

# Nutraceuticals to Treat Joint Pain as An Alternative to Non-Steroidal Anti-Inflammatory Drugs

Adrian Isaza PhD, DC, DABCI, DACBN, CCAP\*

Everglades University, Department of Public Health, US.

## \*Correspondence:

Dr. Adrian Isaza, 8357 38 street circle east, apt 204, Sarasota, FL 34243, United States.

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Anti-Inflammatory drugs, Arthritis, Rheumatism, Cardiovascular diseases.

What is an alternative to non-steroidal anti-inflammatory drugs for the treatment of joint pain? The Arthritis, Rheumatism, and Aging Medical Information System estimates that adverse effects due to NSAIDs are associated with more than 100,000 hospitalizations and more than 16,000 deaths in the U.S. each year. Both nonselective and selective COX-2 inhibitors have now been shown to be associated with an increased risk for cardiovascular events. These studies, together with the outcomes of the recent US Food and Drug Administration decision to require 'black box' warnings regarding potential cardiovascular risks associated with NSAIDs, suggest that the use of COX-2 inhibitors as the sole strategy for gastroprotection in patients with arthritis and other pain syndromes must be reconsidered, particularly among those at risk for cardiovascular events [1].

A few studies have evaluated the risk of cardiovascular complications following the intake of NSAID's. In 2011, Trelle, et al, conducted a meta-analysis of 31 trials and 116429 patients and found that compared to placebo rofecoxib was associated with the highest risk of myocardial infarction, followed by lumiracoxib. Ibuprofen was associated with the highest risk of stroke followed by diclofenac. Etoricoxib and diclofenac were associated with the highest risk of cardiovascular death [2]. These findings were confirmed by a systematic review conducted by Mcgettigan, et al in 2011 [3]. Finally, in 2013, Bhala, et al, conducted a meta-analysis of 280 trials of NSAIDs versus placebo (124,513 participants, 68,342 person-years) and 474 trials of one NSAID versus another NSAID (229,296 participants, 165,456 person-years). This study found that major vascular events were increased by about a third by a COX-2 inhibitor or diclofenac, mainly due to an increase in

major coronary events.

Ibuprofen also significantly increased major coronary events, but not major vascular events. Compared with placebo, of 1000 patients allocated to a COX-2 inhibitor or diclofenac for a year, three more had major vascular events, one of which was fatal. Naproxen did not significantly increase major vascular events. Vascular death was increased significantly by COX-2 inhibitors and diclofenac, non-significantly by ibuprofen, but not by naproxen. Heart failure risk was roughly doubled by all NSAIDs. All NSAID regimens increased upper gastrointestinal complications (COX-2 inhibitors, diclofenac, ibuprofen, and naproxen [4].

These studies lead to a recent official publication of the College of Family Physicians of Canada, Cyclooxygenase-2 (COX-2) inhibitors and traditional NSAIDs except naproxen increase the risk of serious cardiovascular events and death. When prescribing NSAIDs, patients' gastrointestinal (GI) and CV risks should be assessed, with naproxen or low-dose ibuprofen preferentially chosen for patients at risk of CV disease [5].

## Dietary Supplements for Knee, Hip and Spine Osteoarthritis Ginger

In 2015, Bartels, et al, carried out a meta-analysis of five randomized controlled trials involving over 500 patients comparing oral ginger treatment with placebo in adult osteoarthritis patients. This study concluded ginger was modestly efficacious and reasonably safe for treatment of knee and hip osteoarthritis [6].

## Effect on inflammation

In 2016, Mazidi, et al, performed a systematic review and meta-analysis of 9 studies which suggests that ginger supplementation significantly reduces serum C-reactive protein (CRP) [7].

### **Ginger vs NSAIDS**

In 2001, Altman, et al, conducted a randomized, double-blind, placebo-controlled, multicenter, parallel-group of 247 patients with osteoarthritis of the knee and moderate-to-severe pain. In this study ginger extract had a statistically significant effect on reducing symptoms of osteoarthritis of the knee. Moreover, the reduction in intake of acetaminophen was greater in the ginger extract group [8].

In 2012, Drozdov, et al, designed a randomized controlled trial of 43 patients with knee or hip osteoarthritis who were given ginger or diclofenac. This study showed that ginger is as effective as diclofenac but safer in treating osteoarthritis. Moreover, ginger has an increased mucosa-protective potential [9].

In 2013, Paramdeep performed a randomized placebo-controlled open label study of 60 patients of osteoarthritis of the knee who were divided into a diclofenac, ginger and placebo group. The percentage improvement in pain score from baseline in the diclofenac group was 60.31% and 59.11% in the ginger group [10].

### **Curcumin/Turmeric**

In 2016, Daily, et al, published a systematic review and meta-analysis of randomized controlled trials which provided scientific evidence that supports the efficacy of turmeric extract in the treatment of knee and hip osteoarthritis [11].

### **Effect on inflammation**

In 2014, Sahebkar published a meta-analysis of six clinical trials involving over 300 subjects. This study showed that compared with placebo, supplementation with curcumin was associated with a significant reduction in circulating CRP levels [12].

In 2019, Tabrizi, et al, performed a systematic review and meta-analysis of 15 randomized controlled trials. This study suggests that taking curcumin-containing supplements may exert anti-inflammatory by reducing interleukin6 (IL-6), high sensitivity c-reactive protein (hs-CRP), and malondialdehyde (MDA) levels [13].

### **Curcumin vs NSAIDS**

In 2009, Kuptniratsaikul, et al, designed a single-blind randomized controlled trial to evaluate the efficacy of 2,000 mg/day of Curcuma domestica extracts compared with 800 mg/day of ibuprofen in 107 knee osteoarthritis patients for 6 weeks. This study found that curcumin domestica extracts seem to be similarly efficacious as ibuprofen. Moreover, the adverse events for curcumin were 33.3% compared to 44.2% for ibuprofen [14].

In 2012, Kertia, et al, conducted a prospective randomized open-end blinded study of 80 patients with knee osteoarthritis. This study demonstrated that Curcuma domestica extract was not significantly different compared to diclofenac sodium in suppressing the secretion of cyclooxygenase-2 enzyme [15].

In 2014, Kuptniratsaiku, et al, carried out a follow up with better

methodology than the first study. This study was a double-blind randomized controlled trial of 367 knee osteoarthritis patients which indicated that curcuma domestica extracts are as effective as ibuprofen for the treatment of knee osteoarthritis. Moreover, the number of events of abdominal pain and discomfort was significantly higher in the ibuprofen group than that in the C. domestica extracts group [16].

In 2018, Bannuru, et al., performed a systematic review and meta-analysis of eleven randomized controlled trials involving over 1,000 patients. This study suggested that curcuminoids have no statistically significant differences in efficacy outcomes compared to NSAIDs [17].

### **Harpagophytum Procumbens “Devil’s Claw**

In 2004, Gagnier, et al, carried out a systematic review of 12 trials which revealed that there is moderate evidence of effectiveness for the use of a Harpagophytum powder at 60 mg in the treatment of osteoarthritis of the spine, hip and knee. Moreover, the study provided strong evidence for the use of an aqueous Harpagophytum extract at a daily dose of 50 mg in the treatment of acute exacerbations of chronic non-specific low back pain [18].

### **Effect on inflammation**

In 2010, Inaba, et al, tested rats with Harpagophytum ethanol extract which suppressed inflammatory cytokines [interleukin-1beta (IL-1beta), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-alpha)] in mouse macrophages cells [19].

### **Devil’s claw vs NSAIDS**

The study by Gagnier, et al, also found that the use of an aqueous extract of Harpagophytum procumbens at 60 mg had similar efficacy to 12.5 mg of rofecoxib per day for chronic non-specific low-back pain in the short term.

In the year 2000, Chantre, et al, conducted a double-blind, randomized, multicenter clinical study of 122 patients in which 435 mg of powdered Harpagophytum procumbens was compared with diacerhein 100 mg/day (anthraquinone).

This study showed that there was no difference in the efficacy of the two treatments and patients taking Harpagophytum were using significantly less NSAIDs. Furthermore, the most frequent adverse event reported was diarrhea, occurring in 8.1% of harpagophytum patients and 26.7% in diacerhein patients [20].

Although osteoarthritis is a wear and tear condition systemic inflammation may play a role. In 2015, Jin, et al, carried out a systematic review and meta-analysis of 32 studies and found that serum high sensitivity-CRP levels in OA were statistically significantly higher than controls. Moreover, CRP levels were significantly associated with pain and decreased function [21].

Based on the aforementioned evidence, it seems plausible that supplementation with ginger, curcumin and devil’s claw can exert an anti-inflammatory effect and help relieve the pain associated

with osteoarthritis.

## Dietary Supplements for Rheumatoid Arthritis

### OMEGA 3

In 2007, Goldberg, et al, published a meta-analysis of 17 randomized controlled trials measuring the pain-relieving effects of omega 3 in patients with rheumatoid arthritis or joint pain secondary to inflammatory bowel disease and dysmenorrhea. In this study supplementation with omega-3 for 3-4 months reduces patient reported joint pain intensity minutes of morning stiffness number of painful and/or tender and NSAID consumption [22].

### Effect on inflammation

In 2018, Gioxari, et al, performed a systematic review and meta-analysis 20 randomized controlled trials involving over 1200 patients. This study found a significant reduction of leukotriene B4 following omega 3 supplementation [23].

### Omega 3 vs NSAIDS

In 2006, Maroon, et al, designed a study of 250 patients who had been seen by a neurosurgeon and were found to have nonsurgical neck or back disc pain. This study demonstrated equivalent effect in reducing arthritic pain between omega 3 and ibuprofen. Finally, omega-3 fish oil supplements appear to be a safer alternative to NSAIDs for treatment of nonsurgical neck or back pain in this study [24]. In 2012, Lee, et al, conducted a meta-analysis of 10 randomized controlled trials totaling over 300 patients. This study suggests that the use of omega-3 PUFAs at dosages >2.7 g/day for >3 months reduces NSAID consumption by RA patients [25].

Given the above, omega 3 may help relieve the pain associated with rheumatoid arthritis as an alternative to NSAIDS.

### About the author

Adrian Isaza is both a physician and an academic. As an academic he authored a chapter of the book "The Role of Functional Food Security in Global Health". He also teaches graduate students at Everglades University for the Alternative Medicine Degree program.

Adrian holds a diplomate in diagnosis awarded by the American Board of Chiropractic Internists and a diplomate in nutrition awarded by the American Clinical Board of Nutrition. Moreover, he is a Certified Chiropractic Acupuncture Practitioner and has a masters degree in medical science.

He recently obtained his PhD in medical sciences and practices medicine full time in Tampa, Florida. Dr. Isaza has published over 30 papers advocating the use of alternative medicine.

### References

1. Abramson SB, Weaver AL. Current state of therapy for pain and inflammation. *Arthritis Res Ther.* 2005; 7: S1-S6.
2. Trelle S, Reichenbach S, Wandel S, et al. Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis. *BMJ.* 2011; 342: c7086.
3. Mcgettigan P, Henry D. Cardiovascular risk with non-steroidal anti-inflammatory drugs: systematic review of population-based controlled observational studies. *PLoS Med.* 2011; 8: e1001098.
4. Bhala N, Emberson J, Merhi A, et al. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. *Lancet.* 2013; 382: 769-779.
5. Machado GC, Maher CG, Ferreira PH, et al. Non-steroidal anti-inflammatory drugs for spinal pain: a systematic review and meta-analysis. *Ann Rheum Dis.* 2017; 76: 1269-1278.
6. Bartels EM, Folmer VN, Bliddal H, et al. Efficacy and safety of ginger in osteoarthritis patients: a meta-analysis of randomized placebo-controlled trials. *Osteoarthr Cartil.* 2015; 23: 13-21.
7. Mazidi M, Gao HK, Rezaie P, et al. The effect of ginger supplementation on serum C-reactive protein, lipid profile and glycaemia: a systematic review and meta-analysis. *Food Nutr Res.* 2016; 60: 32613.
8. Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. *Arthritis Rheum.* 2001; 44: 2531-2538.
9. Drozdov VN, Kim VA, Tkachenko EV, et al. Influence of a specific ginger combination on gastropathy conditions in patients with osteoarthritis of the knee or hip. *J Altern Complement Med.* 2012; 18: 583-588.
10. Paramdeep G. Efficacy and tolerability of ginger (*Zingiber officinale*) in patients of osteoarthritis of knee. *Indian J Physiol Pharmacol.* 2013; 57: 177-183.
11. Daily JW, Yang M, Park S. Efficacy of Turmeric Extracts and Curcumin for Alleviating the Symptoms of Joint Arthritis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *J Med Food.* 2016; 19: 717-729.
12. Sahebkar A. Are curcuminoids effective C-reactive protein-lowering agents in clinical practice? Evidence from a meta-analysis. *Phytother Res.* 2014; 28: 633-642.
13. Tabrizi R, Vakili S, Akbari M, et al. The effects of curcumin-containing supplements on biomarkers of inflammation and oxidative stress: A systematic review and meta-analysis of randomized controlled trials. *Phytother Res.* 2019; 33: 253-262.
14. Kuptniratsaikul V, Thanakhumtorn S, Chinswangwatanakul P, et al. Efficacy and safety of *Curcuma domestica* extracts in patients with knee osteoarthritis. *J Altern Complement Med.* 2009; 15: 891-897.
15. Kertia N, Asdie AH, Rochmah W, et al. Ability of curcuminoid compared to diclofenac sodium in reducing the secretion of cyclooxygenase-2 enzyme by synovial fluid's monocytes of patients with osteoarthritis. *Acta Med Indones.* 2012; 44: 105-113.
16. Kuptniratsaikul V, Dajpratham P, Taechaarpornkul W, et al. Efficacy and safety of *Curcuma domestica* extracts compared with ibuprofen in patients with knee osteoarthritis: a multicenter study. *Clin Interv Aging.* 2014; 9: 451-458.
17. Bannuru RR, Osani MC, Al-eid F, et al. Efficacy of curcumin and *Boswellia* for knee osteoarthritis: Systematic review and

- 
- meta-analysis. *Semin Arthritis Rheum*. 2018; 48: 416-429.
18. Gagnier JJ, Chrubasik S, Manheimer E. Harpagophytum procumbens for osteoarthritis and low back pain: a systematic review. *BMC Complement Altern Med*. 2004; 4: 13.
  19. Inaba K, Murata K, Naruto S, et al. Inhibitory effects of devil's claw (secondary root of Harpagophytum procumbens) extract and harpagoside on cytokine production in mouse macrophages. *J Nat Med*. 2010; 64: 219-222.
  20. Chantre P, Cappelaere A, Leblan D, et al. Efficacy and tolerance of Harpagophytum procumbens versus diacerhein in treatment of osteoarthritis. *Phytomedicine*. 2000; 7: 177-183.
  21. Jin X, Beguerie JR, Zhang W, et al. Circulating C reactive protein in osteoarthritis: A systematic review and meta-analysis. *Ann Rheum Dis*. 2015; 74: 703-710.
  22. Goldberg RJ, Katz J. A meta-analysis of the analgesic effects of omega-3 polyunsaturated fatty acid supplementation for inflammatory joint pain. *Pain*. 2007; 129: 210-223.
  23. Gioxari A, Kaliora AC, Marantidou F, et al. Intake of  $\omega$ -3 polyunsaturated fatty acids in patients with rheumatoid arthritis: A systematic review and meta-analysis. *Nutrition*. 2018; 45: 114-124.
  24. Maroon JC, Bost JW. Omega-3 fatty acids (fish oil) as an anti-inflammatory: an alternative to nonsteroidal anti-inflammatory drugs for discogenic pain. *Surg Neurol*. 2006; 65: 326-331.
  25. Lee YH, Bae SC, Song GG. Omega-3 polyunsaturated fatty acids and the treatment of rheumatoid arthritis: A meta-analysis. *Archives of Medical Research* 2012; 43: 356-362.