



Complementary and alternative medicines and arthritis

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Dr Zochling reviews the evidence for various CAMs in arthritis management.

When modern medicine is unable to offer complete pain relief, particularly for a chronic disease such as arthritis, patients often seek complementary and alternative medicine (CAM). Up to 50% of Australians use such products, although fewer than half of these people will admit it to their doctors.^{1,2} Whether this is due to a perception that such therapies are not 'medicines', or simply because patients do not want their doctors to think badly of them, is not clear. Either way, it is important that primary caregivers be aware of the range of products available and of what these might add to management.

One of the biggest problems with our knowledge of CAMs is that it is patchy. Evidence based medicine teaches us to look for well structured, randomised placebo-controlled prospective studies (level 2 evidence) and systematic reviews of such studies (level 1 evidence) to support clinical practice, but as yet there are few of these for CAMs. This article focuses on the level 1 and 2 evidence that is available.

Osteoarthritis

There are more than 1.2 million osteoarthritis sufferers in Australia.³ Forty per cent are taking CAMs for their arthritis,⁴ which translates into about half a million Australians.

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Ginger

Ginger (*Zingiber officinale*) has been shown to have a small effect on pain in patients with osteoarthritis. Small but significant pain reductions have been shown with standardised supplements compared with placebo in treating knee osteoarthritis over a six-week period; joint function and quality of life did not show significant changes, and only mild gastrointestinal side effects were reported.⁵ In a randomised controlled crossover study in patients with osteoarthritis of the hip or knee, ginger was ranked between ibuprofen and placebo for analgesic effect; however, the difference between the ginger and placebo arms did not reach statistical significance.⁶

Capsaicin

A meta-analysis of randomised controlled trials of topical capsaicin in osteoarthritis showed it to produce significant reductions in pain compared with placebo.⁷ It has not been compared with other available topical therapies such as methylsalicylates or NSAIDs.

Homeopathy

Homeopathy has been described as 'promising' for osteoarthritis,⁸ but methodological issues exist with the available studies and there are no large randomised controlled trials. This is largely due to the nonstandardised nature of the discipline – doses and ingredients vary greatly between practitioners and are tailored to the patient rather than to a standard formula. A review of four randomised controlled trials did not show a significant therapeutic benefit in osteoarthritis.⁹



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Devil's claw

Devil's claw (*Harpagophytum procumbens*) is a plant that is native to Africa. In a study of patients with osteoarthritis of the hip or knee, it was shown to impart similar improvements to diacerhein (a slow-acting interleukin 1 inhibitor used in osteoarthritis in Europe) in pain, measured using a visual analogue scale, along with significantly fewer people using rescue medications and fewer adverse events.¹⁰ Two French studies gave similar findings at different dosages of *Harpagophytum* for osteoarthritis, with significant decreases in pain severity in the treatment group.^{11,12} A benefit was shown in nonspecific lower back pain in another study.¹³ No comparisons of different dosages are published.

Glucosamine sulfate and chondroitin sulfate

Of all the available CAMs for osteoarthritis, glucosamine sulfate and chondroitin sulfate are closest to breaching the gap between 'alternative' and 'conventional' therapy. Each is effective in reducing pain in osteoarthritis: two large reviews show symptom improvement with glucosamine,^{14,15} and chondroitin has been shown to reduce pain by at least 50% (measured using a visual analogue scale) as shown in a meta-analysis of seven trials measuring similar outcomes.¹⁶ Glucosamine is commercially available in several different salts – the best evidence that is available is for the sulfate form.

Glucosamine forms part of the normal glycosaminoglycans found in cartilage and synovial fluid; glucosamine sulfate

is an aminomonosaccharide derivative synthesised from chitin. This introduces an interesting variant of 'you are what you eat' – just as some cultures believe eating the heart of a lion may infer strength and valour, can we really presume ingesting cartilage might build cartilage? However, evidence of symptom improvement with glucosamine is building to the point where practitioners are accepting it as a routine step in the long term management of osteoarthritis. Of greatest interest is a study by Reginster and colleagues suggesting not merely symptom improvement, but also cartilage structural modification with glucosamine sulfate.¹⁷ In a chronic, disabling and painful condition such as osteoarthritis, it is encouraging that it may be possible to alter the course of the disease and not simply control the symptoms – an achievement that no conventional medical intervention has

been able to replicate.

Chondroitin is a naturally occurring proteoglycan found in cartilage, and most commercial preparations are derived from bovine cartilage or algae. There is a suggestion that it may also play a role in disease modification, retarding the progression of osteoarthritis in the knee and hand. To date, these results have only been published in abstract form and it remains to be seen whether the quality of the studies stands up to critical analysis.

There is no good quality evidence that additional benefit is gained by combining glucosamine and chondroitin.

Avocado and soybean unsaponifiables

A Cochrane review has suggested that preparations of avocado and soybean unsaponifiable constituents decrease pain, improve joint function, reduce the need for NSAIDs, and improve overall well-

being.¹⁸ There has also been evidence of potential structure modification of the cartilage through action on aggrecan production;¹⁹ there are as yet no clinical studies to support this.

Willow bark extract

Willow bark extract (*Salix purpurea daphnoides*) masquerades as a herbal therapy but it contains salicin, which inhibits both COX-1 and COX-2 isoforms of the cyclooxygenase enzyme. A two-week study of willow bark in osteoarthritis of the knee showed good analgesic effect,²⁰ but there have been no good studies of side effects and it might be inferred that use brings increased risk of the gastrointestinal complications seen with other salicylates. This becomes important particularly with patients who might be taking antiplatelet agents or have pre-existing ulcer problems – careful evaluation is warranted.

Stinging nettle

A small crossover trial of a topical stinging nettle (*Urtica dioica*) showed improvement in pain from osteoarthritis of the base of thumb.²¹ This may be mediated by cytokine inhibition, but difficulties in convincing a patient to use nettles for pain relief may in itself preclude regular use.

Boswellia

Ayurvedic herbal preparations have been used in medicine in India for hundreds of years for many complaints. The best studied component is boswellia (*Boswellia serrata*), which is related to frankincense. Small trials show improvements in pain, flexibility, walking distance and swelling in osteoarthritis of the knee,²² but there has been no evidence of radiological improvement. Boswellia inhibits leukotriene biosynthesis, having its effect through the 5-lipo-oxygenase pathway.

Vitamin supplements

Antioxidant vitamins have been linked to improved outcomes. In 640 participants from the Framingham Osteoarthritis Cohort Study, higher doses of vitamin C were associated with a reduced rate of progression in patients who had established disease and with a lower risk of developing knee pain.²³ No effect of vitamin C was seen on the osteoarthritis incidence over the 10-year study period. This study also suggests a reduction in progression of osteoarthritis with beta carotene and vitamin E supplementation. No association was seen between osteoarthritis measures and nonoxidative vitamin supplements.

S-adenosylmethionine

A meta-analysis of good quality trials has failed to show conclusive evidence of pain relief for S-adenosylmethionine (SAME) in treating knee osteoarthritis.²⁴ However,

CAMs with 'best evidence' of benefit

Osteoarthritis*

Glucosamine sulfate
Chondroitin sulfate
Avocado and soybean unsaponifiables
Devil's claw
Topical capsaicin
S-adenosylmethionine (SAME)

Rheumatoid arthritis

Gamma linolenic acid

* Listed in order of decreasing strength of evidence.

level 2 evidence is still convincing for an effect similar to NSAIDs for analgesia.²⁴

Rheumatoid arthritis

There are fewer quality trials of CAMs in rheumatoid arthritis. Boswellia has been

described as 'promising', but so far studies have not been encouraging. Gamma linolenic acid, which is found in evening primrose oil, borage seed oil and black-currant seed oil, has been shown to suppress the release of inflammatory mediators and improve symptoms.¹⁸

Lower level evidence (from observational, noninterventional trials) suggests that patients with rheumatoid arthritis have lower serum levels of several antioxidant vitamins and minerals such as zinc, copper and boron. However, therapeutic trials are few and do not yet support the use of supplements.

Final comments

A recent survey of osteoarthritis sufferers in Sydney showed that over 40% took CAMs for their disease – most commonly, vitamin supplements and various fish oils.⁴ Very few were taking preparations with published evidence supporting use and recognised benefit, as listed in the box on page 65.

Patients have many misconceptions about herbal therapies and arthritis, which is reflected in the frequent use of aloe vera, ginkgo and ginseng for joint pain. The facts that herbal remedies are available at any health store, do not require a prescription and are perceived as 'natural' lull people into the misconception that they are also safe. This introduces the problem of potential toxicity – for example, problems reported with ginseng include 'ginseng abuse syndrome' (i.e. elevated blood pressure, nervousness, insomnia, skin eruptions, and diarrhoea), Stevens–Johnson syndrome, schizophrenia, and significant and potentially dangerous interactions with anticoagulants and monoamine oxidase inhibitors. Ginseng is a good example of a herbal remedy that has serious potential side effects – how many others have similar hazards? In an era when the use of CAMs is increasing, it is of utmost importance that adequate studies are undertaken to assess not just the efficacy but also the safety profile of these treatments.

Of course, no evidence does not necessarily mean negative evidence. Until the studies are done, practitioners must be aware of the compounds that are available and their potential benefits and complications, and be able to educate patients accordingly. Complementary medicines are an integral part of patient-directed management of rheumatic disease. **MT**

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