



Emerging botanicals for joint health

by Kristen McPhee

A ccording to the CDC, osteoarthritis (OA) is the most prevalent musculoskeletal condition in the U.S., affecting more than 30 million Americans. OA is characterized by the progressive deterioration of the articular cartilage and inflammation of the synovium, manifesting as joint pain and stiffness.

The knee is one of the joints most commonly affected by OA, making knee OA the subject of many studies. While there is no known cure, analgesic (e.g., acetaminophen) and anti-inflammatory (e.g., non-steroidal anti-inflammatory drugs [NSAIDs], cyclooxygenase [COX]-2 inhibitors) drugs may help manage symptoms; however, adverse effects such as stomach bleeding can occur with long-term use.¹ In more severe cases, steroid injections for the short-term—and knee replacement surgery for the longer-term—are sometimes among the courses of action.

In recent decades, nutrient and botanical ingredients have offered a safe and effective alternative to pharmaceutical drugs and surgery. Fish oil and connective tissue-derived ingredients such as glucosamine, chondroitin and collagen are well-established options for supporting OA and other musculoskeletal conditions. However, demand for plant-based ingredients has increased. Although turmeric (*Curcuma longa*) has been a popular and viable option in recent years, novel ingredients and innovative formulas are warranted to peak consumers' interest.

French maritime pine (*Pinus pinaster* subsp. *atlantica*) bark offers myriad benefits for OA based on several clinical studies. Three months of daily oral supplementation (as Pycnogenol from Horphag Research) showed a 72% decrease in the inflammatory marker C-reactive protein (CRP), a 30% decrease in reactive oxygen species (ROS, plasma free radicals), and a 40% decrease in joint pain in a double-blind, placebo-controlled study involving participants with knee OA.² In a similar study design, symptom relief was maintained for two weeks after the participants discontinued supplementation, suggesting French maritime pine bark may have lasting reparative effects.³

Polyphenols from Pycnogenol appeared in the joint synovial fluid of participants orally supplemented with 200 mg daily for three weeks but not in the control group, confirming activity in the target areas.⁴ And topical patches may offer an effective alternative to oral supplementation. In one study, 42% of participants reported complete resolution of OA symptoms after applying patches containing 110 mg Pycnogenol twice daily for three weeks.⁵





Haritaki (*Terminalia chebula*) fruit, used extensively in traditional ayurvedic, Unani and Iranian medicine, has demonstrated antioxidant and anti-inflammatory activities in clinical research. In one randomized, double-blind, placebo-controlled clinical trial, haritaki (as AyuFlex from Natreon) reduced knee discomfort and improved knee function during exercise in healthy overweight participants after 12 weeks.⁶ No significant differences occurred between the 250 and 500 mg twice daily doses, validating efficacy with the lower dose. AyuFlex also showed anti-osteoarthritic effects in a rat model by reducing levels of oxidative stress, pro-inflammatory mediators and pro-inflammatory cytokines.⁷ Additionally, haritaki inhibited the progression of OA by decreasing matrix metalloproteinase expression and suppressing synovial membrane and cartilage destruction.



Cucumber (*Cucumis sativus*), a familiar food and topical remedy for various skin problems, has gained traction recently as a dietary supplement ingredient. In a randomized, double-blind, parallel-group clinical trial, cucumber (as Q-actin from IminoTech) extract was significantly more effective at reducing pain and improving mobility than a glucosamine-chondroitin supplement in 122 participants with moderate knee OA.⁸ Oral supplementation included only 10 mg cucumber versus 1,350 mg glucosamine-chondroitin twice daily for six months. Preclinical evidence suggested the iminosugar amino acid, idoBR1, may be partially responsible for cucumber's anti-inflammatory effects by inhibiting sialidase or interacting with CD44-HA signaling.⁹



While most studies are based on a single ingredient, researchers examined the effects of ginger (*Zingiber officinale*) combined with toothache plant (*Acmella oleracea*) in a 2020 experimental pilot study involving 50 participants with knee OA.¹⁰ Two tablets, each containing 37.5 mg ginger and 7.5 mg toothache plant (as Mitidol from Indena S.p.A.), administered daily for one month significantly reduced pain and inflammatory indices, CRP and erythrocyte sedimentation rate. According to in vitro findings, the mechanisms may involve the endocannabinoid system.¹¹ Both botanicals inhibited fatty acid amide hydrolase enzymes while only toothache plant targeted cannabinoid 2 receptors.

Boswellia (*Boswellia serrata*) gum resin is perhaps one of the most well-known of the highlighted botanicals for its usefulness in musculoskeletal disorders. A 2020 systematic review and meta-analysis of seven randomized controlled clinical trials concluded 100-250 mg of boswellia may improve OA-related pain, stiffness and joint function after four weeks.¹ An earlier non-systematic review of a lecithin-based boswellia (as Casperome from Indena S.p.A.) extract highlighted promising evidence for musculoskeletal conditions, including tendonitis, sprains and sports-related injuries.¹² Both reviews included studies that used boswellia alone and in combination with other anti-inflammatory or analgesic ingredients. The mechanisms of action may involve reducing inflammatory markers (e.g., tumor necrosis factor

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[TNF]-alpha, CRP and interleukin [IL]-6) and inhibiting matrix metalloproteinase enzymes, according to one unpublished randomized, double-blind, placebo-controlled clinical trial involving knee OA participants.

One ingredient characteristic that could offer a point of differentiation is a faster time to efficacy. Compared to placebo, a synergistic combination of two proprietary boswellia extracts (as AprèsFlex—formerly Aflapin—from PLT Health Solutions) provided significant improvements in pain score and functional ability in as early as five days of use by study participants with knee OA.¹³ And an unpublished 2014 clinical trial of the same ingredient in knee OA showed a nearly 20% reduction in pain scores over baseline at five days and a 50% reduction in pain scores at 30 days.

Research-based novel botanical ingredients are emerging in the dietary supplement market space to support joint health. Proven beneficial for exercise- and musculoskeletal-related conditions, these ingredients serve as less commonly seen plant-based options to pharmaceutical drugs, well-established turmeric and animal-based dietary supplements. ✨



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