



**Complementary
and alternative
medicines for
the treatment of
rheumatoid arthritis,
osteoarthritis
and fibromyalgia.**

Who are we and what do we do?



Arthritis Research UK is the charity leading the fight against arthritis. We're the UK's fourth largest medical research charity and fund scientific and medical research into all types of arthritis and musculoskeletal conditions. We're working to take the pain away for sufferers with all forms of arthritis and helping people to remain active. We'll do this by funding high-quality research, providing information and campaigning.

Everything we do is underpinned by research.

This report, *Complementary and alternative medicines for the treatment of rheumatoid arthritis, osteoarthritis and fibromyalgia*, has been updated with the latest clinical evidence.

At the back of the report you'll find a glossary of some of the commonly used words. We've underlined these when they're first used.

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Executive summary

Around four out of 10 people in the UK use complementary medicine at some point in their lives, spending over £450 million a year on acupuncture, chiropractic, homeopathy, hypnotherapy, medical herbalism and osteopathy.^{1,2}

People with arthritis and musculoskeletal conditions, whose symptoms are often long-lasting, are particularly attracted to try such medicines, with 60 per cent trying a variety of products.³

This document, written and produced by Arthritis Research UK, is an evidence-based report on the use of complementary and alternative medicines for arthritis and musculoskeletal conditions. It uses data from randomised controlled trials (RCTs) – the type of studies that give the best evidence on whether a treatment is effective or not – and aims to help people with these conditions select which complementary medicines may be useful for them.

This second edition scores medicines according to their effectiveness, with 1 indicating that the available evidence suggests that the compound isn't effective and 5 indicating that there's consistent evidence that the compound is effective. Effectiveness is measured by improvements in pain, movement or general well-being. The report also grades the compounds according to safety, providing traffic-light classifications.

The report reviewed compounds that are taken by mouth (oral) or applied to the skin (topical). Other therapies, such as acupuncture and chiropractic massage, which are commonly used for arthritis and musculoskeletal conditions, are being considered in a separate report.

Despite the number of complementary medicines available and used in the UK, this report found only 31 with evidence available from RCTs. Many of those studied have only been tested in a single or just a few studies, which makes it difficult to be sure whether they work or not.

In terms of safety, much less information is available for complementary medicines in comparison to conventional medicines. However, approximately one fifth of the compounds were given an 'Amber' safety classification, indicating that there were important reported side-effects.

Rheumatoid arthritis

The compounds researched score poorly for rheumatoid arthritis, with 12 out of 17 complementary medicines (71 per cent) scoring just 1. At the other end of the scale, fish body oil scores a maximum 5 for effectiveness, which suggests that it offers real benefits. It also received a green light for safety.

Osteoarthritis

Alternative medicines appear to be more promising for people with osteoarthritis, with only 4 out of 22 approaches (18 per cent) scoring 1 point:

- The nutritional supplement SAMe was found to be well tolerated and scored a 4 for effectiveness.
- Capsaicin, made from chilli peppers, proved the most effective for osteoarthritis, scoring the full 5 points.
- Glucosamine – one of the most widely taken products – has undergone many trials, but the evidence for its effectiveness is mixed; some trials show benefit, while many don't. A recent review and analysis of all the evidence shows that, overall, there's little clinical benefit in terms of pain or changes in the joint, so glucosamine sulphate scored 2 and glucosamine hydrochloride scored 1.

Fibromyalgia

Only four products were assessed for fibromyalgia but none were highly effective, with three scoring just 2 out of 5 and the fourth an ineffective 1.

The research studies used in the report are referenced so you can find out more information if you wish to. In addition, we've published the following papers based on the work in this report:

- Macfarlane GJ, El-Metwally A, De Silva V, Ernst E, Dowds GL, Moots RJ on behalf of the Arthritis Research UK Working Group on Complementary and Alternative Medicines. Evidence for the efficacy of complementary and alternative medicines in the management of rheumatoid arthritis: a systematic review. *Rheumatology (Oxford)*. 2011; 50(9):1672–83.
- De Silva V, El-Metwally A, Ernst E, Lewith G, Macfarlane GJ on behalf of Arthritis Research UK Working Group on Complementary and Alternative Medicines. Evidence for the efficacy of complementary and alternative medicines in the management of osteoarthritis: a systematic review. *Rheumatology (Oxford)*. 2011; 50(5):911–20.
- De Silva V, El-Metwally A, Ernst E, Lewith G, Macfarlane GJ on behalf of Arthritis Research UK Working Group on complementary and alternative medicines. Evidence for the efficacy of complementary and alternative medicines in the management of fibromyalgia: a systematic review. *Rheumatology (Oxford)*. 2010; 49(6):1063–68.

1. Thomas KJ, Coleman P. Use of complementary or alternative medicine in a general population in Great Britain. Results from the National Omnibus Survey. *Journal of Public Health* 2004; 26:152–57.

2. Thomas KJ, Nicholl JP, Coleman P. Use and expenditure on complementary medicine in England: a population based survey. *Complementary Therapies in Medicine* 2001; 9:2–11.

3. Bishop FL, Yardley L, Lewith GT. A systematic review of beliefs involved in the use of complementary and alternative medicine. *Journal of Health Psychology* 2007; 12:851–67.

Introduction

Complementary and alternative medicines (we will call them complementary medicines) are a group of diverse medical and healthcare systems, practices and products that aren't presently considered to be part of conventional medicine. They're defined by the World Health Organisation as 'a broad set of healthcare practices that are not part of the country's own tradition and are not integrated into the dominant healthcare system.'

The use of complementary medicine is more common than ever among people in the UK. Studies have suggested that 46 per cent of us will use complementary medicine at some point in our lives and 10 per cent of us will visit a complementary medicine practitioner each year.^{1,2}

It's estimated that over £450 million is spent annually by individuals on the main types of complementary medicine (acupuncture, chiropractic, homeopathy, hypnotherapy, medical herbalism and osteopathy). One of the most popular complementary medicines for arthritis is glucosamine, and the cost of taking these tablets will typically be around £10 a month. Complementary medicines are used in a variety of ways; some people use them instead of conventional treatments, some alongside. Some people use them regularly and some intermittently.³

People with arthritis and musculoskeletal conditions – whose symptoms are often long-lasting – may be particularly attracted to try such medicines. Evidence suggests that users of complementary medicine:

- want to participate in treatment decisions
- are likely to have active coping styles
- value non-toxic, holistic approaches to health
- tend to believe that psychological and lifestyle factors are important in the development of illness
- believe they can control their health.

Despite the fact that complementary medicines are commonly used, there are many areas that we don't know a lot about. We have little information available on the following:

- how complementary medicines might work in theory or whether they work in practice
- how they compare with available conventional treatments
- what the most effective dose is
- how they interact with drugs, which could change the effectiveness of such conventional treatment – this may be particularly important since many people taking complementary medicines don't tell their doctor
- how well tolerated some complementary medicines really are, despite the frequent assumption that because they're 'natural', they're not harmful.

Unlike medically qualified doctors, most complementary medicine practitioners aren't currently regulated by any government rules, and most herbal medicines in the UK don't need a licence as they're not commercially produced. The Medicines and Healthcare products Regulatory Agency (MHRA), a government body that makes sure medicines are safe and effective before they're licensed and allowed onto the UK market, introduced the Traditional Herbal Medicine Registration Scheme in 2005. Under this scheme, herbal medicine products are required to demonstrate only safety and quality, as it's often difficult for these treatments to be proven effective.

This report provides a resource for people with arthritis and healthcare professionals by giving a summary of the current evidence on commonly used complementary medicines. We've focused on the two most common forms of arthritis, rheumatoid arthritis and osteoarthritis, as well as the chronic musculoskeletal pain disorder fibromyalgia.

Rheumatoid arthritis – the most common inflammatory arthritis – is a chronic disease that affects the joints, often in the wrists, fingers and feet. Common symptoms include pain, stiffness and fatigue.

Osteoarthritis – is an extremely common condition and is often referred to as 'wear and tear' of the joints in the body. The surface of the joint is damaged and the surrounding bone grows thicker. The joints most commonly affected are the knees, hips, hands and spine.

Fibromyalgia – is one of the most common reasons for being referred to a rheumatologist. Symptoms include widespread pain, fatigue and sleep disturbance. The condition doesn't result in any damage to the joints or muscles that can explain the symptoms.

How was the information in this report gathered?

In this report we've only considered compounds which are taken by mouth or applied to the skin, so therapies such as acupuncture, chiropractic and massage, which are commonly used for arthritis and musculoskeletal conditions, haven't been included. These therapies will be the topic of a separate report. A very large number of compounds have been proposed for use in our three target conditions, and this report aims to cover all those where there's been a claim of supporting research evidence. We've considered trials where the compound was compared with a conventional treatment or a placebo (a dummy pill which doesn't contain any active ingredient).

The search for and evaluation of evidence has been conducted by experts in the fields of rheumatology, complementary medicine and nutrition, and it has also included input from a patient representative. Details of those involved are given in the Appendix.

How were complementary medicines classified?

Are complementary medicines effective?

In this report we've evaluated whether there's evidence that each complementary medicine works. Effectiveness might relate to improvement in pain but it also may relate to improvement in movement or general wellbeing.

In assessing compounds, we've relied heavily on data from randomised controlled trials (RCTs). These are studies where participants (people taking part in trials) are randomly allocated to one treatment group. At the end of the study, results are evaluated according to whether participants on a new treatment, for example, had a better outcome than participants on an existing treatment. RCTs of complementary medicines often use a placebo to allow the effect of treatment to be compared when the patients don't know which treatment they received.

RCTs provide the best type of evidence on whether any treatment works. Other types of study, where participants choose the treatments they take, are very difficult to interpret because those with more serious disease might have opted for one treatment and others with milder disease another. Also, participants who choose their treatment do so because they believe it'll be effective, which might influence how they respond to it and evaluate it.

The quality of RCTs can vary, which affects how reliable the results are. To show where results are less reliable, the trials included in this report were judged based on a scoring system called the Jadad scale. This system is commonly used to evaluate the quality of published RCTs in the field of complementary medicine. The Jadad scale has levels from 1 (very poor quality) to 5 (very good quality). To make it easier to use, we've collapsed the scale into two categories:

- good/high quality (Jadad score 3 or above)
- low quality (Jadad score below 3).

We've marked trials with low quality with the symbol[‡]. These studies were given a lower weighting when we came to our conclusions about the compound.

We've also only included trials in which results have been analysed on an 'intention to treat' basis. This means that if a participant is randomly allocated to receive 'treatment A', their results are analysed as if they received that treatment (even if they decided not to take the medication). This is the best method of analysis to avoid bias.

Based on the evidence available from clinical trials and other supporting information, we've categorised each medicine into one of five categories:

1. Overall, there's no evidence to suggest that the compound works or only a little evidence which is outweighed by much stronger evidence that it doesn't work.
2. There's only a little evidence to suggest the compound might work. The evidence in this category often comes from a single study which has reported positive results, and there are therefore important doubts about whether or not it works.
3. There's some promising evidence to suggest that the compound works. The evidence will be from more than one study; however, there may also be some studies showing that it doesn't work. Therefore, we're still uncertain whether compounds in this category work or not.
4. There's some consistency to the evidence, which will come from more than one study, to suggest that the compound works. Although there are still doubts from the evidence that it works, on balance we feel that it's more likely to be effective than not.
5. There's consistent evidence across several studies to suggest that this compound is effective.

These classifications are based on the results of studies overall. In each study, however, there are people who seem to respond to treatment and those who don't. Therefore, for medicines which we think are effective, a greater proportion of people taking this medicine improved compared with, for example, those taking placebo, or roughly the same proportion of people improved compared to another group taking a conventional drug which is known to be effective. It doesn't mean that everyone taking the medicine will improve. Similarly, for medicines which we think aren't effective, the proportion of people reporting improvement when taking these medicines was the same as people taking the placebo, for example.

Sometimes we describe the differences in improvement for participants on one compound as 'significant'. This means that we're fairly sure that the differences between groups didn't happen just by chance, but it doesn't necessarily mean that the differences (e.g. with respect to improvement in pain) are large. In these respects, the interpretation of the data is no different from that used for conventional medicines – the evidence for conventional treatments doesn't reach level 5 in all the conditions for which they're prescribed.

Are complementary medicines safe?

We've also categorised all compounds according to their safety. For many compounds, this isn't easy because there's relatively little information available. Where data are available, we've categorised the compound assuming that it's taken within the range of recommended doses. Compounds which are well tolerated at the recommended doses may have serious side-effects when taken at higher doses.

Again, it should be emphasised that most conventional medicines have side-effects, some serious, but we generally have more information on conventional drugs to work out what these effects are and how often they happen.

We've classified the compounds using a traffic-light system:

	Compounds in this category are reported to have mainly minor and infrequent side-effects. A green classification doesn't mean that the compound has no reported side-effects and users should check what these are in the product information leaflet.
	Compounds with an amber rating have commonly reported side-effects (even if they're mainly minor symptoms) or more serious side-effects.
	Compounds with a red rating have serious reported side-effects. Users should consider carefully before deciding whether to take these medicines.

Some compounds have very little information on side-effects and we've therefore not been able to classify them. These are indicated with an amber rating and the statement, 'No information'.

What else should I know?

Can I take complementary medicines alongside conventional medicines?

Complementary medicines can interact with each other and with conventional medicines. It's important that you check with either a pharmacist or your doctor if particular complementary medicines could interfere with any other medication you're using. We've mentioned some important interactions in the report, but these aren't comprehensive lists – they simply mention the most important interactions or relate to common medications.

The complementary medicine I want information about isn't covered in this report. Why?

Only oral or topical compounds which have been tested in at least one RCT have a specific section in this report. If the compound that you're searching for doesn't appear here, that means we couldn't find any reports of a RCT testing that compound. This means it's not possible for us to tell whether it works or not. We list some of the commonly used complementary medicines that lack RCT support in the tables at the end of the report.

We've restricted the report to compounds that we could source in June 2011 from a national high-street retailer or through a UK-based internet supplier. In a few circumstances we've included overseas retailers where an address and contact details were provided and it was specifically mentioned on their website that they ship to the UK. Please note that availability can change – some compounds which could be sourced at the time of the first report are no longer available, and these are listed at the end of the report.





**This report gives
a summary of the
current evidence
on commonly used
complementary
medicines.**



**We've considered
compounds taken
by mouth or applied
to the skin.**

How do I interpret the data?

Featured compound

The information for each complementary medicine is shown in the following way. The headline name for a compound is the most commonly used name. We also provide information on the family the compound belongs to, its scientific name and any other names by which it's commonly known (including some trade names):

The large letters refer to the condition for which we have been able to find some research evidence to evaluate whether the compound works or not:

- RA** = rheumatoid arthritis
- OA** = osteoarthritis
- F** = fibromyalgia.

What is it?

This section gives a brief explanation of the compound and how it's made.

How does it work?

A summary of the ways the compound is thought to work is presented here.

Is it safe?

This section summarises the information available but doesn't include all side-effects. Little information is available to determine the safety and toxicity of many complementary medicines.

Where do I get it from?

Information on the availability of the compound is given here.

What are the possible interactions?

This information gives information, if available, on how the complementary medicines may affect other drugs. Little is known about possible interactions of many complementary medicines.

What dose should I use?

There is rarely information on appropriate doses for complementary medicines. Where available, the data in this section usually relates to doses used in the trials reported.

The role in treatment of arthritis and musculoskeletal conditions

An overview of results from RCTs examining the effects of complementary medicine in managing osteoarthritis, rheumatoid arthritis or fibromyalgia is listed here.

Conclusion:

The conclusion gives the most important information about the compound. Results from high-quality studies were given more weighting in the final conclusion.

References:

This section gives a list of key references if you'd like to read more about individual studies.

Classification:

Effectiveness score
in osteoarthritis:
5



Effectiveness score
in fibromyalgia:
2



Safety classification:
Green





**Four out of 10
people in the UK
use complementary
medicine at
some point.**

**Sixty per cent of
people with long-
term conditions
will try a variety
of products.**

Where can I get more information about the individual complementary medicines?

At the end of each entry there are some references to scientific papers. These publications report the results of the individual RCTs, or review the results from several RCTs, on which we've based our ratings. Many of these articles can be accessed via PubMed, a publicly available service of the US National Library of Medicine, at www.pubmed.com. There may be a charge for some of the articles.

If you wish to read other publications that provide general information on the use and safety of complementary medicines, or about the evidence, you may find some of the following useful:

- Arthritis Research UK's booklet *Complementary and alternative medicine for arthritis* is a general information booklet on the most common complementary therapies.
- The Medicines and Healthcare products Regulatory Agency provides information on the licensing of medicines in the UK. Their website has a section devoted to the regulation and safety of herbal medicines: www.mhra.gov.uk
- Ernst E, Pittler MH, Wider B, editors. *The Desktop guide to complementary and alternative medicine: an evidence-based approach*. Edinburgh: Mosby Elsevier; 2006. ISBN-3 978-0-7234-3383-5. This book provides a detailed scientific review of the evidence and safety of complementary medicines.
- Ernst E, Pittler MH, Wider B, editors. *Complementary therapies for pain management: an evidenced-based approach*. Philadelphia: Mosby Elsevier; 2007. ISBN-3 978-0-7234-3400-9
- Barnes J, Anderson LA, Phillipson JD, *Herbal Medicines*. 3rd ed. London: Pharmaceutical Press; 2007. ISBN-3 978-0-8536-9623-0
- Encyclopedia of Alternative Medicine: www.enotes.com/alternative-medicine-encyclopedia

If there are several trials which have been conducted, we'll often summarise the information from a published review. We will, however, include the proportion of participants withdrawing and the main reported side-effects from individual studies.

The original report was compiled following detailed discussions by the committee (see Appendix), which were based on a full review of information available in 2008. Emerging information from scientific studies was monitored through mid-2011 and changes have been made to the text and classifications by the chair of the committee where necessary.



1 Andrographis paniculata



Family:

Herbal medicine of the Acanthaceae family

Scientific name:

Andrographis paniculata (Burm.f) Nees

Other names:

Andrographis, Chuan Xin Lian, Kalmegh, king of bitters

What is it?

The Acanthaceae family is native to Asia and the plant is grown throughout the world. Small clusters of white flowers appear in summer and autumn, and the plant is cultivated when these flowers begin to bloom.

How does it work?

Laboratory studies and studies on humans suggest that andrographis may act against infections and viruses, and relieve diarrhoea, fever and pain.

Is it safe?

In studies on humans, Andrographis has only been associated with rare and minor side-effects; however, a small number of cases of urticaria (a skin reaction characterised by sudden wheals or papules, accompanied by severe itching) have been reported. Taking large doses of Andrographis may cause gastric discomfort, vomiting and loss of appetite.

Where do I get it from?

Anthrographis paniculata is available through UK websites.

What are the possible interactions?

Interactions may occur with paracetamol/acetaminophen, anticoagulants, anti-hypertensives, immunosuppressants and insulin/oral hypoglycaemic agents.

What dose should I use?

The trial reported in this section used 30 mg andrographolides, three times a day.

The role in treatment of arthritis and musculoskeletal conditions

In one RCT, 60 people with rheumatoid arthritis were given either Andrographis paniculata tablets containing 30 mg of andrographolides or placebo tablets containing lactose three times a day for 14 weeks.

- Although there was some improvement in joint tenderness and function in the Andrographis group, there were no differences in the outcomes compared to placebo.
- Three of the participants in the Andrographis group reported headaches.

Conclusion

Andrographis paniculata is a herbaceous plant from the Acanthaceae family. Tablets can only be bought over the internet. The effectiveness of Andrographis paniculata in people with musculoskeletal disease hasn't been widely studied: only one RCT has been conducted, which showed that the outcome is the same as with the placebo.

References:

- Burgos RA, Hancke JL, Bertoglio JC, Aguirre V, Arriagada S, Calvo M, Cáceres DD. Efficacy of an Andrographis paniculata composition for the relief of rheumatoid arthritis symptoms: a prospective randomised placebo-controlled trial. *Clinical Rheumatology* 2009; 28:931–46.

Classification:

Effectiveness score:
1



Safety classification:
Green



Andrographis paniculata is a herbaceous plant from the Acanthaceae family, which is native to Asia but grown throughout the world.

2 Anthocyanidins



Family:

Nutritional supplement

Scientific name:

Anthocyanidins

Other names:

Colladeen®

What are they?

Anthocyanidins are a subgroup of flavonoids, which are chemicals that are made from the parts of some plants that don't provide nutrients.

How do they work?

Several laboratory studies have shown that anthocyanidins can act as strong antioxidants. Anthocyanidins can also prevent the destruction of collagen in the muscles, a problem that has been observed in some people with fibromyalgia.

Are they safe?

Reported side-effects on short-term usage include stomach upsets, rashes and problems passing urine. There are no reports on the long-term safety of anthocyanidins.

Where do I get them from?

Anthocyanidins are available over the counter in pharmacies in the form of capsules (Colladeen®). They can also be ordered over the internet.

Anthocyanidins are a subgroup of flavonoids, chemicals that are made from the parts of some plants that don't provide nutrients.

What are the possible interactions?

Interactions with other drugs haven't been well studied.

What dose should I use?

Doses ranging from 40–120 mg a day have been used in a randomised controlled study. No trials have been conducted to find an appropriate dosage in musculoskeletal conditions.

The role in treatment of arthritis and musculoskeletal conditions

A small trial of 12 participants evaluated the role of anthocyanidins in treating fibromyalgia. Participants were given either 120 mg, 80 mg or 40 mg of anthocyanidins or placebo tablets once a day for 3 months. They were asked to report the severity of their pain, the degree of fatigue and sleep problems in a daily diary. The investigator also evaluated the improvement of these symptoms by interviewing the participants once every month.

- Anthocyanidins weren't effective in reducing pain (as evaluated by the participant and the investigator) at any daily doses during any part of the follow-up.
- A similar lack of effect on fatigue was also reported by participants, although some beneficial effect was observed by the investigators during the interviews.
- Based on participants' daily reports, a significant reduction in sleep disturbance was reported by those taking anthocyanidins compared to those on the placebo; however, such beneficial effects weren't confirmed by the investigators during the interviews.
- Participants who were on anthocyanidins reported more side-effects than those who were given placebo capsules.

Conclusion

Anthocyanidins are a subgroup of flavonoids with strong antioxidant properties that can theoretically support and prevent the destruction of collagen in muscles. The effectiveness of these food supplements in the treatment of participants with fibromyalgia was only tested in one small RCT, in which no reduction in pain and an unconfirmed improvement in fatigue and sleeping problems were found. The limited data available doesn't yet allow for reliable evaluation of the role of this treatment for fibromyalgia.

References:

- Edwards AM, Blackburn L, Christie S, Townsend RGN, David J. Food supplements in the treatment of primary fibromyalgia: a double-blind, crossover trial of anthocyanidins. *Journal of Nutrition & Environmental Medicine* 2000; 10:189–99.

Classification:

Effectiveness score:
1



Safety classification:
Amber



3 Antler velvet



Family:

Nutritional supplement of the Cervidae family

Scientific name:

Elk velvet antler

Other names:

Cervus elaphus, deer velvet, velvet deer antler

What is it?

Antler velvet is made from deer or elk antlers in early stages of their growth (during the velvet stage). In ancient China, antler velvet was used as a sexual tonic, but now the powdered form is available in most western countries and marketed as a general tonic, an anti-stress aid and also as a medication for osteoarthritis and rheumatoid arthritis.

How does it work?

Laboratory and animals studies have shown that pilose, a protein found in antler velvet, has an anti-inflammatory effect. Antler velvet is also rich in chondroitin sulphate, collagen and glucosamine sulphate. The properties and make-up of the compound could make it a useful treatment in a variety of types of arthritis.

Is it safe?

No major side-effects have been reported in previous studies on humans lasting 6 months. Androgenic (male hormone type) side-effects have been noted in animal studies.

Where do I get it from?

This compound is only available outside the UK, but at least one supplier provides an address, contact details and indicates specifically that they ship to the UK.

What are the possible interactions?

Interactions haven't been well studied. Theoretically, antler velvet may interact with sexual tonics and hormonal medications (e.g. testosterone).

What dose should I use?

There isn't any available evidence on the best dose in arthritis and related conditions.

The role in treatment of arthritis and musculoskeletal conditions

Two RCTs examined the effect of antler velvet in treating rheumatoid arthritis.

Trial 1* – In the first trial, 40 participants were randomly assigned to receive either 430 mg, 860 mg or 1,290 mg antler velvet capsules or placebo capsules once a day for a month. Participants who received antler velvet didn't show a significant improvement in their disease condition compared to the placebo group.

Trial 2* – In the second trial, 168 participants were randomly selected to receive either antler velvet or placebo capsules. After 6 months of treatment, neither group differed significantly with respect to disease activity, pain experience and overall health status.

In both trials, antler velvet was generally shown to be very well tolerated with no apparent side-effects that forced any participants to stop the medication.

Conclusion

Antler velvet is a nutritional supplement that has anti-inflammatory properties and is rich in glucosamine and other 'building blocks' of cartilage. It has no major side-effects, but based on the results of two RCTs, there's no evidence to suggest that antler velvet is effective in treating rheumatoid arthritis.

References:

- Allen M, Oberle K, Grace M, Russell A. Elk velvet antler in rheumatoid arthritis: phase II trial. *Biological Research for Nursing* 2002; 3(3):111–18.
- Allen M, Oberle K, Grace M, Russell A, Adewale AJ. A randomised clinical trial of elk velvet antler in rheumatoid arthritis. *Biological Research for Nursing* 2008; 9(3):254–56.

Classification:

Effectiveness score:
1



Safety classification:
Green



*A trial of low quality. Results of this trial were given a lower weighting when we came to our conclusion about the compound.

4 Blackcurrant seed oil



Family:

Nutritional supplement

Family:

Herbal medicine of the Saxifragaceae family

Scientific name:

Ribes nigrum

Other names:

Quinsy berries, squinancy berries, cassis, red currant, European blackcurrant, mustaherukka, grosellero negro, siyah frenkuzumu

What is it?

Ribes nigrum is a plant native to northern parts of Europe and Asia. The fruit of this plant is a very dark purple berry containing seeds. The berries and leaves are used for maintaining health and treating several diseases.

How does it work?

Oil produced from blackcurrant seeds contains 13 per cent omega-3 alpha-linolenic acid (ALA) and 17 per cent omega-6 gamma-linolenic acid (GLA).

Is it safe?

No studies appear to have been done to assess the safety of blackcurrant seed oil in people with musculoskeletal conditions; however, studies on other GLA-rich oils suggest that they're relatively well tolerated with no serious side-effects.

Where do I get it from?

The compound is available over the internet from UK-based suppliers.

What are the possible interactions?

Interactions with other drugs haven't been well studied.

What dose should I use?

No trials have been conducted to establish appropriate dosage in musculoskeletal conditions. Doses of 3 g a day and 10.5 g a day have been used in trials.

The role in treatment of arthritis and musculoskeletal conditions

Two RCTs examined the effect of blackcurrant seed oil in treating rheumatoid arthritis.

Trial 1 – In the first RCT, 14 participants were randomly selected to receive 10.5 g blackcurrant seed oil (15 capsules) daily for 24 weeks, while the other 20 participants received placebo capsules made from soybean oil for the same period of time. All participants were asked to continue their usual diets and medications.

- Only 50 per cent of participants in the group allocated blackcurrant seed oil capsules completed the 24-week trial. The main two reasons for stopping the medication were the large amount and size of the capsules, and the perceived lack of effectiveness of the treatment.

- Compared to the placebo group, those in the blackcurrant seed oil group who completed the trial had a significant but moderate reduction in joint tenderness, but only mild and non-significant reduction in pain, morning stiffness and overall disease severity.
- The report states that side-effects of blackcurrant seed oil were negligible and didn't contribute to participants withdrawing from the trial. The nature of the side-effects wasn't reported.

Trial 2 – In the second RCT, 20 participants were randomly selected to receive 3 g blackcurrant seed oil (six capsules) daily for 6 weeks, while the other 10 participants received placebo capsules made of sunflower seed oil for the same period of time. The effects on morning stiffness, grip strength, pain and physical function were measured at the end of the trial and again 6 weeks after treatment.

- Compared to the placebo group, who showed no improvement at both assessment points, participants on blackcurrant seed oil had significant reduction in morning stiffness at the end of the treatment; however, this beneficial effect wasn't observed 6 weeks after the trial had ended.
- Blackcurrant seed oil had no significant effect on improving pain, grip strength and physical function compared with the placebo at both assessment points.

Conclusion

Blackcurrant seed oil is rich in both omega-3 and omega-6 fatty acids that are important for maintaining joints' cell structure and function, and can fight joint inflammation. This nutritional supplement is available over the counter as capsules and as bottled oil. It's considered to be a relatively well-tolerated medication; however, the little available evidence suggests that blackcurrant seed oil may not be effective in treating rheumatoid arthritis.

References:

- Leventhal LJ, Boyce EG, Zuerier RB. Treatment of rheumatoid arthritis with blackcurrant seed oil. *British Journal of Rheumatology* 1994; 33(9):847-52.
- Watson J, Byars ML, McGill P, Kelman AW. Cytokine and prostaglandin production by monocytes of volunteers and rheumatoid arthritis participants treated with dietary supplements of blackcurrant seed oil. *British Journal of Rheumatology* 1993; 32(12):1055-58.

Classification:

Effectiveness score:
1



Safety classification:
Green



5 Borage seed oil



Family:

Herbal medicine of the Boraginaceae family

Scientific name:

Borago officinalis

Other names:

Star flower oil, bee bread, tailwort, common bugloss, echium amoenum

What is it?

Borago officinalis is an annual herb native to the Mediterranean region but grown in other countries, including the UK. The medicinal product is produced from the plant seed oil.

How does it work?

In addition to its content of tannic, oleic and palmitic acid, the oil made from borage seed contains very high levels of two types of polyunsaturated omega-6 essential fatty acids, 20–26 per cent gamma-linolenic acid (GLA) and linolenic acid (LA, which is converted in the body to GLA). Several factors can interfere with the production of GLA from LA in the body, including ageing, dietary deficiencies, viral infections and some diseases. Sunflower oil and other oils generally used in normal diet contain only LA. Borage seed oil is the richest source of pure GLA.

Is it safe?

Reported side-effects include nausea, indigestion, headaches and skin rashes. Borage seed oil contains small amounts of some liver toxins, but preparations free of these toxins are available.

No studies to assess the safety of borage seed oil in people with arthritis and related conditions appear to have been done; however, studies on other GLA-rich oils suggest that they're relatively safe with no serious side-effects.

Where do I get it from?

The compound is available from UK high-street retailers.

What are the possible interactions?

The effects borage seed oil has on drugs haven't been well studied, but interactions with anti-inflammatory drugs (e.g. cortisone) and anticoagulants are possible. Some sedatives and medications for hypertension can suppress borage seed oil's anti-inflammatory properties.

What dose should I use?

No trials have been conducted to find out the best dosage for arthritis-related conditions. Preliminary studies have established that high doses of GLA (more than 1 g a day) are needed to partially relieve symptoms.

The role in treatment of arthritis and musculoskeletal conditions

Two RCTs evaluated the effect of borage seed oil in treating rheumatoid arthritis. All participants were asked to continue with their usual treatment plan during the trial period.

Trial 1 – In the first trial, 37 people with rheumatoid arthritis were randomly assigned to receive either borage seed oil containing 1.4 g GLA or a placebo of cotton seed oil daily for 24 weeks. Compared to the placebo group, who showed no improvement during the trial, participants who received borage seed oil showed an improvement in joint tenderness, number of swollen joints and morning stiffness.

Trial 2 – In the second RCT, 56 participants with rheumatoid arthritis were randomly assigned to take either a daily dose of borage seed capsules containing 2.8 g GLA or placebo capsules of sunflower seed oil for 6 months.

- 64 per cent of those on borage seed oil showed improvement in joint tenderness and morning stiffness, compared to only 21 per cent in those on placebo treatment.
- There was a significant difference in the treatment outcome of the two patient groups in favour of borage seed oil.

In both RCTs, the number of participants withdrawing from the study, due to treatment ineffectiveness or side-effects, was small. Reported side-effects were minor and included belching, diarrhoea and flatulence.

Conclusion

Borage seed oil is rich in essential fatty acids that can regulate the body's immune system and fight joint inflammation. This nutritional supplement can be purchased over the counter from pharmacies and health food shops in the form of capsules or bottled oil. The available evidence suggests that borage seed oil may improve rheumatoid arthritis-related symptoms.

References:

- Leventhal LJ, Boyce EG, Zurier RB. Treatment of rheumatoid arthritis with gamma-linolenic acid. *Annals of Internal Medicine* 1993; 119(9):867–73.
- Zurier RB, Rossetti RG, Jacobson EW, DeMarco DM, Liu NY, Temming JE et al. Gamma-linolenic acid treatment of rheumatoid arthritis. A randomised, placebo-controlled trial. *Arthritis & Rheumatism* 1996; 39(11):1808–17.

Classification:

Effectiveness score:

3



Safety classification:

Green



6 Capsaicin



Family:

Herbal medicine extracted from chilli peppers
(Capsicum family)

Scientific name:

Capsaicin

Other names:

Axsain®, Zacin®, chilli, pepper gel, cayenne

What is it?

Capsaicin is the main medicinally active component of chilli peppers. It's extracted from the plant's tissues.

How does it work?

Several studies have found that capsaicin can use up Substance P, which plays an important role in the transmission of pain signals from nerve endings to the brain and is involved in activating inflammatory substances in joints.

Is it safe?

There are no major safety concerns in applying capsaicin gel/cream to a painful area of the body, although most people will feel a burning sensation when the gel comes into contact with their skin. This is because capsaicin also binds to specific receptors in nerve endings called VR1, producing a burning sensation which isn't caused by any tissue damage. Brief skin redness is common, but high doses of capsaicin can cause skin blisters. A review of topical capsaicin for the treatment of chronic pain (not specifically related to osteoarthritis, rheumatoid arthritis or fibromyalgia) concluded that approximately a third of people experience a reaction around the area where the treatment is applied. It's important to keep capsaicin away from the eyes, mouth and open wounds as it's highly irritant.

Where do I get it from?

Capsaicin is available on prescription as a cream and is licensed in the UK for the treatment of pain associated with osteoarthritis.

What are the possible interactions?

There have been no reported drug interactions.

What dose should I use?

Most trials have used either 0.025 per cent or 0.075 per cent of capsaicin gel applied to the skin four times a day.

The role in treatment of arthritis and musculoskeletal conditions

Capsaicin has been tested for its effect in both osteoarthritis and fibromyalgia. The information on osteoarthritis has been taken from three individual trials and a review article which summarised the results of three separate RCTs. One RCT investigated the topical application of capsaicin gel in fibromyalgia.

Osteoarthritis

Review article (1994) – The trials included in this article investigated the effectiveness of topical application of capsaicin gel in treating osteoarthritis when compared to a placebo gel. In the three trials, capsaicin (0.025 per cent in two trials and 0.075 per cent in one) was applied four times a day for a treatment period ranging between 4 and 12 weeks.

- Capsaicin was found to be more effective than the placebo in all three trials.
- When data from the trials were analysed together to get a single estimate of effectiveness, it was found that capsaicin was four times more effective in improving pain and joint tenderness in participants with osteoarthritis as compared to placebo gel.

Trial 1 – A separate trial published in 1994 randomly selected 113 people with osteoarthritis to apply either capsaicin cream or a placebo to their affected joint four times a day for 12 weeks.

- Significantly more participants using capsaicin cream had a reduction in pain, as assessed by a doctor and by the participants themselves.
- The severity of pain and joint tenderness was significantly reduced in participants using capsaicin.

Trial 2 – In an RCT published in 2000, 200 participants with osteoarthritis were randomly selected to apply one of the following to their affected joint for 6 weeks: 0.025 per cent capsaicin cream; glyceryl trinitrate cream; a cream containing both ingredients; a placebo cream.

- Participants given any of the three active treatments had a significant reduction of both joint pain and painkiller use compared to participants who received the placebo cream.
- Participants who used the cream that contained both active treatments had the greatest improvement in pain and the most significant reduction of painkiller use.

Similar beneficial results were found in another RCT, which evaluated the effectiveness of an ointment containing several herbal compounds, including 0.015 per cent capsaicin (Arthritis Relief Plus), in treating joint pain and stiffness in 36 people with osteoarthritis.

Trial 3*—In the most recent trial, 100 women with mild to moderate osteoarthritis of the knee received either 0.0125 per cent capsaicin gel or a placebo gel three times a day for 4 weeks. This was followed by 1 week with no treatment, then another 4 weeks of the treatment they hadn't previously used. Greater improvements in pain, stiffness and function were reported in relation to the capsaicin gel compared to the placebo gel.

Fibromyalgia

Trial 1—In this trial, 45 participants were randomised to apply either 0.025 per cent capsaicin gel or placebo gel to areas with pain four times a day for 4 weeks. Participants who used capsaicin reported less tenderness and experienced significant increase in grip strength when compared to participants on the placebo.

Conclusion

Capsaicin, which is extracted from chilli peppers, is available on prescription in pharmacies in the form of gel, cream and plasters. It works mainly by its ability to reduce Substance P, a pain transmitter in human nerves. Results from RCTs evaluating its role in treating osteoarthritis indicate that it has no major safety problems and can be effective in reducing pain and tenderness in affected joints. Evidence for its effectiveness for fibromyalgia is related to a single trial.

References:

- Zhang WY, Li Wan Po A. The effectiveness of topically applied capsaicin. A meta-analysis. *European Journal of Clinical Pharmacology* 1994; 46(6):517–22.
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- McCleane G. The analgesic efficacy of topical capsaicin is enhanced by glyceryl trinitrate in painful osteoarthritis: a randomised, double-blind, placebo-controlled study. *European Journal of Pain* 2000; 4(4):355–60.
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- McCarty DJ, Csuka M, McCarthy G, Trotter D. Treatment of pain due to fibromyalgia with topical capsaicin: a pilot study. *Seminars in Arthritis & Rheumatology* 1994; 23 (Suppl 3):41–47.
- Kosuwon W, Sirichatiwapee W, Wisanuyotin T, Jeeravipoolvarn P, Laupattarakasem W. Efficacy of symptomatic control of knee osteoarthritis with 0.0125% of capsaicin versus placebo. *Journal of the Medical Association of Thailand* 2010; 93(10):1188–95.

Classification:

Effectiveness score
in osteoarthritis:
5



Effectiveness score
in fibromyalgia:
2



Safety classification:
Green



*A trial of low quality. Results of this trial were given a lower weighting when we came to our conclusion about the compound.



7 Cat's claw



Family:

Herbal medicine of the Rubiaceae family

Scientific name:

Uncaria tomentosa

Other names:

Life-giving vine of Peru, una de gato

What is it?

Cat's claw is extracted from the stem and root of some woody vines native to South and Central America.

How does it work?

Laboratory studies have found that cat's claw can prevent the activation of several inflammatory substances in the body, which has been confirmed by studies on animals. Studies have also shown that cat's claw has antioxidant properties (meaning they can prevent cell damage in the body by interacting with harmful molecules, known as free radicals, which are produced within the cells).

Is it safe?

There's a lack of data on the clinical safety of cat's claw. No serious side-effects were reported in one trial whose participants had rheumatoid arthritis; however, there was an isolated report of serious kidney problems in a woman with lupus.

Where do I get it from?

Cat's claw is available in high-street stores in the UK.

What are the possible interactions?

Cat's claw may increase the effect of drugs used to treat hypertension so should be taken with caution by people using this type of medication. Laboratory studies have also found that cat's claw can stimulate the production of certain immune hormones called cytokines. These cells are important for immunity. For that reason, people who are on immunosuppressants should be cautious when taking this compound.

What dose should I use?

A dose of 60 mg a day of the active component (*Uncariae tomentosae*) was used in one trial; however, no studies have been conducted to find an appropriate dosage for musculoskeletal conditions.

The role in treatment of arthritis and musculoskeletal conditions

One RCT has been conducted to evaluate the role of cat's claw in treating rheumatoid arthritis. In this trial, 40 participants with the condition who were all on conventional treatment with sulfasalazine or hydroxychloroquine were randomised to receive either cat's claw tablets (60 mg of *Uncariae tomentosae*) or placebo tablets once a day for 24 weeks (phase A). Participants in both treatment groups were then asked to take cat's claw for an additional 28 weeks (phase B). All participants in both phases were asked to continue their usual treatment during both phases of the trial.

- 53 per cent of participants allocated cat's claw in phase A reported a significant reduction in the number of painful joints compared to only 24 per cent of participants who were on placebo tablets during the same phase.
- Participants in both groups didn't differ with respect to morning stiffness and number of tender or swollen joints during this period.
- Significant beneficial effects on all clinical aspects were observed in participants who were given cat's claw for a total of 52 weeks when compared to the placebo group in phase A.
- Minor side-effects (e.g. stomach upsets) were reported in participants who received cat's claw.

Conclusion

Cat's claw is a herbal remedy with antioxidant and anti-inflammatory properties that's available over the counter in pharmacies and health food shops in the form of capsules. Only one RCT was conducted to evaluate its role in treating rheumatoid arthritis, which showed some clinical benefits with only minor side-effects when taken along with conventional medications.

References:

- Mur E, Hartig F, Eibl G, Schirmer M. Randomised double-blind trial of an extract from the pentacyclic alkaloid-chemotype of *Uncaria tomentosa* for the treatment of rheumatoid arthritis. *Journal of Rheumatology* 2002; 29(4):678–81.

Classification:

Effectiveness score:
2



Safety classification:
Amber



8 Cetylated fatty acids (CFAs)



Family:

Nutritional supplement

Scientific name:

Cetylated fatty acids

Other names:

Individual CFAs (e.g. cetyl myristoleate), combinations of CFAs (e.g. Celadrin®)

What is it?

Cetyl myristoleate (a specific CFA) was proposed as a possible treatment for musculoskeletal conditions in the 1970s by an American chemist who found that this fatty acid might be responsible for protecting mice against the development of rheumatoid arthritis.

How does it work?

The exact ways that CFAs work in treating musculoskeletal conditions haven't been formally studied. It's been proposed that they may have a lubricant effect on joints. Similar to omega fatty acids, they theoretically have anti-inflammatory effects by improving the production of chemicals in the body called prostaglandins.

Is it safe?

No serious side-effects have been reported.

Where do I get it from?

CFAs are available in creams and 350 mg capsules from high-street retailers.

What are the possible interactions?

Interactions with other medications haven't been examined.

What dose should I use?

The best dose hasn't been established, but a treatment plan consisting of three capsules of Celadrin® containing 350 mg of CFAs per day has been used in studies.

The role in treatment of arthritis and musculoskeletal conditions

Two RCTs evaluated the role of CFAs in treating osteoarthritis of the knee.

Trial 1* – In the first trial, 64 participants were randomly assigned to receive either active capsules (350 mg of CFAs) or placebo capsules six times a day for 68 days, while continuing their current osteoarthritis medication.

- No improvement in knee extension was reported in either group.
- Participants in the active treatment group had significantly increased knee flexion.

Trial 2* – Participants in the second trial were randomly selected to receive a topical treatment of either CFA cream or a placebo cream. All 40 participants were asked to apply the cream to their knee twice a day for 30 days.

- Those in the active treatment group experienced significant improvement in climbing stairs and standing up from a sitting position.
- The overall range of motion of the knee was markedly improved in participants who used CFA cream.

In both trials, the medication was well tolerated with no serious side-effects.

Conclusion

CFA nutritional supplements are available as capsules and creams over the counter in pharmacies and health food shops. There's a little evidence that the cream may be effective in improving some aspects of range of motion in the knees of participants with osteoarthritis; however, how it works, its safety and its effectiveness in relation to conventional medications is still unclear.

References:

- Hesslink R Jr, Armstrong D 3rd, Nagendran MV, Sreevatsan S, Barathur R. Cetylated fatty acids improve knee function in participants with osteoarthritis. *Journal of Rheumatology* 2002; 29(8):1708-12.
- Kraemer WJ, Ratamess NA, Anderson JA, Maresh CM, Tiberio DP, Joyce ME et al. Effect of a cetylated fatty acid topical cream on functional mobility and quality of life of participants with osteoarthritis. *Journal of Rheumatology* 2004; 31(4):767-74.

Classification:

Effectiveness score:
2



Safety classification:
Green



* A trial of low quality. Results of this trial were given a lower weighting when we came to our conclusion about the compound.

9 Chondroitin



Family:

Nutritional supplement

Scientific name:

Chondroitin sulphate

Other names:

CSA, CDS, CSC

What is it?

Chondroitin is a complex sugar produced from the cartilage of cows, pigs and sharks.

How does it work?

Chondroitin is found naturally in the body and is a vital part of cartilage, giving it elasticity by helping it retain water. Laboratory studies have found that chondroitin can reduce the activity of enzymes and substances that break down collagen in joints. Other studies have demonstrated that it has several anti-inflammatory properties. Research on animals has found that chondroitin can prevent the breakdown of cartilage and can also stimulate repair mechanisms.

Is it safe?

Side-effects, which are usually mild and infrequent, can include stomach upsets, headaches, increased intestinal gas, diarrhoea and rashes.

Where do I get it from?

This nutritional supplement is widely available in pharmacies and supermarkets in the form of capsules. It's usually sold in combination with glucosamine sulphate.

What are the possible interactions?

Theoretically, chondroitin might increase the risk of bleeding if taken with anticoagulants. For that reason, people on these medications are advised to take chondroitin under a doctor's supervision. People with asthma should take chondroitin with caution as it might make breathing problems worse.

What dose should I use?

Most trials have used a daily dose of between 800 mg and 1,200 mg taken in divided amounts.

The role in treatment of arthritis and musculoskeletal conditions

Chondroitin is one of the most commonly investigated complementary medications for osteoarthritis. The information below has been taken from two review articles that investigated the effectiveness of this supplement in treating osteoarthritis of the knee and hip, and three separate trials into osteoarthritis of the knee.

Review article (2007) – In the 19 trials assessed, the number of participants ranged from 46–631. The trials lasted between 13–132 weeks. Sixteen trials compared the potential benefits of chondroitin with that of a placebo. The data from the other three came from conference abstracts, meaning only a summary of results is available or they had poorly defined comparison groups.

- Twelve trials out of the 16 found that chondroitin was significantly superior to the placebo in relieving pain.
- Of the 16 trials that compared the role of chondroitin with the placebo, five investigated the potential beneficial effect of chondroitin on increasing the width of joint space. Most of these studies found that chondroitin had a small and insignificant effect, compared to the placebo, on the progression of joint space narrowing.
- Of the 16 trials that compared the clinical effectiveness of chondroitin with that of the placebo in terms of reducing painkiller use, 12 found that the chondroitin was more effective. The other four trials found that chondroitin and the placebo had similar effects.
- In the vast majority of the trials, the number and severity of side-effects reported by participants who received chondroitin was less than or similar to those taking the placebo.
- Overall, evidence from trials with a good study design in allocating participants to treatment groups and trials that used the most appropriate statistical methods had lower estimates of effectiveness of chondroitin, particularly in terms of reduction in joint pain.

Trial 1 – In this trial, 364 participants received either three 400 mg chondroitin sulphate capsules or one 300 mg avocado soybean unsaponifiable capsule per day.

- Both groups reported decreased pain and stiffness at the end of the 6-month trial and for 2 months afterwards, but there was no difference between the groups.
- There was no difference in minor side-effects reported between the groups.

Trial 2 – A second RCT randomly assigned 622 participants to receive either one 800 mg sachet of chondroitin sulphate or a sachet of placebo once a day for 2 years.

- After 6 months of treatment, those who received chondroitin sulphate reported a greater improvement in pain, and both participants' and their doctors' overall assessment suggested that the treatment was effective.
- There were no differences between groups in stiffness and physical function and no differences between the groups at the end of the study.

Trial 3[#] – The 662 participants of this study received either 400 mg chondroitin sulphate, 500 mg glucosamine, a combination of glucosamine and chondroitin sulphate, 200 mg celecoxib (a non-steroidal anti-inflammatory drug, or NSAID) or a placebo three times a day over 24 months. In comparison to the placebo, no treatment demonstrated improvement in pain or function.

Review article (2010) – In the most recent review, the authors concluded that chondroitin (or its combination with glucosamine) didn't reduce joint pain to any clinically meaningful extent or change clinical aspects of the joint.

Conclusion

Chondroitin is found naturally in the body and is a vital part of cartilage. It can be bought in the form of capsules, usually in combination with glucosamine sulphate. Laboratory and animal studies have found that taking chondroitin can prevent cartilage breaking down and can also stimulate its repair mechanisms. The role of chondroitin in the treatment of osteoarthritis has been the subject of at least 22 RCTs. Evidence from these RCTs is inconsistent but many have demonstrated that this dietary supplement has significant clinical benefits in reducing pain and painkiller use. Higher quality trials were, however, less likely to show benefit. The medication appears to be well tolerated for short-term use, but its long-term safety and effectiveness are still unclear.

References:

- Pavelka K, Coste P, Géher P, Krejci G. Efficacy and safety of piasclidine 300 versus chondroitin sulphate in a 6 months' treatment plus 2 months' observation in participants with osteoarthritis of the knee. *Clinical Rheumatology* 2010; 29: 659–70.
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- Wandel S, Jüni P, Tendal B, Nüesch E, Villiger PM, Welton NJ, Reichenbach S, Trelle S. Effects of glucosamine, chondroitin, or placebo in participants with osteoarthritis of hip or knee: network meta-analysis. *British Medical Journal* 2010; 341:c4675.

Classification:

Effectiveness score:
2



Safety classification:
Green



Chondroitin is found naturally in cartilage. The supplement is produced from the cartilage of cows, pigs and sharks.

10 Collagen



Family:

Nutritional supplement

Scientific name:

Collagen hydrolysate

Other names:

Hydrolyzed collagen, purified gelatin, HCP, collagen type 2

What is it?

Collagen is extracted from beef, pork or fish bones and skins after being processed to make it more digestible.

How does it work?

Collagen hydrolysate supplements are rich in a number of amino acids that play an important role in the creation of collagen. It's been suggested that taking collagen hydrolysate can improve the symptoms of osteoarthritis by stimulating the production of joint collagen. Type II collagen is one of the main proteins in cartilage.

Some studies have suggested that autoimmune diseases, like rheumatoid arthritis, where the immune system attacks the body's own tissues, may be treated by oral tolerance. This is where the body's reaction to a foreign antigen is suppressed by taking it orally. It has been suggested that taking collagen orally may introduce some chemicals that cause joint inflammation into the body and create oral tolerance to these antigens, reducing the effects of inflammatory arthritis.

Is it safe?

Collagen is considered to be well tolerated with no major side-effects. Minor side-effects include a feeling of heaviness in the stomach, mild diarrhoea and skin rashes.

Where do I get it from?

Collagen capsules are available from high-street retailers.

What are the possible interactions?

There are no well-known drug interactions.

What dose should I use?

Dosage hasn't been well established. Daily doses of between 1–10 g collagen hydrolysate and 0.1–10 mg of chicken or bovine type II collagen have been used in previous studies.

The role in treatment of arthritis and musculoskeletal conditions

Collagen has been assessed for the treatment of both rheumatoid arthritis and osteoarthritis. For rheumatoid arthritis, four trials tested collagen against a placebo and one tested it against methotrexate. Of the osteoarthritis trials, four compared collagen with a placebo and one compared it with glucosamine hydrochloride plus chondroitin.

Rheumatoid arthritis

The trials for rheumatoid arthritis involved between 60 and 503 participants.

- Collagen type II showed fewer swollen joints, joint tenderness and better walk time in only one of the trials against a placebo.
- Although people in both groups improved in the collagen type II and methotrexate trial, improvement was greatest in the methotrexate participants.
- There was no evidence of increased side-effects in people taking collagen type II, although trials did report participants withdrawing because they believed the collagen wasn't improving their symptoms.

Osteoarthritis

Trial 1 – In the first trial, 81 participants were randomly selected to receive placebo tablets or one of three gelatine (collagen hydrolyse) preparations. Participants in the active treatment groups were treated daily with 10 g of each gelatine product (0.5 g each tablet) for 2 months.

- All three gelatine preparations were significantly superior to the placebo in reducing pain at the end of the trial period, but they didn't cause any radiological or laboratory changes.
- The most common side-effect was heaviness in the stomach.

Trial 2 – This trial included 389 people with osteoarthritis across 20 sites in the UK, USA and Germany. Participants were randomised to receive either 10 g of collagen hydrolysate or placebo tablets for 24 weeks.

- Collagen hydrolysate was relatively well tolerated but had no significant effect on reducing pain and improving physical function in the total study group.
- There was a beneficial effect in participants who had severe symptoms at the start of the study.

Trial 3 – In this trial, 250 people with primary osteoarthritis of the knee were randomised to receive either 10 g collagen hydrolysate or a placebo daily for 6 months.

- Those who received collagen reported a greater reduction in pain.
- The most frequently reported side-effects were migraines, headaches and gastrointestinal effects.

Trial 4 – Trial 4 included 29 people with mild to moderate osteoarthritis of the knee. Participants received either a collagen formulation (Fortigel®) or a placebo for 24 weeks. There were no differences in reported pain, stiffness, function or walking at the end of the study.

Trial 5 – In the final RCT for osteoarthritis, 52 participants whose knees were affected by the condition were given 10 mg bioactive undenatured type II collagen or glucosamine hydrochloride plus chondroitin once a day for 3 months.

- There were no differences in pain or functional scores across the 3-month trial; however, there were differences at some time points which favoured the collagen group when function was measured in a second way.
- There was no difference in the proportion of reported side-effects between the groups.

Conclusion

Collagen is a nutritional supplement extracted from animal or fish materials. It can be bought from pharmacies and health food shops in the form of capsules. Collagen is rich in amino acids that play an important role in the building of joint cartilage. It's also been suggested that it can have anti-inflammatory effects, although the way this might work isn't yet clearly understood.

Trials on collagen's role in treating osteoarthritis are scarce and gave mixed results. Studies into the role of collagen type II in treating rheumatoid arthritis suggest that it doesn't have a significant effect in reducing pain and joint inflammation, although this hasn't been found to be consistently reproduced across trials.

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collagen hydrolysate, for improving joint comfort. *International Journal of Food Sciences and Nutrition* 2009; 60 (S2):99–113.

- McAlindon TE, Nuite M, Krishnan N, Ruthazer R, Price LL, Burstein D, Griffith J, Flechsenhar K. Change in knee osteoarthritis cartilage detected by delayed gadolinium enhanced magnetic resonance imaging following treatment with collagen hydrolysate: a pilot randomised controlled trial. *Osteoarthritis and Cartilage* 2011; 19:399–405.

Classification:

Effectiveness score
in rheumatoid arthritis:
1



Effectiveness score
in osteoarthritis:
2



Safety classification:
Green



* A trial of low quality. Results of this trial were given a lower weighting when we came to our conclusion about the compound.



11 Devil's claw



Family:

Herbal medicine of the Bignoniaceae family

Scientific name:

Harpagophytum procumbens

Other names:

Grapple plant, wood spider, Doloteffin®, Rivoltan®, iridoid glycoside, WS 1531

What is it?

Devil's claw is a plant native to deserts of South and South East Africa. Extracts from the plant root are used medicinally to treat several diseases.

How does it work?

As yet, we don't completely understand how devil's claw works. Laboratory studies found that extracts from the plant root can block several pathways which cause joint inflammation. These anti-inflammatory properties have been attributed to its active ingredient, harpagoside, but animal studies found that its painkilling properties can't be explained by this ingredient alone.

Is it safe?

Although uncommon, serious side-effects of abnormal heart rhythm and bleeding can occur in participants taking devil's claw. Other, less serious side-effects include rashes, stomach upsets and diarrhoea, headaches and loss of appetite.

Where do I get it from?

The compound is available from high-street retailers.

What are the possible interactions?

Drug interactions have been documented with anticoagulants, painkillers (e.g. ibuprofen), heart drugs (e.g. digoxin) and stomach acid drugs (e.g. famotidine).

What dose should I use?

A dose of 500–1,500 mg of dried root or capsules three times daily has been established.

The role in treatment of arthritis and musculoskeletal conditions

The potential therapeutic effect of devil's claw in treating osteoarthritis of the hip or the knee have been investigated in five RCTs dating from 1980, as reported in a systematic review.

Three studies (two of which were considered to be of high quality) compared devil's claw with a placebo. Participants who were allocated devil's claw in these studies had a significant improvement in osteoarthritis-related pain compared to those who were on a placebo.

One high-quality study compared the level of pain improvement in participants randomly selected to receive devil's claw with that of participants assigned to take phenylbutazone (an NSAID). Participants taking devil's claw reported fewer side-effects and had slightly better pain improvement.

Another high-quality study compared the overall disease-related symptoms in two groups of participants who were randomly assigned to take either devil's claw or diacerhein*, a conventional therapy for osteoarthritis. The level of symptom improvement was similar in both groups following treatment, but participants allocated devil's claw experienced fewer side-effects.

A more recently published scientific article reviewed the same clinical trials and found that results of the high-quality trials suggest that devil's claw is effective in the reduction of osteoarthritis-related symptoms.

Conclusion

Devil's claw is a herbal medicine that can be bought over the counter in the form of capsules, tinctures (a medicine made by dissolving the active ingredient in alcohol) and fluid extract. How it works is still poorly understood, but evidence suggests that devil's claw is as effective as conventional medicines for osteoarthritis. Side-effects remain a concern.

References:

- Gagnier JJ, Chrubasik S, Manheimer E. Harpagophytum procumbens for osteoarthritis and low back pain: a systematic review. *BMC Complementary and Alternative Medicine* 2004; 4:13.
- Brien S, Lewith GT, McGregor G. Devil's claw (Harpagophytum procumbens) as a treatment for osteoarthritis: a review of efficacy and safety. *Journal of Alternative and Complementary Medicine* 2006; 12(10):981–93.

Classification:

Effectiveness score:
3



Safety classification:
Amber



*NB: Diacerhein can be spelt with or without the 'h'.

12 Duhuo Jisheng Wan (DJW)



Family:

Traditional Chinese herbal medicine

Scientific name:

Duhuo Jisheng Wan

Other names:

Du Huo Ji Sheng Tang, Du Huo Ji Shang, Du Huo Ji Sheng Wan, Duhuojishengwan, Guang Ci Tang, Plum Flower

What is it?

Duhuo Jisheng Wan is a medicinal formula made up of at least seven Chinese herbs, including *Radix angelicae pubescentis* and *Herba taxilli*.

How does it work?

According to traditional theories, Duhuo Jisheng Wan can relieve pain by 'expelling wind, clearing dampness and removing obstruction in Qi (energy)'. The ways it works haven't been well examined, but some laboratory studies have shown that Duhuo Jisheng Wan can clear inflammation by activating specific anti-inflammatory cells in the body.

Is it safe?

Reported side-effects include raised blood pressure, dizziness and drowsiness, nausea and vomiting, and diarrhoea and constipation.

Where do I get it from?

Duhuo Jisheng Wan tablets are available to buy over the internet under different brand names (Guang Ci Tang, Plum Flower, Du Huo Ji Sheng Wan herbal pills) from UK-based suppliers.

What are the possible interactions?

No data about interactions with other medications is available.

What dose should I use?

One study used 3 g of Duhuo Jisheng Wan, three times a day.

The role in treatment of arthritis and musculoskeletal conditions

One RCT examined the effect of this compound in treating osteoarthritis of the knee. In this trial, 200 participants were randomly assigned to receive either 75 mg diclofenac tablets, 9 g Duhuo Jisheng Wan tablets, placebo tablets identical to the diclofenac or placebo tablets identical to the Duhuo Jisheng Wan once a day. The four groups were compared with respect to side-effects and effectiveness over a 4-week period.

- Compared to the corresponding placebo groups, participants who received either Duhuo Jisheng Wan or diclofenac had significantly lower scores for pain and stiffness.
- Compared to diclofenac, the beneficial effects of Duhuo Jisheng Wan were slower to develop.
- Around 30 per cent of participants in both groups receiving diclofenac and Duhuo Jisheng Wan reported side-effects; however, both groups also reported significantly more side-effects than the placebo groups.

Conclusion

Duhuo Jisheng Wan is a Chinese herbal medicine which is available in tablet form and can be purchased over the internet. The compound seems to activate specific anti-inflammatory cells in the body, but there's little evidence available on treating osteoarthritis with Duhuo Jisheng Wan. The only randomised trial suggests it has an equal effect to NSAIDs, but more evidence is needed before a conclusion on effectiveness and safety can be reached.

References:

- Teekachunhatean S, Kunanusorn P, Rojanasthien N, Sananpanich K, Pojchamarnwiputh S, Lhieochaiphunt S et al. Chinese herbal recipe versus diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomised controlled trial. *BMC Complementary and Alternative Medicine* 2004; 4:19–27.

Classification:

Effectiveness score:
2



Safety classification:
Amber



Duhuo Jisheng Wan is made up of at least seven Chinese herbs, including *Radix angelicae pubescentis* and *Herba taxilli*.

13 Evening primrose oil (EPO)



Family:

Herbal medicine of the Onagraceae family

Scientific name:

Oenothera biennis

Other names:

Tree primrose, fever plant, night willowherb, King's-cure-all, scabish, scurvisch, sun drop, suncups

What is it?

EPO is a biennial plant native to North America but which is now found all over the world. The medicinal product is produced from the plant's seeds.

How does it work?

EPO is a rich source of two types of polyunsaturated omega-6 essential fatty acids: 2–15 per cent gamma-linolenic acid (GLA) and 70 per cent linolenic acid (LA, which is converted in the body to GLA). Several factors can interfere with the production of GLA from LA in the body, including ageing, dietary deficiencies, viral infections and some diseases. Sunflower oil and other oils generally used in normal diet contain only LA. EPO is one of the richest sources of pure GLA.

Is it safe?

If taken in the correct dose, EPO has no major safety problems. Common side-effects include nausea, diarrhoea and skin rashes. People with epilepsy or seizure disorder shouldn't take this product as it can cause seizures.

Where do I get it from?

EPO capsules (500–1,300 mg) or oil (150 ml) is available from high-street retailers.

What are the possible interactions?

Interactions haven't been well studied, but EPO may interact with anti-inflammatory drugs (e.g. cortisone) and anticoagulants.

What dose should I use?

No recommended safe doses have been found for the use in musculoskeletal conditions. A dose of 6 g (540 mg GLA) a day has been used in trials.

The role in treatment of arthritis and musculoskeletal conditions

Two RCTs examined the effect of this compound in treating rheumatoid arthritis.

Trial 1 – In this trial, 49 people with rheumatoid arthritis who were on NSAIDs were randomised to take either 6 g (540 mg GLA) EPO, EPO with fish oil or placebo tablets once a day for 12 months. Participants were asked to take their normal dose of NSAIDs (e.g. ibuprofen) during the first 3 months of the trial but were advised to reduce or stop it according to their symptoms thereafter.

- The difference in treatment outcomes between active treatments and placebo were significant – 94 per cent of participants who got EPO alone and 93 per cent who received EPO combined with fish oil reported a significant improvement of disease-related symptoms, including pain and morning stiffness, compared to only a 30 per cent improvement in participants in the placebo group.

- EPO was also significantly effective in reducing the NSAIDs intake during the trial period.
- It didn't seem to modify the long-term disease activity, as symptoms relapsed in most of the participants during the 3 months that followed treatment.
- Two of the participants on EPO withdrew from the trial because of nausea and diarrhoea.

Trial 2 – Researchers evaluated the outcome of 40 people with rheumatoid arthritis who received daily doses of either 6 g EPO (540 mg GLA) or olive oil for 6 months.

- Participants allocated EPO had a significant improvement in morning stiffness compared to participants assigned olive oil, but there were no significant differences between both treatment groups with respect to pain reduction and overall disease severity.
- Most participants in this trial didn't stop taking NSAIDs.
- Four out of 19 participants taking EPO had to withdraw because of nausea, flu-like symptoms or deteriorating disease condition.

Conclusion

EPO is rich in polyunsaturated omega-6 fatty acids that can help in the regulation of pain and inflammation with no major safety problems. Products containing this compound are available in most pharmacies, health food shops and supermarkets. Evidence for the effectiveness of EPO in reducing joint pain in rheumatoid arthritis isn't conclusive, but there's some evidence that it can improve morning stiffness. EPO doesn't seem to modify long-term disease activity, so it should be taken along with conventional therapy.

References:

- Brzeski M, Madhok R, Capell HA. Evening primrose oil in participants with rheumatoid arthritis and side-effects of non-steroidal anti-inflammatory drugs. *British Journal of Rheumatology* 1991; 30(5):370–72.
- Belch JJF, Ansell D, Madhok R, Dowd AO, Sturrock RD. Effects of altering dietary essential fatty acids on requirements for non-steroidal anti-inflammatory drugs in participants with rheumatoid arthritis: a double-blind placebo-controlled study. *Annals of Rheumatic Diseases* 1988; 47(2):96–104.

Classification:

Effectiveness score:
3



Safety classification:
Green



14 Feverfew



Family:

Perennial plant of the sunflower (Compositae) family

Scientific name:

Chrysanthemum parthenium, tanacetum parthenium

Other names:

Bachelor's buttons, featherfew, Santa Maria, Mother-herb, altamisa, featherfoil, flirtwort, midsummer daisy, febrifuge plant

What is it?

Feverfew is a perennial plant originally native to Eastern Europe and Asia Minor but now cultivated throughout Europe and America. Compounds that are used for medicinal purposes are prepared from the leaves.

How does it work?

Feverfew is believed to have painkilling and anti-inflammatory properties. It's been suggested that it reduces the release of an inflammatory substance, serotonin, from blood cells and slows down the production of a chemical transmitter in the body called histamine. Both serotonin and histamine play an important role in migraines.

Is it safe?

No major safety problems have been identified in short-term use, but the long-term safety isn't known. Reported side-effects from previous studies (mainly on participants who have migraines) include mouth ulceration, indigestion and heartburn, colicky abdominal pain, dizziness and rashes.

Where do I get it from?

Feverfew is available from high-street retailers.

What are the possible interactions?

Interactions with other drugs haven't been widely studied; however, feverfew might increase the risk of bleeding if taken with anticoagulants.

What dose should I use?

No recommended safe doses have been found for the use in musculoskeletal conditions. Previous RCTs of feverfew in migraine participants, which showed encouraging results, used doses between 50 and 140 mg of powdered or granulated leaf preparations daily.

The role in treatment of arthritis and musculoskeletal conditions

One RCT evaluated the effectiveness of feverfew in treating rheumatoid arthritis. Twenty participants were randomly selected to take one capsule containing 70–86 mg of powdered feverfew leaf, while the other 21 participants were randomly selected to take a placebo capsule daily for 6 weeks. Both treatment groups were asked to continue their usual medications.

- No significant differences were found between the two groups in the clinical and laboratory presentation of the disease at the end of the treatment.
- One patient in the treatment group reported minor ulcerations and a sore tongue.

Conclusion

Feverfew is believed to have anti-inflammatory and painkilling properties. It can be bought over the counter from pharmacies, health food shops and supermarkets. The current evidence is limited but it suggests that this compound has only minor side-effects in the short-term, although it doesn't have a therapeutic benefit for rheumatoid arthritis.

References:

- Patrick M, Heptinstall S, Doherty M. Feverfew in rheumatoid arthritis: a double-blind, placebo-controlled study. *Annals of Rheumatic Diseases* 1989; 48(7):547–49.
- Ernst E, Pittler MH. The efficacy and safety of feverfew (*Tanacetum parthenium* L.): an update of a systematic review. *Public Health Nutrition* 2000; 3(4A):509–14.

Classification:

Effectiveness score:
1



Safety classification:
Green



15 Fish oil



Family:

Nutritional supplement

Scientific name:

Fish oil (fish body oil and/or fish liver oil)

What is it?

Fish body oil is made from tissues of fatty fish like sardines, sprat, salmon, and mackerel.

Fish liver oil is made by pressing the cooked liver of halibut, shark or, most commonly, cod.

How does it work?

Fish oils are rich in omega-3 essential fatty acids, which have strong anti-inflammatory properties. Firstly, they significantly reduce the release of several pro-inflammatory elements from white blood cells. Secondly, they form the building blocks for prostaglandins.

Omega-3 fatty acids also play a role in lowering cholesterol and triglyceride levels in the blood, so they can reduce the risk of heart disease and stroke in people with inflammatory arthritis.

Fish liver oil contains high levels of vitamins A and D. Vitamin A is a strong antioxidant (meaning it can prevent cell damage in the body by interacting with free radicals, harmful molecules which are produced within the cells). Vitamin D plays an important part in the production of proteoglycan in cartilage as well as helping to maintain a healthy musculoskeletal system.

Is it safe?

Fish oil is considered to be well tolerated at therapeutic doses. However, certain environmental chemicals such as methylmercury and polychlorinated biphenyls (PCBs) can contaminate fish supplies and there's a concern that taking very high doses of fish oil can cause a build-up of these chemicals in the body. This is also a concern for people who eat fish frequently.

Side-effects, at therapeutic doses, are usually minor and uncommon. The most common is stomach upsets, but flatulence and diarrhoea may also be experienced.

It's important not to take large amounts of fish liver oil because it can provide more than the recommended dietary allowance of vitamin A. Taking too much vitamin A can lead to liver problems and hair loss. It may also harm unborn babies, so fish liver oil and vitamin A supplements should be avoided during pregnancy. Fish liver oil that hasn't been well purified can contain some contaminants (e.g. mercury, and dioxins), which can lead to health problems, but most supplement companies test fish liver oil for purity before it becomes publicly available.

Where do I get it from?

Fish oil is available from high-street retailers and internet sites based abroad which specifically mail to the UK.

What are the possible interactions?

Fish oil can interfere with blood clotting so shouldn't be taken with anticoagulants.

What dose should I use?

In the UK, dietary guidelines recommend eating two portions of fish a week, including one oily. This works out at about 0.45 g per day of omega-3 fatty acids.

The role in treatment of arthritis and musculoskeletal conditions

One RCT assessed fish liver oil in the treatment for osteoarthritis, while another evaluated the role of capsules containing a combination of fish liver oil and fish body oil (SSMO1) in treating rheumatoid arthritis.

Data from 10 trials from 1985 onwards have been combined in a report to assess the potential therapeutic effect of fish body oil in rheumatoid arthritis. A more recent review article gave an overview of results from 17 RCTs into the same subject.

Fish liver oil

Rheumatoid arthritis

In this 9-month trial, 97 people with rheumatoid arthritis were randomly selected to receive either 10 capsules of SSMO1 (containing 1 g of fish liver oil per capsule) or 10 placebo capsules once a day.

- There was no difference in outcome after 12 weeks of the trial, but participants given SSMO1 had a modest improvement in pain after 24 and 36 weeks compared to the placebo group.
- Of the active treatment group, 39 per cent reported a significant reduction in their daily NSAID need, compared to just 10 per cent in the placebo group (this was a significant difference).
- Approximately 65 per cent of participants in the fish liver oil group completed the trial, compared to 54 per cent of the placebo group. Withdrawal from the trial wasn't put down to side-effects, but it might have been related to the large number of capsules participants were asked to take every day.
- In those who completed the trial, there was no significant difference in the number or type of side-effects reported, most of which were mild and gastrointestinal in nature.
- Because we can't tell whether the results were caused by the fish liver oil, the fish body oil or the combination of the two, we haven't been able to make a conclusion about the use of fish liver oil to treat rheumatoid arthritis based on this RCT alone.

Osteoarthritis

In this trial of fish liver oil, 86 people with osteoarthritis were randomly allocated to receive 10 ml of either cod liver oil or olive oil once a day for 24 weeks. Participants in both groups were asked to continue taking their regular NSAIDs through the trial period.

- There was no significant difference between the two treatment groups in the amount by which the participants' pain and disability changed during the study.
- Both treatments failed to significantly reduce pain and disability symptoms of osteoarthritis.
- Approximately 70 per cent of participants in the group taking fish liver oil completed the 24-week trial (compared to 79 per cent who were given olive oil), but side-effects from treatments were not the main reasons for withdrawal; similar proportions of participants in the fish liver oil (30 per cent) and olive oil (24 per cent) groups reported minor side-effects, including stomach upsets and dry skin.

Fish body oil

Report – The quality of the trials included in this report into fish body oil for the treatment of rheumatoid arthritis ranged between low and moderate, and results were combined because of the small number of participants.

- Compared to the placebo treatments, fish body oil significantly decreased the number of tender joints and shortened the duration of morning stiffness.
- However, it failed to make a significant change in a number of other disease measures (e.g. grip strength, blood tests for disease activity and the overall disease severity).

Review article – Trials included in this article used daily doses of between 1.6–7.1 g (average 3.5 g) omega-3 fatty acids. The evidence suggests that fish oil supplements were generally well tolerated and significantly reduced the following measures:

- joint pain
- the duration of morning stiffness
- fatigue time
- the number of tender or swollen joints
- the use of painkillers.

Conclusion

Fish body oil and fish liver oil are rich in omega-3 essential fatty acids, which can regulate the body's immune system and fight joint inflammation. Fish liver oil is also a rich source of vitamin A (a strong antioxidant) and vitamin D (which is important for maintaining healthy joints).

Fish oil in capsule and bottle form is widely available in supermarkets, pharmacies and health food shops.

Evidence suggests that both fish body and liver oils are well tolerated with no major side-effects if taken at therapeutic doses. There's good evidence that fish body oil can result in improvement in the symptoms of rheumatoid arthritis and some unconfirmed evidence that the combined treatment of fish body and liver oils might also be of long-term benefit, particularly in reducing daily NSAID use. Evidence for the use of fish liver oil for osteoarthritis is based on insufficient data.

References:

- Cleland LG, Caughey GE, James MJ, Proudman SM. Reduction of cardiovascular risk factors with long-term fish oil treatment in early rheumatoid arthritis. *Journal of Rheumatology* 2006; 33(10):1973–79.
- Fortin PR, Lew RA, Liang MH. Validation of a meta-analysis: the effects of fish oil in rheumatoid arthritis. *Journal of Clinical Epidemiology* 1995; 48(11):1379–90.
- Kris-Etherton PM, Harris WS, Appel LJ; American Heart Association. Nutrition Committee. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* 2002;106(21):2747–57.
- Calder PC. Polyunsaturated fatty acids, inflammation and immunity. *Lipids* 2001; 36(9):1007–24.
- Calder PC. n-3 polyunsaturated fatty acids, inflammation and inflammatory diseases. *American Journal of Clinical Nutrition* 2006; 83(6 Suppl):1505S–1519S.
- Stammers T, Sibbald B, Freeling P. Efficacy of cod liver oil as an adjunct to non-steroidal anti-inflammatory drug treatment in the management of osteoarthritis in general practice. *Annals of Rheumatic Diseases* 1992; 51(1):128–29.
- Galarraga B, Ho M, Youssef HM, Hill A, McMahon H, Hall C et al. Cod liver oil (n-3 fatty acids) as a non-steroidal anti-inflammatory drug sparing agent in rheumatoid arthritis. *Rheumatology (Oxford)* 2008; 47(5):665–69.

Classification:

Effectiveness score
of fish body oil in
rheumatoid arthritis: 5



Effectiveness score
of fish liver oil in
osteoarthritis: 1



Safety classification:
Green



**There are two types
of fish oil: fish body
oil (from fatty fish
tissue) and fish liver
oil (from pressed
fish livers).**

16 Flaxseed oil



Family:

Herbal medicine of the Linaceae family

Scientific name:

Linum usitatissimum

Other names:

Linseed, brown, golden flaxseed

What is it?

The flax plant is native to Egypt but cultivated in many places, including Europe and the United States. Oil from the plant seeds is used to treat several diseases.

How does it work?

Flaxseed oil contains alpha-linolenic acid (ALA), an omega-3 essential fatty acid. Flaxseed oil also contains some chemicals called lignans, which have antioxidant properties, so they've been used to prevent cardiovascular disease.

Is it safe?

Side-effects include stomach discomfort, rashes and breathing difficulties. In theory, flaxseed may increase blood sugar level and the risk of bleeding.

Where do I get it from?

Flaxseed oil is available from high-street retailers.

What are the possible interactions?

Flaxseed might increase the risk of bleeding if taken with anticoagulants.

What dose should I use?

No recommended safe doses have been established for the use of flaxseed in musculoskeletal conditions.

The role in treatment of arthritis and musculoskeletal conditions

One RCT of 22 people investigated flaxseed's potential role in the treatment of rheumatoid arthritis. Participants were randomly selected to be treated with either flaxseed oil or a placebo medication for 3 months.

- Results found that the levels of EPA and DHA in patients' blood didn't rise.
- The two treatment groups showed no difference with respect to symptom reporting, laboratory findings and clinical signs on physical examination.

Conclusion

Flaxseed oil, which can be bought over the counter in capsule form, is rich in ALA. This fatty acid can help in reducing joint inflammation. We don't yet know how safe flaxseed oil is, but the limited evidence suggests that it's not effective in the treatment of rheumatoid arthritis.

References:

- Nordstrom DC, Honkanen VE, Nasu Y, Antila E, Friman C, Konttinen YT. Alpha-linolenic acid in the treatment of rheumatoid arthritis. A double-blind, placebo-controlled and randomised study: flaxseed vs. safflower seed. *Rheumatology International* 1995; 14(6):231–34.

Classification:

Effectiveness score:
1



Safety classification:
Amber



17 Ginger



Family:

Herbal medicine of the ginger (Zingiberaceae) family

Scientific name:

Zingiber officinale

Other names:

Gan Jiang, zingiber, EV.EXT35, African ginger, black ginger, chayenne ginger, Zinaxin®

What is it?

Ginger is a plant native to China, South East Asia, West Africa and the Caribbean. The herbal preparation is extracted from the rhizome, which is part of the stem of the plant.

How does it work?

Some laboratory and animals studies have found ginger extracts can reduce the production of several chemical substances (including leukotrienes) that promote joint inflammation. Ginger also contains salicylates, which is transformed by the body into a chemical substance called salicylic acid. Salicylic acid inhibits the production of certain prostaglandins in the nerves and this relieves pain and discomfort.

Is it safe?

Ginger is a relatively well-tolerated herbal remedy with minor side-effects. The most commonly reported side-effects are stomach upset and mouth irritation.

Where do I get it from?

Ginger is available from high-street retailers.

What are the possible interactions?

Treatment with ginger might increase the risk of bleeding if taken with anticoagulants.

What dose should I use?

No recommended safe and effective doses have been found for use in musculoskeletal conditions. Doses ranging from 510–1,000 mg a day have been used in RCTs.

The role in treatment of arthritis and musculoskeletal conditions

Three RCTs evaluated the role of ginger in the treatment of osteoarthritis.

Trial 1 – In this trial, 67 participants with osteoarthritis of the hip or knee were given either 170 mg capsules of ginger extract, 400 mg ibuprofen tablets or a placebo three times a day for 3 weeks. Participants were given paracetamol as a 'rescue drug' for pain relief during the study.

- Participants who were given ibuprofen or ginger had a significant reduction in pain scores and reported taking less paracetamol compared to those who got placebo tablets.
- Ibuprofen was more effective than ginger in both treatment outcomes.

Trial 2 – Trial 2 included 29 people with knee osteoarthritis. Participants were given either 250 mg of ginger capsules or placebo capsules four times a day for 3 months (phase A). The groups then swapped treatments for 3 months (phase B).

- At the end of phase A, participants who were treated with ginger had a significant reduction in pain and disease-related disability when compared to participants who were allocated a placebo during the same phase.
- No significant difference between treatment groups was observed at the end of phase B.

Trial 3 – In the final trial, 247 participants with knee osteoarthritis were given either 255 mg of ginger capsules or placebo capsules twice a day for 6 months. Paracetamol was given as a rescue drug for pain relief during the study.

- Of the participants who were treated with ginger, 63 per cent had significant reduction in knee pain, compared to 50 per cent of the placebo group.
- The severity of pain and overall improvement of osteoarthritis-related symptoms were also significantly reduced in the group taking ginger compared to the placebo group.
- Both groups were similar with respect to their perceived improvement in quality of life.
- The ginger group reported more gastrointestinal side-effects (e.g. heartburn), but they were relatively mild and tolerable.

Conclusion

Ginger extracts are available over the counter in pharmacies in the form of capsules and oil. Theoretically, ginger can reduce the activity of several chemical substances that promote joint inflammation. Results from RCTs evaluating its role in treating participants with osteoarthritis found that it has a high safety profile and can have moderately beneficial effects in reducing pain and disability.

References:

- Bliddal H, Rosetzký A, Schlichting P, Weidner MS, Andersen LA, Ibelt HH et al. A randomised, placebo-controlled, cross-over study of ginger extracts and ibuprofen in osteoarthritis. *Osteoarthritis Cartilage* 2000; 8(1):9–12.
- Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in participants with osteoarthritis. *Arthritis & Rheumatology* 2001; 44(11):2531–8.
- Wigler I, Grotto I, Caspi D, Yaron M. The effects of Zintona EC (a ginger extract) on symptomatic gonarthrosis. *Osteoarthritis Cartilage* 2003; 11(11):783–9.

Classification:

Effectiveness score:
3



Safety classification:
Green



18 Glucosamine



Family:

Nutritional supplement

Scientific name:

Glucosamine sulphate, glucosamine hydrochloride

Other names:

GS, amino monosaccharide, sulfated monosaccharide, chitosamine, D-glucosamine

What is it?

Glucosamine is an amino sugar made from shellfish or prepared in the laboratory.

How does it work?

Glucosamine is found naturally in the body. It plays an important role in making glycosaminoglycans and glycoproteins, which are essential building blocks of many structures of the joints, including the ligaments, tendons, cartilage and synovial fluid. It's been suggested that the way joint structures are built and maintained contributes to the development and the progression of osteoarthritis. Animal studies have found that giving glucosamine can delay the breakdown of cartilage as well as rebuild it. It's available in two forms: glucosamine sulphate and glucosamine hydrochloride.

Is it safe?

Side-effects, which are usually mild and infrequent, include stomach upsets, constipation, diarrhoea, headaches and rashes. Glucosamine shouldn't be taken by people who are allergic to shellfish, although shellfish-free options are available.

Where do I get it from?

This nutritional supplement is widely available from high-street retailers.

What are the possible interactions?

There are several reports of interaction between glucosamine and anti-diabetic treatments. Glucosamine might increase blood sugar level in people with diabetes requiring therapeutic adjustments to their diabetic control. There are also some reports of possible interaction with chemotherapy drugs and drugs that lower blood cholesterol.

What dose should I use?

Most trials used a standard dose of 500 mg of glucosamine sulphate or glucosamine hydrochloride taken three times a day.

The role in treatment of arthritis and musculoskeletal conditions

Glucosamine sulphate

A review article of 18 trials investigating the effectiveness of glucosamine sulphate in treating osteoarthritis was published in 2005. A further four trials published since 2007 evaluated the effect of glucosamine sulphate in the treatment of hip and knee osteoarthritis. A second review article compared the clinical effectiveness and safety of glucosamine sulphate with those of NSAIDs.

Review article (2005) – The number of participants in the RCTs included in this article ranged from 30 to 319. The trials lasted from 3 weeks to 3 years.

- Seven trials out of 13 which compared glucosamine sulphate to a placebo found that the glucosamine sulphate was significantly better than the placebo in relieving pain.
- In all 13 RCTs, the number and severity of side-effects reported by participants who were given glucosamine sulphate weren't significantly different from those reported by participants who got the placebo.
- Three trials out of five found that glucosamine sulphate was significantly better than the placebo in improving problems associated with walking and other daily activities.
- No trials found that glucosamine sulphate was significantly effective, as compared to a placebo, in improving all the main osteoarthritis-related symptoms (pain, disability and joint stiffness).
- Trials that used one company's supplement (Rotta Pharm) showed a positive effect for pain and function while those that used other brands didn't.
- Trials that used the best methods to make sure that participants didn't know which treatment they were getting didn't show significant benefits in pain relief and improved physical function in those who received glucosamine sulphate.

Trial 1 – The first trial involved 222 people over 2 years. The supplement didn't show any beneficial effects, compared to a placebo, in relieving pain and improving function.

Trial 2 – In this 6-month trial, which included 318 participants, glucosamine had a clear significant benefit over a placebo and an even stronger effect than paracetamol in improving both pain and function.

Trial 3[†] – The 64 participants with osteoarthritis of the knee in this study received either 500 mg glucosamine sulphate three times a day or 400 mg vitamin E made from palm oil once a day for 6 months. Both groups improved in pain and function, but there was no difference between them.

Trial 4 – 60 participants with primary osteoarthritis in either one or both knees were randomised to receive a 1500 mg sachet of glucosamine sulphate or a placebo. After 12 weeks, there were no improvements in the placebo group but those who received glucosamine reported significant improvements in resting and moving pain, overall pain, stiffness and function. The improvements in these final three measures lasted for 20 weeks. In the treatment group, reported side-effects were heartburn and an all-over itch.

Review article – This review article summarised results of four trials:

- Two trials out of three found that glucosamine sulphate was significantly more effective than NSAIDs in reducing pain, while the third found that both treatments had similar effects.
- One trial out of two found that glucosamine sulphate was significantly better than NSAIDs in improving physical function, while the second trial found that both medications had similar effects.
- Three trials out of four found that the number and severity of side-effects reported by participants taking glucosamine sulphate were significantly less than those reported by participants who were given NSAIDs.

Glucosamine hydrochloride

Two RCTs were conducted to evaluate the role of glucosamine hydrochloride in the treatment of knee osteoarthritis. A review article also looked at its effects for hip and knee osteoarthritis.

Trial 1 – The first trial included 118 people and lasted 8 weeks. Participants were randomly selected to receive 1,500 mg a day of glucosamine hydrochloride or a placebo.

- 49 per cent of participants in the treatment group reported that they were ‘better than at the start of the trial’; however, the same positive response was reported by 40 per cent of the participants who got placebo capsules, suggesting that glucosamine hydrochloride isn’t significantly better than placebo in improving osteoarthritis-related symptoms.
- In addition, this trial found that glucosamine hydrochloride wasn’t significantly better than the placebo in reducing pain, stiffness and physical function.

Trial 2* – In the second trial, 1,583 people with knee osteoarthritis were randomly assigned to receive 1,500 mg glucosamine hydrochloride, 1,200 mg chondroitin sulphate, both treatments, celecoxib (an NSAID) or placebo capsules once a day for 24 weeks.

- Participants who received glucosamine hydrochloride or chondroitin sulphate didn’t report a significant improvement in pain, stiffness and physical function when compared to participants who were assigned the placebo.
- The only groups who achieved significant improvement in osteoarthritis-related symptoms when compared to placebo were those who were assigned celecoxib, and those who had moderate-to-severe knee pain at the outset of the trial and were given the glucosamine hydrochloride/chondroitin sulphate combination.
- Two years after treatment, 662 people were reassessed. None of the treatments were reported to give greater improvements than the placebo in pain and function measurements.

In RCTs generally, side-effects of glucosamine hydrochloride were only mild and infrequent.

Review article (2010) – Taking glucosamine (or its combination with chondroitin) didn’t result in a clinically meaningful reduction in joint pain or change clinical aspects of the joint.

Conclusion:

Glucosamine is a nutritional supplement which is made from shellfish or prepared in the laboratory. It’s widely available in pharmacies, health food shops and supermarkets in two preparations: glucosamine sulphate and glucosamine hydrochloride. Animal studies have found that glucosamine can both delay the breakdown of and repair damaged cartilage.

The role of glucosamine in the treatment of osteoarthritis has been subject to more trials than any other compound included in this review. The results are mixed – some trials have demonstrated the effectiveness of glucosamine sulphate when compared to placebo, but others have not. The size of effect is also, overall, modest. There’s some evidence that more recent trials and those using higher-quality methods are less likely to show a benefit. Evidence from trials on glucosamine hydrochloride is scarce and not convincing. The supplement, in both its sulphate and hydrochloride preparations, appears to be well tolerated with only mild and infrequent side-effects.

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- Wandel S, Jüni P, Tendal B, Nüesch E, Villiger PM, Welton NJ, Reichenbach S, Trelle S. Effects of glucosamine, chondroitin, or placebo in participants with osteoarthritis of hip or knee: network meta-analysis. *British Medical Journal* 2010 Sep 16; 341:c4675.

Classification:

Effectiveness score for glucosamine sulphate:
2



Effectiveness score for glucosamine hydrochloride:
1



Safety classification:
Green



[†] A trial of low quality. Results of this trial were given a lower weighting when we came to our conclusion about the compound.



19 Green-lipped mussel



Family:

Nutritional supplement

Scientific name:

Perna canaliculus

Other names:

New Zealand mussel, greenshell mussel, Seaton®, GLM, Lyprinol®

What is it?

Green-lipped mussel is a nutritional supplement taken from *perna canaliculus*, a bivalve mollusc native to New Zealand.

How does it work?

We don't yet fully understand how green-lipped mussel works, but we know that extracts contain omega-3 fatty acids, amino acids, minerals and carbohydrates. Laboratory and animal studies have shown that omega-3 fatty acids have anti-inflammatory properties and are important for maintaining joint cell structure and function, and this might be one of the ways green-lipped mussel works in some people.

Is it safe?

Green-lipped mussel seems to be relatively well tolerated, although gastrointestinal discomfort (e.g. nausea and flatulence) have occasionally been reported.

Where do I get it from?

Green-lipped mussel is available from high-street retailers.

What are the possible interactions?

Interactions with other drugs haven't been well studied, but it may affect anticoagulants.

What dose should I use?

No recommended safe doses have been found for use in musculoskeletal conditions.

The role in treatment of arthritis and musculoskeletal conditions

One review article summarised the results of four published RCTs investigating the effectiveness of green-lipped mussel in treating osteoarthritis. A recent review of medical literature summarised results of a further four RCTs into the effects on rheumatoid arthritis.

Rheumatoid arthritis

The number of participants with rheumatoid arthritis included in these trials ranged from 6–47 and the trials lasted from 3–6 months.

- All except one trial found that green-lipped mussel was no better than a placebo in improving the health of participants with rheumatoid arthritis.

Osteoarthritis

Review article[†] – The number of participants involved in the trials included in this review ranged from 30–80. The trials lasted between 3 and 6 months. Three of these trials (two of which were low quality) compared the potential beneficial effects of green-lipped mussel supplements with placebo capsules. The fourth trial, also of low quality, compared the effectiveness of two forms of the compound (the lipid extract versus powder).

- Green-lipped mussel was more effective than a placebo in reducing pain, improving function and improving overall quality of life when taken along with usual painkillers (e.g. paracetamol) and NSAIDs.
- Both lipid extract and powder were effective, with 73 per cent of the lipid group and 87 per cent of the powder group showing significant improvement.

Conclusion

Green-lipped mussel is a nutritional supplement taken from a type of mussel native to New Zealand. It can be bought over the counter in the form of capsules. How it works is poorly understood, but it contains omega-3 fatty acids, which have anti-inflammatory and joint-protecting properties. Current evidence suggests that this compound might be of some benefit to people with osteoarthritis when taken along with paracetamol or NSAIDs; however, it's not effective in treating rheumatoid arthritis.

References:

- Cobb CS, Ernst E. Systematic review of a marine nutriceutical supplement in clinical trials for arthritis: the effectiveness of the New Zealand green-lipped mussel *Perna canaliculus*. *Clinical Rheumatology* 2006; 25(3):275–84.
- Brien S, Prescott P, Coghlan B, Bashir N, Lewith G. Systematic review of the nutritional supplement *Perna canaliculus* (green-lipped mussel) in the treatment of osteoarthritis. *QJM* 2008; 101(3):167–79.

Classification:

Effectiveness score
in rheumatoid arthritis:
1



Effectiveness score
in osteoarthritis:
3



Safety classification:
Green



[†] A trial of low quality. Results of this trial were given a lower weighting when we came to our conclusion about the compound.

20 Homeopathy



What is it?

Homeopathy is a form of treatment founded by Samuel Hahnemann in the 18th century. According to the Society of Homeopaths, homeopathy is based on the theory of 'treating like with like' and an observation that symptoms of an illness are identical to those experienced by a healthy person treated for that illness. Homeopathic remedies are produced by diluting an active substance that causes similar symptoms in the belief that this will reduce the likelihood of harm.

How does it work?

Similar to traditional Chinese medicine, homeopathy is a holistic method of treatment. We don't fully understand how homeopathic treatments work. Remedies are often diluted to the point where there may be no molecules of active ingredient left.

Is it safe?

Homeopathic remedies are considered to be well tolerated, although allergic reactions (e.g. rashes) have been reported. Some people also find their symptoms become worse at the start of treatment.

Where do I get it from?

Homeopathy is a system of treatment practised by professional homeopaths who are qualified to prescribe remedies according to their diagnosis. However, homeopathic granules, tablets, powders and drops are readily available over the counter in pharmacies and health food shops throughout the UK.

What are the possible interactions?

Interactions with other drugs haven't been well studied, although they're unlikely given the high dilution of the remedies.

What dose should I use?

Many homeopathic remedies can be used in the treatment of various forms of arthritis, and dosage hasn't been well studied. The homeopath or homeopathic pharmaceutical company should recommend a dose.

The role in treatment of arthritis and musculoskeletal conditions

A systematic review identified three RCTs into the use of homeopathic treatment for rheumatoid arthritis. The results from a more recent RCT are also summarised. A second systematic review identified three RCTs of oral or topical homeopathic treatment of osteoarthritis; two trials were conducted on participants with knee osteoarthritis and one trial involved participants with hip and/or knee osteoarthritis. Two separate trials investigated homeopathic treatment for fibromyalgia.

Rheumatoid arthritis

Systematic review – Results were inconsistent, with one trial (of reasonable quality but with a high withdrawal rate) showing significant benefit from homeopathy and two trials (one of reasonable quality) showing no significant effect.

Trial 1 – In this larger RCT, 112 participants compared the potential beneficial effects of a mixture of 42 oral homeopathic medicines with that of placebo tablets for 3 months. No evidence was found that homeopathy improved the pain, morning stiffness and mobility in rheumatoid arthritis.

Conclusion

Homeopathic remedies are widely available over the counter in pharmacies and health food shops throughout the UK. The way they work isn't clear, but there's no evident safety risk and interactions with drugs are unlikely.

Even though isolated reports have suggested that homeopathy may have positive effects in the treatment of fibromyalgia, evidence is still not conclusive. Trials which investigated the role of these remedies in osteoarthritis and rheumatoid arthritis gave inconsistent results.

Osteoarthritis

Systematic review – Three trials were identified in this systematic review. The first trial compared oral administration of homeopathic remedies *Rhus toxicodendron* and *Lac Vaccinum* with placebo drops and paracetamol tablets in 65 people for one month. The second trial also investigated oral administration of *Rhus toxicodendron*, but here it was compared 600 mg a day fenoprofen (an NSAID), placebo tablets and placebo drops in 36 people for 2 weeks.

The third trial compared the topical application of SRL, a homeopathic remedy, with piroxicam (an NSAID gel) in 184 people for 4 weeks.

- In the first trial, a significant but similar reduction of pain was observed in the two treatment groups.
- In the second trial, only participants taking fenoprofen reported significant pain reduction.
- Participants who were given SRL in the third trial reported a greater reduction in pain when walking.

Fibromyalgia

Trial 1 – Oral homeopathic drops, prescribed by a homeopath, were compared to oral placebo drops in 62 people for 4 weeks. Participants who took the homeopathic remedy showed significantly greater improvement in the number of tender points, pain levels and quality of life compared to the placebo group.

Trial 2 – The oral administration of Rhus toxicodendron was compared to placebo tablets in 30 people for 4 weeks. Participants assigned the homeopathic drops showed significantly greater improvement in number of tender points and quality of life compared to the placebo group.

References:

- Jonas WB, Linde K, Ramirez G. Homeopathy and rheumatic disease. *Rheumatic disease clinics of North America* 2000; 26(1):117–23.
- Soeken KL. Selected CAM therapies for arthritis-related pain: the evidence from systematic reviews. *Clinical Journal of Pain* 2004; 20(1):13–8.
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- Fisher P, Greenwood A, Huskisson EC, Turner P, Belon P. Effect of homeopathic treatment on fibrositis (primary fibromyalgia). *British Medical Journal* 1989; 299(6695):365–66.

Classification:

Effectiveness score
in rheumatoid arthritis:
1



Effectiveness score
in osteoarthritis:
1



Effectiveness score
in fibromyalgia:
2



Safety classification:
Green



* A trial of low quality. Results of this trial were given a lower weighting when we came to our conclusion about the compound.



21 Indian frankincense



Family:

Ayurvedic medicine of the Burseraceae family

Scientific name:

Boswellia serrata

Other names:

Resin, olibanum, salai guggal, 11-keto β -boswellic acid, acetyl-11-keto β -boswellic acid (AKBA), African elemi, Arabian incense (Bakhour), Boswellia serrata gum resins, boswellic acids, boswellic, Sallaki®, S-compound®, 5-LOXIN®

What is it?

Ayurvedic medicine is a Hindu system of alternative treatment which originated in India. Indian frankincense is a plant extract used as an Ayurvedic remedy to treat a number of diseases.

How does it work?

Indian frankincense prevents the production of hormone-like substances in the body that act as triggers for joint inflammation.

Is it safe?

The compound is safe to use in a daily dose of 1 g, but high doses can have serious side-effects on the liver.

Where do I get it from?

The compound is available from high-street retailers.

What are the possible interactions?

Interactions with other medications haven't been well studied.

What dose should I use?

A daily dose of 1 g has been used in RCTs in participants with osteoarthritis, but dosage hasn't been well studied.

The role in treatment of arthritis and musculoskeletal conditions

Four RCTs examined the use of Indian frankincense in treating osteoarthritis of the knee.

Trial 1 – In the first trial, 30 participants were randomly given either 333 mg Indian frankincense capsules three times a day or placebo tablets for 8 weeks.

- The Indian frankincense group had moderate improvement in pain, knee flexion and walking distance compared to the placebo group.
- The compound was well tolerated by participants, with only minor stomach upsets reported.

Trial 2 – The potential beneficial effects of 333 g Indian frankincense were compared with valdecoxib (an NSAID) in treating knee osteoarthritis in 66 people over 6 months.

- Participants in both groups showed considerable improvement in pain, stiffness and ability to perform physical activity during the trial, but the onset of action was slower in participants who were given Indian frankincense.
- One month after treatment had finished, those in the Indian frankincense group experienced a significant improvement in symptoms compared to participants who received valdecoxib, which might indicate that this compound has a relatively long-lasting effect.
- Only minor gastrointestinal side-effects were reported by participants in both treatment groups.

Trial 3 – The effectiveness and safety of 5-LOXIN®, a drug made of Indian frankincense extract enriched with an anti-inflammatory acid called AKBA was evaluated. The 75 participants were randomly allocated to receive 100 mg of 5-LOXIN®, 250 mg of 5-LOXIN® or placebo tablets once a day for 3 months.

- Compared to the placebo group, participants who were on either dose of 5-LOXIN® had a significantly greater improvement in pain and physical function. Those on 250 mg had the quickest improvement (as early as 7 days after the start of treatment).
- The level of an inflammatory and cartilage-destroying chemical in the knee fluid was significantly reduced in participants taking 5-LOXIN®.
- Only minor side-effects (gastrointestinal problems and mild fever) were reported by participants across all treatment groups.

Trial 4 – In this trial, 60 people with knee osteoarthritis were given 50 mg 5-LOXIN® tablet, 50 mg Aflapin® tablet (made of *Boswellia serrata* extract enriched with at least 20 per cent AKBA), 50 mg *Boswellia serrata* non-volatile oil tablet or a placebo twice a day for 3 months.

- All groups reported improvements in pain, function and stiffness.
- Those who received 5-LOXIN® reported a greater improvement in pain and stiffness than the placebo group; meanwhile those who received Aflapin® reported greater improvements in pain, stiffness and function in comparison with the placebo group.
- Those who received 5-LOXIN® or Aflapin® reported improvements in pain and physical ability as early as 7 days after beginning the treatment and continued to improve throughout the study.

Conclusion

Indian frankincense is an Ayurvedic remedy that can be purchased over the counter in capsule form. It can prevent the production of inflammatory substances in the joints. Current evidence, based on four RCTs, suggests that it might have some beneficial effects in treating participants with knee osteoarthritis which might last for a period of time after treatment is stopped.

References:

- Kimmattkar N, Thawani V, Hingorani L, Khiyani R. Efficacy and tolerability of *Boswellia serrata* extract in treatment of osteoarthritis of knee – a randomised, double blind, placebo-controlled trial. *Phytomedicine* 2003;10(1):3–7
- Sontakke S, Thawani V, Pimpalkhute S, Kabra P, Babulkar S, Hingorani L. Open, randomised, controlled clinical trial of *Boswellia serrata* extract as compared to valdecoxib in osteoarthritis of knee. *Indian Journal of Pharmacology* 2007; 39:27–29.
- Sengupta K, Krishnaraju AV, Vishal AA, Mishra A, Trimurtulu G, Sarma KVS, Raychaudhuri SK, Raychaudhuri SP. Comparative efficacy and tolerability of 5-LOXIN® and Aflapin® against osteoarthritis of the knee: a double-blind, randomised, placebo-controlled clinical study. *International Journal of Medical Sciences* 2010; 7(6):366–77.
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Classification:

Effectiveness score:

4



Safety classification:

Green



22 MSM



Family:

Organic sulphur (nutritional mineral)

Scientific name:

Methylsulfonylmethane

Other names:

OptiMSM®

What is it?

Methylsulfonylmethane is a sulphur (a chemical) found in fresh raw foods including fruits, vegetables and meat. The therapeutic compound, MSM, is a white crystalline substance that contains 34 per cent sulphur.

How does it work?

Laboratory studies have found that MSM has anti-inflammatory and antioxidant effects. Sulphur, which is a major component of MSM, plays an important role in making collagen and glucosamine, both of which are vital for healthy bones and joints, and in the production of immunoglobulins, which offer many benefits to the immune system.

Is it safe?

Current evidence suggests that MSM is well tolerated as a short-term treatment, even with high doses. Only mild side-effects have been reported, the most common of which was gastrointestinal discomfort. The long-term side-effects of MSM haven't yet been studied.

Where do I get it from?

MSM is available from high-street retailers.

What are the possible interactions?

There are no well-known interactions but MSM has been reported to improve the effect of glucosamine in reducing pain and swelling in osteoarthritis.

What dose should I use?

A daily dose of 1,500 mg per day for up to 3 months was used in one RCT in participants with osteoarthritis; however, doses up to 2,600 mg per day have been used in non-RCT studies.

The role in treatment of arthritis and musculoskeletal conditions

Three RCTs examined MSM's effect in treating osteoarthritis.

Trial 1 – In the first trial, 118 participants with knee osteoarthritis were randomly given 1.5 g glucosamine, 1.5 g MSM capsules, both glucosamine and MSM or placebo capsules once a day for 12 weeks.

- Compared to participants who were given a placebo, a significant improvement in pain and joint swelling was achieved by participants allocated MSM or glucosamine.
- The degree of pain reduction was similar in both groups, but glucosamine seemed to have a better effect in reducing joint swelling.

- The group who were assigned both glucosamine and MSM had the most significant reduction in both pain and swelling compared to the other three treatment groups.
- The combined treatment group had the best functional ability of joints at the end of the trial period.
- MSM was well tolerated with no significant side-effects reported.

Trial 2 – In the second RCT, 50 participants with osteoarthritis-related knee pain were given either 6 g MSM capsules or placebo capsules for 12 weeks.

- Only 25 per cent of participants taking MSM showed some improvement of pain and physical function compared to those who took the placebo.
- There was no difference in stiffness.

Trial 3 – This trial has only been published as a conference summary so the quality is unknown. Sixty participants with knee osteoarthritis were randomised to take either 3.375 g MSM capsules or placebo capsules once a day for 12 weeks.

- Participants who were on MSM showed improvement in pain and general functional well-being compared to those who took the placebo.
- MSM didn't have an effect on improving knee function (e.g. walking, climbing stairs).

Conclusion

MSM is rich in organic sulphur, an important 'building block' for healthy bones and joints, and it offers many benefits to the immune system. MSM capsules and ointments are sold over the counter.

The small amount of evidence available from short-term RCTs shows that MSM may have a moderate effect in improving joint pain and swelling as well as general functional well-being in people with osteoarthritis. In a single trial this effect was greater when MSM was combined with glucosamine.

References:

- Usha PR, Naidu MU. Randomised, double-blind, parallel, placebo-controlled study of oral glucosamine, methylsulfonylmethane and their combination in osteoarthritis. *Clinical Drug Investigation* 2004; 24(6):353–63.
- Kim LS, Axelrod LJ, Howard P, Buratovich N, Waters RF. Efficacy of methylsulfonylmethane (MSM) in osteoarthritis pain of the knee: a pilot clinical trial. *Osteoarthritis and Cartilage* 2006; 14(3):286–94.
- Debi R, Fichman G, Bar Ziv Y, Kardosh R, Debbi E, Halperin N et al. The role of MSM in knee osteoarthritis: a double-blind, randomised, prospective study. *Osteoarthritis and Cartilage* 2007; 15(Suppl 3):C231.

Classification:

Effectiveness score:
2



Safety classification:
Green



23 Pine bark extracts



Family:

Herbal extract and nutritional supplement

Scientific name:

Pinus pinaster ssp. Atlantica

Other names:

French pinus maritime bark, Pycnogenol®, pinus maritima, pygenol, PYC

What is it?

Pinus pinaster is a type of pine native to France. The water extract of its bark is used to treat several diseases, including some types of arthritis.

How does it work?

Pine bark extract, which is available in the UK under the trade name Pycnogenol®, is rich in plant pigments called bioflavonoids. Several laboratory studies have found that some of these bioflavonoids have anti-inflammatory and antioxidant properties. Other studies have found that it can reduce the production of specific enzymes that break down cartilage.

Is it safe?

No major side-effects have been reported in previous trials, although minor side-effects include stomach upsets and headaches.

Where do I get it from?

Pine bark is available from high-street retailers.

What are the possible interactions?

Pine bark can theoretically lower blood pressure and blood sugar level, and these effects have also been reported in some RCTs. For that reason, people with hypertension or diabetes should be careful while taking this compound.

What dose should I use?

The best dose hasn't been established, but a treatment plan of two 50 mg Pycnogenol® capsules per day has been used in studies.

The role in treatment of arthritis and musculoskeletal conditions

Two RCTs have been conducted to evaluate the role of pine bark in treating osteoarthritis.

Trial 1 – In the first trial, 156 participants with pain that wasn't well controlled with NSAIDs were randomly selected to receive either 100 mg daily of pine bark or placebo capsules. Participants in both groups were free to use NSAIDs throughout the trial. The trial lasted for 3 months.

- There was a 56 per cent reduction in pain in the pine bark group compared to only a 10 per cent reduction in the placebo group.
- Significant improvements in foot and ankle swelling, joint stiffness and physical function were achieved by the group on the active treatment. Pine bark was significantly more effective than the placebo in all these aspects.
- The use of NSAIDs dropped by 58 per cent in participants taking the active treatment compared to only one per cent in the placebo group.
- The pine bark group had a significant reduction in gastrointestinal symptoms compared to almost no reduction in the placebo group. This might be related to their lower NSAID use.

Trial 2 – In the second trial, 100 people with mild knee osteoarthritis were randomly allocated to receive either 150 mg Pycnogenol® or a placebo for 3 months. Participants receiving Pycnogenol® reported an improvement in function and lower levels of pain in comparison to the group taking the placebo, who showed no improvement.

Conclusion

Pine bark is a herbal extract which is available in the UK under the trade name Pycnogenol®. It's rich in several bioflavonoids that have both anti-inflammatory and antioxidant effects. The little evidence available suggests that pine bark extract may result in an improvement in osteoarthritis-related symptoms.

References:

- Belcaro G, Cesarone MR, Errichi S, Zulli C, Errichi BM, Vinciguerra G et al. Treatment of osteoarthritis with Pycnogenol. The SVOS (San Valentino Osteo-arthrosis Study). Evaluation of signs, symptoms, physical performance and vascular aspects. *Phytotherapy Research* 2008; 22(4):518–23.

Classification:

Effectiveness score:
3



Safety classification:
Green



24 Rosehip



Family:

Herbal medicine of the Rosaceae family

Scientific name:

Rosa canina

Other names:

Rose hips, rosehip drink, LitoZin, Hyben Vital, Burr rose, camellia rose, Cherokee rose, chestnut rose, cabbage rose, Cili, coumaric acid, dog rose, French rose, gooseberry rose, hansa, hedge-pedgies, hips, hip berry, Japanese rose, Virginia rose

What is it?

Rosa canina is a species of wild rose native to some regions in Europe, Africa and Asia. Rosehip is made from the fruits that usually develop after the bloom has died.

How does it work?

Rosehip extract contains polyphenols and anthocyanins, which are believed to help relieve joint inflammation and prevent joint damage. It's also rich in vitamin C, which has antioxidant properties.

Is it safe?

Side-effects are usually mild but include allergic reactions, constipation, diarrhoea and heartburn.

Where do I get it from?

Rosehip is available from high-street retailers.

What are the possible interactions?

Interactions with other medications haven't been well studied.

What dose should I use?

Trials have used 5 g a day of rosehip, but dosage hasn't been well studied.

The role in treatment of arthritis and musculoskeletal conditions

One RCT has evaluated the potential beneficial effect of rosehip on rheumatoid arthritis.

Two systematic reviews identified two RCTs that examined the clinical effectiveness of rosehip in osteoarthritis. The results of a third trial are also summarised below.

Rheumatoid arthritis

Trial 1 – In this trial, 89 participants were randomly assigned 5 g of rosehip powder or placebo powder once a day for 6 months.

- Those who received rosehip reported greater improvements in disease activity, quality of life, physical function and physical global assessment than the placebo group.
- There were more dropouts and side-effects in the placebo group.
- One person in the rosehip group developed vasculitis, but it was unclear whether this was related to the treatment as they were also on several other medications.

Osteoarthritis

Systematic reviews – In the first trial in the reviews, 100 people with hip and/or knee osteoarthritis were randomly assigned to receive either LitoZin tablets (5 g rosehip) or a placebo once a day for 4 months. The second trial involved 112 people with osteoarthritis in multiple sites. Participants were randomly assigned to receive either Hyben Vital tablets (5 g rosehip) or a placebo once a day for 3 months.

- In the first trial, rosehip significantly improved hip flexion when compared with the placebo, but it didn't significantly improve the range of rotation of the hip and the degree of flexion of the knee.
- Significantly more participants in the active treatment group reported a reduction in pain compared with the placebo group.
- Of those given rosehip in the second trial, 66 per cent reported a significant reduction in pain, compared to 36 per cent of participants who received the placebo.
- The rosehip group also had a reduction in some disease-related symptoms (e.g. morning stiffness) and a significant decline in painkiller use.
- In both trials, the active treatment was well tolerated with only minor gastrointestinal side-effects (e.g. diarrhoea).

Trial 1 – The treatment outcome of LitoZin (5 g rosehip) was compared with a placebo in 94 people with osteoarthritis.

- After 3 weeks of treatments, rosehip resulted in a significant reduction in pain scores and painkiller use compared to the placebo, but it didn't significantly reduce stiffness and disability or improve the overall disease severity.
- After 15 weeks, participants who were given rosehip had a significant reduction in pain, stiffness, disability and painkiller use as well as significant improvement in overall disease severity compared to participants on the placebo.

Conclusion

Rosehip is a herbal medication with anti-inflammatory properties. It's available over the counter in capsule form. The evidence available suggests that rosehip may be relatively well tolerated and may be effective in relieving some symptoms associated with osteoarthritis and rheumatoid arthritis.

References:

- Rossnagel K, Roll S, Willich SN. [The clinical effectiveness of rosehip powder in participants with osteoarthritis. A systematic review.] *MMW – Fortschritte der Medizin* 2007; 149(11):51–56. [Article in German].
- Chrubasik C, Duke RK, Chribasik S. The evidence for clinical efficacy of rose hip and seed: a systematic review. *Phytotherapy Research* 2006; 20(1):1–3.
- Rein E, Kharazmi A, Winther K. A herbal remedy, Hyben Vital (stand. powder of a subspecies of Rosa canina fruits), reduces pain and improves general wellbeing in participants with osteoarthritis – a double-blind, placebo-controlled, randomised trial. *Phytomedicine* 2004; 11(5):383–91.
- Warholm O, Skaar S, Hedman E, Molmen HM, Eik L. The effects of a standardized herbal remedy made from a subtype of Rosa canina in participants with osteoarthritis: a double-blind, randomised, placebo-controlled clinical trial. *Current Therapeutic Research* 2003; 64:21–31.

- Willich SN, Rossnagel K, Roll S, Wagner A, Mune O, Erlendson J, Kharazmi A, Sørensen H, Winther K. Rose hip herbal remedy in participants with rheumatoid arthritis – a randomised controlled trial. *Phytomedicine* 2010; 17:87–93.
- Winther K, Apel K, Thamsborg G. A powder made from seeds and shells of a rose-hip subspecies (*Rosa canina*) reduces symptoms of knee and hip osteoarthritis: a randomised, double-blind, placebo-controlled clinical trial. *Scandinavian Journal of Rheumatology* 2005; 34(4):302–08.

Classification:

Effectiveness score
in rheumatoid arthritis:
2



Effectiveness score
in osteoarthritis:
3



Safety classification:
Green



25 SAMe



Family:

Nutritional supplement

Scientific name:

S-adenosylmethionine

What is it?

SAMe is a chemical compound made from methionine, an amino acid also found in protein-rich foods, and adenosine triphosphate (ATP), a nucleic acid and the end product of all energy-gaining reactions in the human body. SAMe was discovered in 1952 and was first studied as a possible treatment for depression.

How does it work?

SAMe is found naturally in the body. It contributes to several biochemical pathways and in the building of hormones and neurotransmitters. Laboratory studies suggested that SAMe has some painkilling activity and stimulates the production of collagen and proteoglycans, the major building blocks of cartilage. The way SAMe may work as an antidepressant is still unknown.

Is it safe?

Side-effects, which are usually mild and infrequent, include nausea, restlessness, headaches, a dry mouth and stomach upsets. Severe side-effects of anxiety and mania have also been reported in people with depression.

Where do I get it from?

This nutritional supplement is available from UK-based internet retailers.

What are the possible interactions?

Theoretically, SAMe might increase the risk of bleeding if taken with anticoagulants. For that reason, people on these medications are advised to take SAMe under a doctor's supervision. The drug can also increase the activity of antidepressants.

What dose should I use?

Optimal dose hasn't been well established, but most studies have used daily doses of 400–1,600 mg.

The role in treatment of arthritis and musculoskeletal conditions

Four trials investigated the effects of SAMe in fibromyalgia. A review article analysed 11 RCTs that investigated the effectiveness of SAMe in treating osteoarthritis. Two separate trials are also included below.

Osteoarthritis

Review article (2002) – Of the 11 trials in this review, one compared the effect of SAMe with that of a placebo, nine compared SAMe with aspirin or another NSAID, and one compared SAMe with a placebo and an NSAID. The number of participants included ranged from 36–493 and the trials lasted from 10–84 days. Six trials used a dosage of 1,200 mg SAMe per day, three trials used 600 mg per day, one trial used 400 mg per day and in the final trial the dose varied between participants. Data from all these trials were combined and reanalysed.

- SAMe was significantly better than a placebo and had an effect similar to that of NSAIDs in reducing functional limitations caused by osteoarthritis.
- In terms of pain reduction, SAMe had an effect equivalent to that of NSAIDs.
- Two trials compared the effect of SAMe versus that of a placebo in reducing osteoarthritis related-pain. Both of them reported SAMe to be significant better than the placebo.
- The combined reanalysis of the 10 trials which compared NSAID with SAMe found that participants taking the active treatment were 58 per cent less likely to experience side-effects than those treated with NSAIDs, regardless of the dose of SAMe and the length of treatment.

Trial 1 – This trial, published in 2004, compared the effectiveness of SAMe to celecoxib (a COX-2 inhibitor, which is a type of NSAID) for pain control, functional improvement and reported side-effects in people with osteoarthritis. The trial lasted for 16 weeks and found that SAMe worked more slowly but was as effective as celecoxib in relieving pain and improving the physical function.

Trial 2 – In this trial, 134 people of Asian origin with knee osteoarthritis were randomly allocated to receive either 400 mg SAMe three times a day or nabumetone (an NSAID) for 8 weeks.

- Both groups reported improvements in pain, stiffness and function.
- The participants' overall assessment of disease and the physicians' assessment of the participants' response to therapy also reported improvement, with no differences between the groups.

Fibromyalgia

Three out of four published RCTs found that SAMe was effective, when compared to a placebo, in reducing the number of tender points and/or the intensity of tenderness of these points in people with fibromyalgia. The three studies also found that SAMe was effective, compared to placebo, in reducing depressive symptoms.

The fourth RCT found that SAMe wasn't significantly better than a placebo in reducing almost all disease-related symptoms; however, the number of participants who took part in these four trials was small (17–44 participants) and length of treatment was short (10 days–6 weeks).

Conclusion

SAMe is a chemical compound found naturally in the body. In addition to its potential antidepressant properties, laboratory studies suggest that SAMe has some painkilling activities. It also stimulates the production of major parts of cartilage. The chemical compound can be purchased over the internet in the form of capsules.

Evidence from RCTs suggests that SAMe is effective in reducing functional limitations and, to a lesser extent, pain in osteoarthritis. Evidence for its effectiveness for fibromyalgia, from a small number of trials only, suggests that SAMe might be of benefit in reducing body tenderness and depressive symptoms.

References:

- Najm WI, Reinsch S, Hoehler F, Tobis JS, Harvey PW. S-adenosyl methionine (SAMe) versus celecoxib for the treatment of osteoarthritis symptoms: a double-blind cross-over trial. *BMC Musculoskeletal Disorders* 2004; 26:5–6.
- Kim J, Lee EY, Koh E, Cha H, Yoo B, Lee CK, Lee YL, Ryu H, Lee KH, Song YW. Comparative clinical trial of S-adenosylmethionine versus nabumetone for the treatment of knee osteoarthritis: an 8-week, multicenter, randomised, double-blind, double-dummy, phase IV study in Korean participants. *Clinical Therapeutics* 2009; 31(12):2860–72.
- Soeken KL, Lee WL, Bausell RB, Agelli M, Berman BM. Safety and efficacy of S-adenosylmethionine (SAMe) for osteoarthritis. *Journal of Family Practice* 2002; 51(5):425–30.
- Sarac AJ, Gur AJ. Complementary and alternative medical therapies in fibromyalgia. *Current Pharmaceutical Design* 2006; 12(1):47–57.

Classification:

Effectiveness score
in osteoarthritis:
4



Effectiveness score
in fibromyalgia:
2



Safety classification:
Green



SAMe, a chemical compound found in the body, was first studied as a possible treatment for depression.

26 Selenium



Family:

Nutritional supplement

Scientific name:

Selenium

Other names:

Selenomethionine

What is it?

Selenium is a trace mineral which is important for many vital functions in the body. For medicinal purposes, the mineral is usually produced from yeast.

How does it work?

Some previous studies have found that people with rheumatoid arthritis have low levels of selenium in their blood compared to people without the disease. How selenium may work to treat arthritis and musculoskeletal conditions isn't well understood, but it might be related to its antioxidant properties. Selenium is a crucial part of a number of enzymes, some of which are involved in specific pathways in the body that can prevent cell damage (usually by interacting with harmful molecules produced within the cells known as free radicals).

Is it safe?

The daily recommended dietary allowance of selenium is 80–200 micrograms (μg), and it's well tolerated if no more than this is taken; however, selenium can be toxic if taken in high doses and may cause gastrointestinal symptoms, liver and kidney problems, skin changes and hair loss.

Where do I get it from?

Selenium is available from UK high-street retailers.

What are the possible interactions?

Interactions with other medications are unlikely if selenium is taken in low or moderate doses.

What dose should I use?

No recommended effective and safe dose has been found for use in musculoskeletal conditions, but most trials used a dose of 200 μg .

The role in treatment of arthritis and musculoskeletal conditions

A recent review article identified three complete reports of RCTs of selenium treatment in rheumatoid arthritis.

Review article – The number of participants included in the trials ranged from 40–70 and the trials lasted from 3–6 months. The active treatment in all trials was selenium capsules (200 μg per day in two trials and 256 μg per day in one trial). The control group in all trials was made up of participants on placebo capsules.

- In the first trial (40 participants over 6 months), there was no significant difference between those who were assigned selenium or placebo in all aspects of disease severity, including pain, morning stiffness and number of swollen joints.
- In the second trial[†] (55 people over 3 months), there was no significant difference between participants taking selenium or placebo in pain reduction, morning stiffness and number of swollen joints. Participants on selenium had better arm movement and a perception of better general health.
- The third trial (70 people over 3 months) found that there was no significant difference between participants who were on selenium or placebo in terms of pain reduction, morning stiffness, number of swollen joints and the use of NSAIDs.

Conclusion

Selenium is a dietary supplement that's available to buy over the counter from pharmacies and health food shops, mainly as an ingredient in multivitamin capsules. How selenium works to treat arthritis isn't well understood, but it might be related to its antioxidant properties. Current evidence, based on published RCTs, suggests that selenium supplements aren't effective in treating rheumatoid arthritis.

References:

- Canter PH, Wider B, Ernst E. The antioxidant vitamins A, C, E and selenium in the treatment of arthritis: a systematic review of randomised clinical trials. *Rheumatology (Oxford)* 2007; 46(8):1223–33.

Classification:

Effectiveness score:

1



Safety classification:

Green



[†]A trial of low quality. Results of this trial were given a lower weighting when we came to our conclusion about the compound.

27 Stinging nettle



Family:

Herbal medicine of the nettle (Urticaceae) family

Scientific name:

Urtica dioica

Other names:

Common perennial nettle

What is it?

Stinging nettle is a plant native to Europe, Asia, and North America.

How does it work?

Nettle leaves are covered in tiny hairs which have a high silicon content, meaning they're extremely brittle. When the leaf touches the skin, the round tips of the hairs break off. The sharp point of the hair then penetrates the skin and several chemicals, including histamine and serotonin, are produced. These chemicals can be effective in reducing pain by stimulating pain neurons, so the skin irritation overrides musculoskeletal pain.

Is it safe?

The compound is applied to the skin around the painful area. Common side-effects include itching and a tingling sensation.

Where do I get it from?

Although stinging nettle is available in capsules from high-street retailers, the trials below used topical applications.

What are the possible interactions?

Interactions are unlikely because the compound is applied topically to the skin.

What dose should I use?

Little information is available on dosage, but nettle leaves were applied to the painful area for two 30-second periods for 1 week in one study.

The role in treatment of arthritis and musculoskeletal conditions

Two RCTs evaluated the role of stinging nettle in the treatment of osteoarthritis.

Trial 1 – The effects of nettle as a possible local painkiller were examined in 27 people with osteoarthritis-related pain at the base of their thumb. Participants were told that the study was testing two types of nettle leaf but were randomly allocated to apply either a nettle leaf or a placebo leaf daily for 1 week to the painful area. Participants continued on their usual treatment during this period. They then stopped using the leaf for 5 weeks and applied the other leaf for 1 week afterwards.

- Participants using nettle leaves reported less pain and disability compared to those who used the placebo leaves.
- The difference in pain reduction remained significant during the first week following treatment and then disappeared gradually thereafter.

Trial 2 – The potential beneficial effects of stinging nettle were examined in 42 people with knee osteoarthritis. Participants were randomly allocated to apply either stinging nettle or another type of nettle (which isn't thought to treat osteoarthritis) to their knees for 1 week.

- Participants in both groups had a similar mild but insignificant reduction in pain scores.
- Those using stinging nettle had only minor and short-term skin irritation.

Conclusion

Stinging nettle is a topical medication that's used to relieve osteoarthritis-related pain. When applied to the skin, the compound gives a counterirritant effect which can override musculoskeletal pain. There's little evidence available on the use of nettle leaves for osteoarthritis; one study suggested a positive effect in the short-term treatment of osteoarthritis of the thumb but another found no beneficial effect in the short-term treatment of knee osteoarthritis.

References:

- Randall C, Randall H, Dobbs F, Hutton C, Sanders H. Randomised controlled trial of nettle sting for treatment of base-of-thumb pain. *Journal of the Royal Society of Medicine* 2000; 93(6):305–09.
- Randall C, Dickens A, White A, Sanders H, Fox M, Campbell J. Nettle sting for chronic knee pain: a randomised controlled pilot study. *Complementary Therapies in Medicine* 2008; 16(2):66–72.

Classification:

Effectiveness score:
1



Safety classification:
Green



28 Turmeric



Family:

Nutritional supplement of the ginger (Zingiberaceae) family

Scientific name:

Curcuma domestica

Other names:

C. rotunda L., C. xanthorrhiza Naves and Amomum curcuma Jacq

What is it?

Turmeric is a perennial plant native to southern Asia. It's widely grown both for domestic and medicinal purposes.

How does it work?

Studies on animals have shown that turmeric products have anti-inflammatory properties.

Is it safe?

Human clinical trials haven't found turmeric to be toxic when given at doses of 1–10 g a day.

Where do I get it from?

Turmeric is widely available from high-street retailers.

What are the possible interactions?

Turmeric increased the effects of anticoagulants or antiplatelet drugs in laboratory studies, but the effects on antiplatelet drugs haven't been demonstrated in humans.

What dose should I use?

In studies in humans, participants received doses of approximately 1–1.5 g a day but also up to 8 g a day.

The role in the treatment of arthritis and musculoskeletal conditions

One RCT has investigated the use of turmeric in 107 people with primary knee osteoarthritis.

Trial 1 – Participants were randomised to receive either 2 g turmeric or 800 mg ibuprofen per day for 6 weeks.

- Both groups' pain levels when walking and when climbing stairs improved, as did their knee function.
- Those who received turmeric found that their pain when climbing stairs improved more than those who received ibuprofen.
- There was no difference in reported side-effects between the groups, and the most commonly reported were heartburn and dizziness.
- Those who received ibuprofen were better at taking their treatment than those who received turmeric.

Conclusion

Turmeric is believed to have anti-inflammatory properties. It can be bought over the counter from health food shops, pharmacies and supermarkets in the form of powder. The effectiveness of turmeric in osteoarthritis is uncertain due to the limited trial evidence, but it suggests that it only has minor side-effects.

References:

- Kuptniratsaikul V, Thanakhumtorn S, Chinswangwatanakul P, Wattanamongkonsil L, Thamlikitkul V. Efficacy and safety of Curcuma domestica extracts in patients with knee osteoarthritis. *Journal of Alternative and Complementary Medicine* 2009; 15(8):891–97.

Classification:

Effectiveness score:
2



Safety classification:
Green



Turmeric is a perennial plant native to southern Asia. It's widely grown for both domestic and medicinal purposes.

29 Vitamins A, C and E (antioxidant vitamins)



Family:

Nutritional supplement

Scientific name:

Vitamin A (retinoids), vitamin C (L-ascorbate) and vitamin E (tocopherols and tocotrienols)

What are they?

Vitamins are nutritional substances that are needed in small amounts in the diet. Vitamins A and E are fat-soluble vitamins, meaning they're stored in the body in fat cells, but they need to have their levels topped up at regular intervals. Vitamin C is a water-soluble vitamin. All water-soluble vitamins except for vitamin B12 are stored in the body for only a brief period (several weeks to several months) and then excreted through urine. For that reason, water-soluble vitamins need to be taken daily. Vitamins can be found in foods (natural vitamins) or can be produced in laboratories (synthetic vitamins).

How do they work?

Vitamins A, C and E have antioxidant properties. Some laboratory and animal studies have also found that vitamin E might have the potential to treat osteoarthritis by stimulating the growth of cartilage cells. Other studies have found that it has some anti-inflammatory properties. Studies on vitamin C have found that it can stimulate the production of collagen and proteoglycan (both of which are important parts of joint cartilage) and can protect against the breakdown of cartilage in animal studies.

Are they safe?

Vitamin C is considered to be a very well-tolerated vitamin because if the body has too much, it can get rid of it through the urine; however, because vitamins A and E are stored in the body, having too much of these vitamins can cause health problems. If more than 50,000 units of vitamin A are taken over a long period, it can cause vitamin A toxicity. Symptoms of this can include dry skin or rashes, bone pain, hair loss, sleep problems and gastrointestinal problems.

Most adults can tolerate up to 100–800 mg a day of vitamin E, but long-term intake of large doses (more than 1,000 mg daily) can cause headaches, nausea, blurred vision and disturbed functions of the thyroid gland. Recently, it has been recommended that high-dose intake of vitamin E (more than 400 mg a day) should be avoided.

Where do I get them from?

Antioxidant vitamins are readily available from high-street retailers.

What are the possible interactions?

No serious drug interactions have been reported with a low or medium intake of antioxidant vitamins.

What dose should I use?

No recommended effective and safe doses have been found for use in arthritis and related conditions. Most trials used daily doses of 1,200 mg vitamin E, 50,000 international units (IU) vitamin A and 1,000 mg vitamin C.

The role in treatment of arthritis and musculoskeletal conditions

A review article identified eight reports of RCTs of antioxidant vitamin treatment of osteoarthritis. A separate study from 2009 looked specifically at vitamin E.

Another review article identified four reports of RCTs of antioxidant vitamin treatment of rheumatoid arthritis. A fifth trial investigated the role of vitamin E.

Rheumatoid arthritis

Review article – Three of the trials in the review investigated the potential beneficial role of vitamin E, while the fourth studied the effectiveness of selenium ACE treatment.

- In the first trial[†] (42 people over a 12-week period), there was no significant difference between participants on 1,200 mg per day vitamin E supplements or a placebo in morning stiffness, number of swollen joints and degree of joint tenderness, but there was a significant difference in pain reduction in favour of participants taking vitamin E.
- In both the second trial (41 people over a 3-week period) and the third trial (85 people over a 3-week period), there was no significant difference between participants allocated 1,200 mg a day vitamin E supplements or participants given 150 mg diclofenac a day in all aspects of disease severity at the end of the trial.
- In the fourth trial[‡] (20 people over a 6-month period), there was no significant difference between participants who received selenium ACE supplements or participants on a placebo in all aspects of disease severity at the end of the trial.

Osteoarthritis

Review article – Six of the trials in the review investigated the potential beneficial role of vitamin E, while one studied the effectiveness of vitamin C and another looked at selenium ACE. The number of participants included in these trials ranged from 30–136 and the trial period ranged from 10 days–2 years.

- Two trials out of four demonstrated the effectiveness of vitamin E supplements in reducing pain and overall symptoms in osteoarthritis when compared to placebo treatment. The other two trials found they had no significant benefits.
- Two RCTS out of two found no significant difference between participants who received vitamin E supplements or diclofenac with respect to pain reduction and overall improvement of most symptoms.
- One trial of 133 people compared the treatment outcome of participants with osteoarthritis who were randomly selected to receive either 1 g vitamin C

supplements or placebo tablets once a day for 2 weeks. Compared to the placebo group, participants on vitamin C reported a significant improvement in joint pain and physical function at the end of the trial.

- Another study[‡] compared the treatment outcome of 30 people with osteoarthritis who were randomised to receive either selenium ACE supplements or placebo tablets for 6 months. There was no significant difference in the level of pain reduction and the degree of general health improvement at the end of the trial period.

Trial 1[‡] – In this trial, 64 participants with osteoarthritis of the knee received either daily doses of 400 mg vitamin E (produced from palm oil) or 500 mg glucosamine sulphate three times a day for 6 months. Both groups improved but there were no differences between the groups in pain or function.

Trial 2 – This trial looked at 102 people who received either vitamin E, conjugated linolenic acids (CLAs), a combination of vitamin E and CLAs or a placebo over a 3-month period.

- The participants' conditions as assessed by the physician, pain (morning, night, post-activity), morning stiffness, number of swollen and tender joints and disease activity improved in all groups except the placebo group.
- The greatest improvements were in those taking CLAs alone or in combination with vitamin E.

Conclusion

Vitamins are organic essential nutrients which are available in most pharmacies in the form of capsules. Vitamins A, C and E have antioxidant activity, so theoretically they can play a role in the treatment of arthritis-related conditions by preventing bone and joint cell damage.

Laboratory and animal studies have found some scientific basis for their use, but current evidence from studies on humans suggests that antioxidant vitamins aren't effective in treating rheumatoid arthritis. Evidence from trials of the effectiveness of vitamin E in treating osteoarthritis provided mixed results. Results for trials into the use of vitamin C in treating osteoarthritis are encouraging, but still preliminary, and need confirmation by larger trials.

References:

- Aryaeian N, Shahram F, Djalali M et al. Effect of conjugated linoleic acids, vitamin E and their combination on the clinical outcome of Iranian adults with active rheumatoid arthritis. *International Journal of Rheumatic Diseases* 2009; 12:20–28.
- Canter PH, Wider B, Ernst E. The antioxidant vitamins A, C, E and selenium in the treatment of arthritis: a systematic review of randomised clinical trials. *Rheumatology (Oxford)* 2007; 46(8):1223–33.
- Haflah NHM, Jaarin K, Abdullah S, Omar M. Palm vitamin E and glucosamine sulphate in the treatment of osteoarthritis of the knee. *Saudi Medical Journal* 2009; 30(11): 1432–38.

Classification:

Effectiveness score
in rheumatoid arthritis:
1



Effectiveness score
in osteoarthritis:
2



Safety classification:
Green



[‡]A trial of low quality. Results of this trial were given a lower weighting when we came to our conclusion about the compound.



30 Vitamin B complex (non-antioxidant vitamins)



Family:
Nutritional supplement

Scientific names:
Vitamin B3 (niacinamide), vitamin B12 (Cobalamin),
vitamin B9 (folic acid)

What is it?

Vitamins are nutritional substances that are needed in small amounts in the diet. Vitamin B complex is a water-soluble vitamin. Except for vitamin B12, which can be stored in the liver for up to 4 years, all water-soluble vitamins are stored for only a brief period (several weeks to several months) and then excreted through urine. For that reason, water-soluble vitamins need to be taken daily. Vitamins can be found in foods (natural vitamins) or can be produced in laboratories (synthetic vitamins).

How does it work?

Several studies have found that vitamin B12 plays a role in regulating bone metabolism. Another study found that people with osteoarthritis have low intake of vitamin B9 (folic acid).

Is it safe?

Folic acid supplements are safe, even with high doses. Apart from occasional gastrointestinal symptoms and itching, vitamin B12 has a high safety profile.

Where do I get it from?

Vitamin B complex is readily available from high-street retailers.

What are the possible interactions?

No serious drug interactions have been reported with low or medium intake of non-antioxidant vitamins.

What dose should I use?

No recommended effective and safe doses have been found for use in the treatment of arthritis-related conditions, but RCTs have used daily doses of 3 g of vitamin B3, 6,400 µg of vitamin B9 and 20 µg of vitamin B12.

The role in treatment of arthritis and musculoskeletal conditions

Two RCTs were conducted to evaluate the role of non-antioxidant vitamins in treating osteoarthritis. One trial evaluate the role of vitamin B6 in rheumatoid arthritis.

Rheumatoid arthritis

Trial 1[#] – In this trial, 43 participants were randomly allocated to receive 5 mg vitamin B9 with or without 100 mg vitamin B6 once a day for 12 weeks.

- There was no reported difference in change in the disease activity score or number of painful or swollen joints.

- Those who received the Vitamin B9 and B6 combination demonstrated significantly greater reductions in some markers of inflammation.
- No side-effects were recorded.

Osteoarthritis

Trial 1 – In the first trial, 72 people with osteoarthritis were randomly selected to receive either 3 g vitamin B3 or placebo tablets once a day for 12 weeks.

- Neither treatment group reported reduction of pain, but the overall symptoms improved by 29 per cent in participants assigned the vitamin and worsened by 10 per cent in participants on the placebo.
- In particular, vitamin B3 seemed to be effective in improving joint mobility compared to the placebo.
- No major side-effects were reported, but the number of side-effects was higher in the vitamin B3 group.

Trial 2 – In the second RCT, 29 people with hand osteoarthritis were randomised to receive either 6,400 µg vitamin B9, a combination of 6,400 µg vitamin B9 and 20 µg vitamin B12 or placebo tablets once a day for 2 months.

- Participants who received vitamin B9 and B12 had significantly better hand grip values compared to the other two treatment groups.

Conclusion

Vitamin B complex is a type of non-antioxidant vitamin. The way vitamins belonging to this group may treat arthritis-related conditions isn't well studied, but they're relatively well tolerated.

Evidence from trials of vitamin B supplements in osteoarthritis suggests that vitamins B3, B9 and B12 might be of some benefit, particularly in improving joint mobility and hand grip. In participants with rheumatoid arthritis, vitamin B6 may reduce levels of markers of inflammation, but there's no evidence from trials that it improve clinical measures.

References:

- Wang Y, Prentice LF, Vitetta L, Wluka AE, Cucutini FM. *The effect of nutritional supplements on osteoarthritis* Alternative Medicine Review 2004; 9(3):275–96.
- Huang S-C, Wei JC-C, Wu DJ, Huang Y-C. Vitamin B6 supplementation improves pro-inflammatory responses in participants with rheumatoid arthritis. *European Journal of Clinical Nutrition* 2010; 64:1007–13.
- Jonas WB, Rapoza CP, Blair WF. The effect niacinamide on osteoarthritis: a pilot study. *Inflammation Research* 1996; 45(7):330–34.
- Flynn MA, Irvin W, Krause G. The effect of folate and cobalamin on osteoarthritic hands. *Journal of the American College of Nutrition* 1994; 13(4):351–56.

Classification:

Effectiveness score
in rheumatoid arthritis:
1



Effectiveness score
in osteoarthritis:
2



Safety classification:
Green



[#]A trial of low quality. Results of this trial were given a lower weighting when we came to our conclusion about the compound.

31 Willow bark



Family:

Herbal medicine of the willow (Salicaceae) family

Scientific name:

Willow

Other names:

Salix spp., basket willow, bay willow, beta-salicin, black willow, brittle willow, crack willow, daphne willow, populin, purple willow, salicin, salicortin, salicylsalicin, salicyl alcohol, salicylate, salicylic acid, salicyluric acid, salidroside, saligenin, salipurposide, Salix alba, Salix daphnoides, Salix fragilis L., Salix pentandra, Salix purpurea, white willow, white willow bark, willow tree, willowprin

What is it?

The bark of some species of Salix trees has been used for treating inflammatory and arthritis-related conditions since ancient times. Extracts from the following species of Salix trees have been used as sources of willow: Salix purpurea (purple willow), Salix fragilis (crack willow), Salix alba (white willow), Salix daphnoides (violet willow) and Salix pentandra (bay willow). These Salix species are also considered the natural source of acetylsalicylic acid, also known as aspirin.

How does it work?

Willow bark contains an ingredient called salicin, which is transformed in the body into another chemical substance called salicylic acid. Similar to acetylsalicylic, salicylic acid reduces the production of certain prostaglandins in the nerves, and this relieves pain and discomfort. Willow bark showed anti-inflammatory activity in several laboratory-based studies.

Is it safe?

Willow bark should be used with caution in participants with gastrointestinal and liver problems, and diabetes. Common side-effects include stomach upsets, increased blood pressure and allergic reactions. Overdose can lead to serious consequences, including stomach ulcers and bleeding.

Where do I get it from?

Willow bark capsules are available from UK-based internet retailers.

What are the possible interactions?

Similar to aspirin, willow bark interacts with anticoagulants, acetazolamide, anti-hypertensives and anti-inflammatory drugs.

What dose should I use?

A daily dose of 240 mg of salicin has been used in previous studies on participants with osteoarthritis and rheumatoid arthritis. Assalix®, a commercial willow bark preparation, contains 240 mg of salicin per tablet.

The role in treatment of arthritis and musculoskeletal conditions

Two RCTs were found examining the effectiveness of willow bark in treating hip and knee osteoarthritis. One trial evaluated the potential therapeutic effects of willow bark in participants with rheumatoid arthritis.



Rheumatoid arthritis

Trial 1 – In this trial, 26 participants were randomly selected to receive either willow bark (240 mg salicin) or placebo tablets once a day for 6 weeks. Participants taking willow bark achieved a 15 per cent reduction in pain compared to a four per cent reduction in the placebo group, but the study's authors concluded that this difference may be due to chance.

Conclusion

Willow bark is a herbal preparation that's available over the counter in the form of tablets. Its pain-relieving effect is caused by its active ingredient, salicin, which reduces the production of pain-inducing chemicals in the nerves.

The limited evidence available suggests that willow bark may have a moderate effect in treating osteoarthritis and rheumatoid arthritis-related pain. In the single study evaluating willow bark against an NSAID for osteoarthritis, it wasn't as effective for pain relief. It appears relatively well tolerated when taken in recommended doses.

Osteoarthritis

Trial 1 – In the first trial, 127 participants were randomised to receive willow bark (240 mg of salicin), 100 mg diclofenac or a placebo once a day for 6 weeks.

- Participants who were on diclofenac had the best levels of pain relief.
- Those assigned willow bark didn't significantly differ from the placebo group.

Trial 2 – In the second trial, 78 participants were randomly assigned to either willow bark (240 mg of salicin) or placebo tablets once a day for 2 weeks. Participants taking willow bark achieved a 14 per cent reduction in pain, compared to only two per cent in the placebo group.

Willow bark was well-tolerated by participants who received it in both RCTs. Lack of effectiveness was the most common reason for withdrawal.

References:

- Schmid B, Ludtke R, Selbmann HK, Kotter I, Tschirdewahn B, Schaffner W et al. Efficacy and tolerability of a standardized willow bark extract in participants with osteoarthritis: randomised placebo-controlled, double blind clinical trial. *Phytotherapy Research* 2001; 15(4):344–50.
- Biegert C, Wagner I, Ludtke R, Kotter I, Lohmuller C, Gunaydin I et al. Efficacy and safety of willow bark extract in the treatment of osteoarthritis and rheumatoid arthritis: results of 2 randomised double-blind controlled trials. *Journal of Rheumatology* 2004; 31(11):2121–30.

Classification:

Effectiveness score
in rheumatoid arthritis:
1



Effectiveness score
in osteoarthritis:
2



Safety classification:
Amber



Bark from some species of *Salix* trees, such as willow bark, has been used for medicinal purposes since ancient times.



Other compounds

Only compounds which have been tested in at least one RCT and which are available to buy in the UK have an entry in the previous section. If the compound that you're searching for doesn't appear, it means that you can't buy it in the UK or that we couldn't find any reports of an RCT in which it was tested. This means it's not possible for us to tell whether this compound works or not. In this section we list some commonly used complementary medicines for which we couldn't find any RCTs.

Two of the compounds included in this list have been studied in RCTs but only as an ingredient of a multicomponent medication – milfoil as an ingredient of gitadyl and poplar bark as an ingredient of reumalex – but the individual effectiveness wasn't investigated using RCTs.

Although we couldn't find any RCTs investigating the safety and effectiveness of the compounds included in this list, most of them have been studied in the laboratory,

on animals and/or in humans in non-randomised studies; however, we can't make complete assessments for the following reasons:

- Laboratory studies can only provide data on how the compounds work and their toxicity. Animal studies can help us to start understanding the compounds' safety and effectiveness, but this can't necessarily be directly applied to humans.
- Non-randomised trials are experimental studies in humans where participants aren't randomly allocated to get either the active treatment or placebo. This type of study is affected by differences in the treatment applied but also by differences in the characteristics of the participants.

Therefore, RCTs are needed before a conclusion can be reached on the safety and effectiveness of these compounds.

Compounds for which no RCTs were identified (with other names and components in brackets)

• 5-HTP	• Milfoil (yarrow, Achillea millefolium)
• Aloe vera (lily of the desert, plant of immortality, medicine plant)	• Nicotinamide adenine dehydrogenase (NADH)
• Artrósilium (organic silica, currant of the meadow, Queen of the meadow, meadowsweet)	• Noni juice (<i>Morinda citrifolia</i>)
• Basil (holy basil, tulsi, <i>Ocimum sanctum</i>)	• Organic silica (<i>Bambusa vulgaris</i>)
• Bee stings (bee venoms, Nectar Ease®)	• Phosphatidyleserine
• Black cohosh (<i>Actaea racemosa</i>)	• Poplar bark (American aspen, white poplar)
• Chlorella pyrenoidosa (green algae)	• Qianggu
• Cider vinegar (apple cider vinegar)	• Sarsaparilla (<i>Smilax</i>)
• Co-enzyme Q10 (CellSparsc 360° combined with fish oil and tocotrienols)	• Serum dehydroepiandrosterone sulphate (DHEAS)
• Echinacea	• Solidago virgaurea (<i>Solidago canadensis</i> , goldenrod)
• Emu oil (emuline)	• St John's wort (<i>hypericum perforatum</i>)
• Garlic (<i>Allium sativum</i>)	• Tipi (contains Indian ginseng, Indian frankincense and turmeric)
• Gingko biloba	• Valeriana officinalis (valerian)
• Ginseng (Siberian ginseng)	• White royal jelly
• Green tea	• Wintergreen oil (contains methyl salicylate)
• Guaiacum resin	• Withania somnifera (ashwagandha, Indian ginseng, winter cherry)
• Kava kava (<i>Piper methysticum</i>)	• zinc and copper
• Melatonin	

Compounds for which there is randomised controlled trial evidence, but which aren't available in the UK*

- | | |
|---|------------------------------|
| • Articulin-F | • Passion fruit peel extract |
| • Avocado-soybean unsaponifiables (ASU) | • Phytodolor |
| • Biqi capsule | • Reumalex |
| • Cannabis oral spray ** | • SKI 306X |
| • Eazmov | • Thunder god vine |
| • Gitadyl | • Tong luo kai bi |

* many of these were included in the first edition of the report

** not available for the conditions considered in this report

Glossary

Alpha-linolenic acid (ALA) – an essential fatty acid that's important for maintaining a joint's cell structure and function. ALA is converted into two important compounds within the body – DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid). Both DHA and EPA play a significant role in the production of anti-inflammatory substances in the blood called prostaglandins.

Amino acids – a group of chemical compounds that provide the basic structure for all the different proteins within the body.

Anticoagulants – a group of drugs used to prevent or treat abnormal blood clotting. They may be given as tablets (e.g. aspirin, warfarin) or by injection (e.g. heparin) and may increase the risk of bleeding.

Anti-hypertensive – a drug or treatment to lower and control high blood pressure (hypertension), for example, beta-blockers.

Antioxidants – substances that can neutralise harmful molecules, known as free radicals, which are produced within the cells and which may cause tissue damage or disease. The body produces its own antioxidants but it's thought that antioxidants in the diet (such as vitamin C) help destroy excess free radicals.

Cartilage – a layer of tough, slippery tissue that covers the ends of the bones in a joint. It acts as a shock-absorber and allows smooth movement between bones.

Collagen – the main substance in the white, fibrous connective tissue that is found in tendons, ligaments and cartilage. This very important protein is also found in skin and bone.

Diclofenac – a type of non-steroidal anti-inflammatory drug (NSAID).

Effectiveness – a measure of how well something works when completely different subjects are compared with each other. If a particular treatment, for example, is found to be better than another, but they're entirely different treatments (e.g. care from a general practitioner versus care from a herbal medicine practitioner), it's described as effective. This is because we can't be sure precisely what aspect of the care resulted in a better outcome due to the differences in the treatments.

Efficacy – how well something works when tested under strictly controlled conditions, for example when all aspects of treatment are exactly the same apart from one aspect (e.g. real capsule versus placebo capsule).

Essential fatty acids – fats that the body can't make itself and must be taken through foods or nutritional supplements.

Fibromyalgia – a long-term (chronic) form of widespread pain in the muscles and soft tissues surrounding the joints throughout the body.

Gamma-linolenic acid (GLA) – an essential fatty acid that's important for maintaining a joint's cell structure and function. GLA is converted in the body to hormone-like substances called prostaglandins, which regulate the immune system and fight joint inflammation. GLA might also suppress inflammatory responses by directly acting on some inflammatory cells.

Immunosuppressants – drugs that suppress the actions of the immune system. They're often used in conditions such as rheumatoid arthritis where the immune system attacks the body's own tissues.

Ligaments – tough, fibrous bands anchoring the bones on either side of a joint and holding the joint together. In the spine they're attached to the vertebrae and restrict spinal movements, therefore giving stability to the back.

Non-steroidal anti-inflammatory drugs (NSAIDs) – a large family of drugs prescribed for different kinds of arthritis that reduce inflammation and control pain, swelling and stiffness. Common examples include ibuprofen, naproxen and diclofenac.

Osteoarthritis – the most common form of arthritis (mainly affecting the joints in the fingers, knees, hips), causing cartilage thinning and bony overgrowths (osteophytes) and resulting in pain, swelling and stiffness.

Placebo – a drug that contains no active ingredients. Placebos are often used as control treatments that an active ingredient can be compared against so investigators can tell whether the active treatment works or not. Placebos should look like the active treatment to make sure that the participant doesn't know which treatment they were given.

Prostaglandins – hormone-like substances that regulate the immune system and fight joint inflammation.

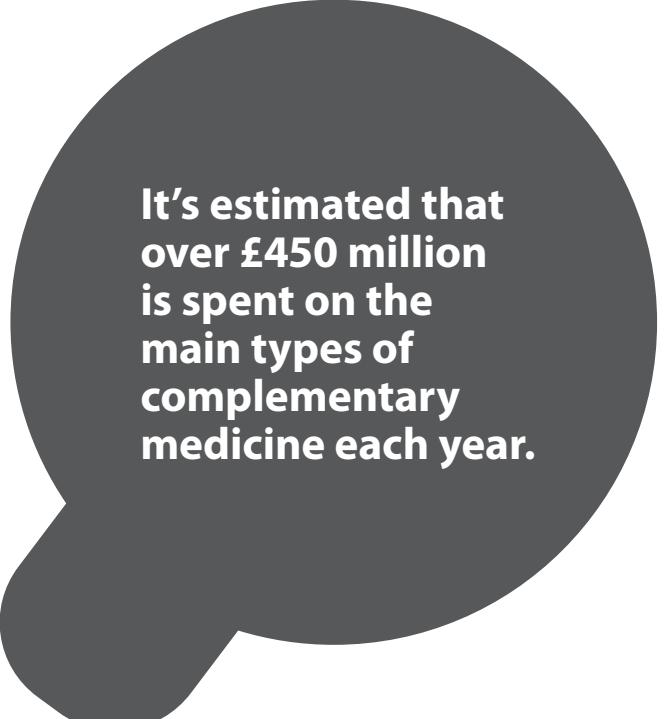
Randomised controlled trial (RCT) – an experiment in which two or more treatments are given to participants who have been put into groups at random. The active treatment is often compared against a control treatment or no treatment. RCTs provide the best evidence on effectiveness.

Rheumatoid arthritis – an inflammatory disease affecting the joints, particularly the lining of the joint. It most commonly starts in the smaller joints in a symmetrical pattern – that is, for example, in both hands or both wrists at once.

Significant – a result is considered to be significant when investigators are fairly sure that differences between two different treatments assessed weren't due to chance. It doesn't mean that any differences were clinically important.

Synovial fluid – the fluid produced within the joint capsule that helps to nourish the cartilage and lubricate the joint.

Tendons – strong, fibrous bands or cords that anchor muscle to bone.



It's estimated that over £450 million is spent on the main types of complementary medicine each year.

Summary table

Compound	Condition	Effectiveness score	Safety classification
Andrographis paniculata	Rheumatoid arthritis	1 ●●●●●●●●	● Green
Anthocyanidins	Fibromyalgia	1 ●●●●●●●●	● Amber
Antler velvet	Rheumatoid arthritis	1 ●●●●●●●●	● Green
Blackcurrant seed oil	Rheumatoid arthritis	1 ●●●●●●●●	● Green
Borage seed oil	Rheumatoid arthritis	3 ●●●●●●●●	● Green
Capsaicin	Fibromyalgia	2 ●●●●●●●●	● Green
	Osteoarthritis	5 ●●●●●●●●	● Green
Cat's claw	Rheumatoid arthritis	2 ●●●●●●●●	● Amber
Cetylated fatty acids (CFAs)	Osteoarthritis	2 ●●●●●●●●	● Green
Chondroitin	Osteoarthritis	2 ●●●●●●●●	● Green
Collagen	Osteoarthritis	2 ●●●●●●●●	● Green
	Rheumatoid arthritis	1 ●●●●●●●●	● Green
Devil's claw	Osteoarthritis	3 ●●●●●●●●	● Amber
Duhuo Jisheng Wan (DJW)	Osteoarthritis	2 ●●●●●●●●	● Amber
Evening primrose oil (EPO)	Rheumatoid arthritis	3 ●●●●●●●●	● Green
Feverfew	Rheumatoid arthritis	1 ●●●●●●●●	● Green
Fish liver oil	Osteoarthritis	1 ●●●●●●●●	● Green
Fish body oil	Rheumatoid arthritis	5 ●●●●●●●●	● Green
Flaxseed oil	Rheumatoid arthritis	1 ●●●●●●●●	● Amber
Ginger	Osteoarthritis	3 ●●●●●●●●	● Green
Glucosamine sulphate	Osteoarthritis	2 ●●●●●●●●	● Green
Glucosamine hydrochloride	Osteoarthritis	1 ●●●●●●●●	● Green
Green-lipped mussel	Osteoarthritis	3 ●●●●●●●●	● Green
	Rheumatoid arthritis	1 ●●●●●●●●	● Green
Homeopathy	Fibromyalgia	2 ●●●●●●●●	● Green
	Osteoarthritis	1 ●●●●●●●●	● Green
	Rheumatoid arthritis	1 ●●●●●●●●	● Green
Indian frankincense	Osteoarthritis	4 ●●●●●●●●	● Green
MSM	Osteoarthritis	2 ●●●●●●●●	● Green
Pine bark extracts	Osteoarthritis	3 ●●●●●●●●	● Green
Rosehip	Osteoarthritis	3 ●●●●●●●●	● Green
	Rheumatoid arthritis	2 ●●●●●●●●	● Green
SAME	Fibromyalgia	2 ●●●●●●●●	● Green
	Osteoarthritis	4 ●●●●●●●●	● Green
Selenium	Rheumatoid arthritis	1 ●●●●●●●●	● Green
Stinging nettle	Osteoarthritis	1 ●●●●●●●●	● Green
Turmeric	Osteoarthritis	2 ●●●●●●●●	● Green
Vitamins A, C and E	Osteoarthritis	2 ●●●●●●●●	● Green
	Rheumatoid arthritis	1 ●●●●●●●●	● Green
Vitamin B complex	Osteoarthritis	2 ●●●●●●●●	● Green
	Rheumatoid arthritis	1 ●●●●●●●●	● Green
Willow bark	Osteoarthritis	2 ●●●●●●●●	● Amber
	Rheumatoid arthritis	1 ●●●●●●●●	● Amber

Notes

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The authors thank Kate Boddy of the University of Exeter for providing support for the bibliographical literature search for this review. We would like also to thank Dr Vijitha de Silva of the University of Aberdeen for reviewing parts of the manuscript and individual studies included in this report. Ms Gillian Dowds undertook the search strategies for the revised report and drafted the parts of the report which required updating.



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Appendix

Below is a list of the members of the working group for the first edition of *Complementary and alternative medicines for the treatment of rheumatoid arthritis, osteoarthritis and fibromyalgia*. Revisions to the report for the second edition were undertaken by Professor Gary Macfarlane.

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