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File: ■ Zingiberaceae Extracts
■ Pain
■ Systematic Review/Meta-analysis

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RE: Meta-analysis Indicates Zingiberaceae Extracts Are Clinically Effective for Relieving Persistent Pain Arising from a Variety of Causes

Lakhan SE, Ford CT, Tepper D. Zingiberaceae extracts for pain: a systematic review and meta-analysis. *Nutr J*. May 14, 2015;14:50. doi: 10.1186/s12937-015-0038-8.

Many plants in the Zingiberaceae family are used in traditional medicine. For example, turmeric (*Curcuma longa*, Zingiberaceae) root has been used for gastrointestinal complaints, and its bioactive component curcumin has been shown to be an anti-inflammatory.[1] Ginger (*Zingiber officinale*, Zingiberaceae) root, used traditionally and currently for multiple digestive complaints,[1] also contains anti-inflammatory compounds. Javanese ginger (*C. zanthorrhiza*) and galangal (*Alpinia galanga*, Zingiberaceae) also contain anti-inflammatory compounds. This systematic review and meta-analysis investigates these members of the Zingiberaceae family for use in chronic pain.

The PubMed, Science Direct, and Cochrane Library databases were searched using the following terms: turmeric, curcumin, ginger, galangal, Zingiberaceae, *Curcuma*, *Zingiber*, *Kaempferia*, *Alpinia*, curcuminoid, turmerone, gingerol, shogaol, zingiberene, zingiberol, zingerone, curcumene, galangin, and zanthorrhizol, along with pain or visual analogue score (VAS). Included studies in the systematic review were published before December 2014, were randomized, had a chronic pain group as defined by pain more than 24 hours, used extracts of Zingiberaceae plants only in combination with agents for bioavailability, had a treatment duration of longer than 24 hours, and had pain assessment as one measured outcome. Studies in the systematic review that were not placebo-controlled, double-blinded, or did not measure pain with a VAS were not included in the meta-analysis. The meta-analysis used pain as measured with a VAS as the primary outcome across studies, and in studies with multiple treatments, the treatment groups with the highest dosages and/or "least processed" plant material were assessed. Also, the longest time point was assessed in studies with varied time points, with one exception when pain diminished over time in the placebo group.

In summary, from 43 studies located, 18 randomized studies in total were reviewed, with only eight used for the meta-analysis (they were double-blinded, placebo-controlled, and included VAS as pain assessment). For studies involving osteoarthritis and knee arthritis, ginger extract was utilized at dosages of 340, 510, and 1,000 mg/day; ginger and galangal extracts were used in combination at 510 mg/day; curcumin was tested at 1,000 mg/day; a mixture of curcuminoids was used at 1,500 mg/day; and turmeric extract was incorporated at 1,000 and 1,500 mg/day. In two studies, ginger extract was found to significantly reduce pain in

comparison with placebo; was shown to have similar efficacy as the drug diclofenac (a nonsteroidal anti-inflammatory drug [NSAID] for pain) with less adverse side effects; was significantly more effective in combination with diclofenac as compared with either ginger extract or diclofenac with placebo; and ginger and galangal extracts together "moderately" reduced pain. Turmeric was observed to significantly reduce pain in those suffering from knee osteoarthritis as compared to a placebo group, and turmeric was shown to be equally efficacious in pain treatment when compared with ibuprofen. Also in the studies of patients with knee osteoarthritis, the mixture of curcuminoids decreased pain significantly as compared with placebo, and curcumin together with diclofenac was found to be no different for pain as compared to diclofenac alone.

When tested for efficacy in patients with dysmenorrhea, ginger extract (1,000 mg/day) was found to decrease pain comparable with mefenamic acid (another NSAID for pain) and ibuprofen. In another trial, ginger extract (1,500 mg/day) significantly decreased pain severity and duration as compared with placebo. Exercising subjects given ginger extracts (raw or heat-treated at 2,000 mg/day) experienced decreased muscle soreness as compared with placebo. In thigh muscles of exercised subjects, curcumin (400 mg/day) significantly reduced exercise-related pain. Curcumin (2,000 mg/day) also significantly reduced pain following cholecystectomy (gallbladder removal surgery) after one and three weeks, as compared with placebo. Turmeric extract (72 and 144 mg/day) was found at both doses to significantly decrease pain in those with irritable bowel syndrome (IBS), but Javanese ginger extract (60 mg/day) was not different than placebo for pain alleviation. Lastly, curcumin (6,000 mg/day) failed to significantly reduce pain due to radiation in patients with breast cancer as compared with placebo.

The meta-analysis was conducted on five studies of ginger extracts, two of curcuminoids, and one of Javanese ginger extract. Studies included four in those with arthritis, and one each for patients with IBS, dysmenorrhea, recent surgery, and exercise-related soreness; all patients and subjects were over 18 years old. From the analysis, pain in those receiving the Zingiberaceae treatments was significantly less than in the control group (P=0.004); however, study heterogeneity was considered "very high." A scatter plot diagram suggested a linear dose-effect relationship for pain.

Overall, the botanical extracts included in this review and meta-analysis show beneficial effects for chronic pain. However, the typical definition of "chronic pain" was reduced in this review from ≥ three months to ≥ 24 hours. The authors surmise that study heterogeneity may be explained by differences in doses and types of preparations used. Also, no information is given here about what plant parts are used, origin, or how the extracts were produced. It is cautioned that, in previous preclinical literature, these preparations have been found to cause adverse side effects such as liver toxicity, problems with blood clotting, and nausea. Discussed limitations include the small sample size of studies and a heavy bias for more female patients than male. Although likely efficacious for persistent pain, attention to dosage may be important for ensuring avoidance of adverse side effects.

—Amy C. Keller, PhD

Reference

[1]Blumenthal M, Goldberg A, Brinckmann J, eds. *Herbal Medicine: Expanded Commission E Monographs*. Austin, TX: American Botanical Council; Newton, MA: Integrative Medicine Communications; 2000.

Referenced article can be accessed at http://www.nutritionj.com/content/14/1/50.