random number table, using a computer random number generator, coin tossing, shuffling cards or envelopes, throwing dice, drawing of lots, minimisation (minimisation may be implemented without a random element, and this is considered to be equivalent to being random).

There is a high risk of selection bia*s* if the investigators describe a non-random component in the sequence generation process, such as: sequence generated by odd or even date of birth, date (or day) of admission, hospital or clinic record number; or allocation by judgement of the clinician, preference of the participant, results of a laboratory test or a series of tests, or availability of the intervention. Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Allocation concealment (selection bias)

Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment

There is a low risk of selection bias if the participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomization); sequentially numbered drug containers of identical appearance; or sequentially numbered, opaque, sealed envelopes.
There is a high risk of bias if participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; or other explicitly unconcealed procedures.
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Blinding of participants

Performance bias due to knowledge of the allocated interventions by participants during the study

There is a low risk of performance bias if blinding of participants was ensured and it was unlikely that the blinding could have been broken; or if there was no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding.
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Blinding of personnel or care providers (performance bias)

Performance bias due to knowledge of the allocated interventions by personnel or care providers during the study

There is a low risk of performance bias if blinding of personnel was ensured and it was unlikely that the blinding could have been broken; or if there was no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding.
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Blinding of outcome assessors (detection bias)

Detection bias due to knowledge of the allocated interventions by outcome assessors

There is low risk of detection bias if the blinding of the outcome assessment was ensured and it was unlikely that the blinding could have been broken; or if there was no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding, or:

- for patient-reported outcomes in which the patient was the outcome assessor (e.g. pain, disability): there is a low risk of bias for outcome assessors if there is a low risk of bias for participant blinding (Boutron 2005);
- for outcome criteria that are clinical or therapeutic events that will be determined by the interaction between patients and care providers (e.g. co-interventions, length of hospitalisation, treatment failure), in which the care provider is the outcome assessor: there is a low risk of bias for outcome assessors if there is a low risk of bias for care providers (Boutron 2005);
- for outcome criteria that are assessed from data from medical forms: there is a low risk of bias if the treatment or adverse effects of the treatment could not be noticed in the extracted data (Boutron 2005).

Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Incomplete outcome data (attrition bias)

Attrition bias due to amount, nature or handling of incomplete outcome data

There is a low risk of attrition bias if there were no missing outcome data; reasons for missing outcome data were unlikely to be related to the true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data were balanced in numbers, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with the observed event risk was not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, the plausible effect size (difference in means or standardised difference in means) among missing outcomes was not enough to have a clinically relevant impact on observed effect size, or missing data were imputed using appropriate methods (if drop-outs are very large, imputation using even "acceptable" methods may still suggest a high risk of bias) (van Tulder 2003). The percentage of withdrawals and drop-outs should not exceed 20% for short-term follow-up and 30% for long-term follow-up and should not lead to substantial bias (these percentages are commonly used but arbitrary, not supported by literature) (van Tulder 2003).
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Selective reporting (reporting bias)

Reporting bias due to selective outcome reporting

There is low risk of reporting bias if the study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way, or if the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).
There is a high risk of reporting bias if not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study.
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Group similarity at baseline (selection bias)

Bias due to dissimilarity at baseline for the most important prognostic indicators.

There is low risk of bia*s* if groups are similar at baseline for demographic factors, value of main outcome measure(s), and important prognostic factors (examples in the field of back and neck pain are duration and severity of complaints, vocational status, percentage of patients with neurological symptoms) (van Tulder 2003).
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Co-interventions (performance bias)

Bias because co-interventions were different across groups

There is low risk of bias if there were no co-interventions or they were similar between the index and control groups (van Tulder 2003).
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Compliance (performance bias)

Bias due to inappropriate compliance with interventions across groups

There is low risk of bias if compliance with the interventions was acceptable, based on the reported intensity or dosage, duration, number and frequency for both the index and control intervention(s). For single-session interventions (e.g. surgery), this item is irrelevant (van Tulder 2003).
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Intention-to-treat-analysis

There is low risk of bias if all randomized patients were reported or analysed in the group to which they were allocated by randomization.
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Timing of outcome assessments (detection bias)

Bias because important outcomes were not measured at the same time across groups

There is low risk of bias if all important outcome assessments for all intervention groups were measured at the same time (van Tulder 2003).
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

Other bias

Bias due to problems not covered elsewhere in the table

There is a low risk of bias if the study appears to be free of other sources of bias not addressed elsewhere (e.g. study funding).
Unclear' reflected the fact that there was insufficient information to determine whether this criterion was fulfilled or not.

WHAT'S NEW

Last assessed as up-to-date: 31 August 2013.

Date	Event	Description
11 September 2014	New citation required but conclusions have not changed	The review authors conducted a new search, added four new studies to the review, and used up-to-date methods. The new studies examined the effects of topical capsaicin, acupressure with lavender oil, comfrey root extract, and Brazilian arnica on chronic soft tissue and lower back pain
11 September 2014	New search has been performed	The review authors conducted a new search, added four new trials to the review, and used up-to-date methods. The newly included trials examined the effects of topical capsaicin, acupressure with lavender oil,

(*Continued*)

		comfrey root extract, and Brazilian arnica on chronic soft tissue and lower back pain

HISTORY

Protocol first published: Issue 4, 2003

Review first published: Issue 2, 2006

Date	Event	Description
11 June 2008	Amended	Converted to a new review format
11 June 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

HNO wrote the body of the review, screened trials for inclusion, assessed methodological quality and evidence, and prepared the manuscript for submission to the CBRG.

JJG screened trials for inclusion, assessed methodological quality and grading, edited and wrote the body of the review.

MVT resolved author disagreements on inclusion of articles, translated articles from German to determine inclusion, and edited the final version of the review.

CB edited versions of the protocol and review.

BB edited versions of the protocol and review.

CR updated and edited final version of the review.

DECLARATIONS OF INTEREST

The senior review author, JJG, previously worked as a scientist with a company that produced and sold ingredients reviewed in this Cochrane Review. MVT is a Co-ordinating Editor of the CBRG and editors are required to conduct at least one Cochrane Review. A Cochrane editor who is a Cochrane Review author is excluded from editorial decisions on the Cochrane Review of which they are contributors. Therefore, this involvement does not seem to be a source of conflict of interest in the Cochrane Collaboration.

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Internal sources

- No sources of support supplied

External sources

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- National Center for Complementary and Alternative Medicine, USA.

INDEX TERMS

Medical Subject Headings (MeSH)

*Phytotherapy; Acute Pain [drug therapy]; Benzyl Alcohols [therapeutic use]; Capsicum; Chronic Pain [drug therapy]; Cyclooxygenase 2 Inhibitors [therapeutic use]; Glucosides [therapeutic use]; Harpagophytum; Lactones [therapeutic use]; Low Back Pain [*drug therapy]; Randomized Controlled Trials as Topic; Salix; Sulfones [therapeutic use]

MeSH check words

Adult; Humans