

NUHS Journal Club

Topic: Devil's Claw for OA

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Group Members:

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Patient: A 62 yo white F pt. has a hx of bilateral (R>>L) hip osteoarthritis. PMH includes four children but otherwise unremarkable. She was on rofecoxib (Vioxx) for pain management until discontinued by primary care physician (PCP). Her PCP wants to continue treatment with celecoxib (Celebrex), but she is concerned about possible cardiovascular side effects. She does not tolerate NSAIDs well (GI) and as not found any OTCs that alleviate her pain to any great extent. “Is there something ‘natural’ I can take that might help?”

<u>P</u> atient, Population, Disease	62 yo white female with hip OA
<u>I</u> ntervention	Harpagophytum procumbens (Devil’s Claw)
<u>C</u> omparison (optional)	COX-2 inhibitors, NSAIDs, mild analgesics
<u>O</u> utcome	Clinical improvement (analgesic effects)

Question: Is there a botanical alternative as effective as COX-2 inhibitors, NSAIDs, or other analgesics in providing symptomatic relief for hip osteoarthritis?

OR

Is there a botanical medicine that is effective in improving clinical outcomes in adults with osteoarthritis?

Search Strategy - Group

- Search Program(s):
 - PubMed
- Databases searched:
 - Medline
- Key Search Terms:
 - Hip, osteoarthritis – search returned 2716 articles
- Operators used:
 - Hip AND osteoarthritis
- Limits Used:
 - Reviews – search returned 271 review articles
- Additional Strategies used:
 - With PubMed, checked “related articles”
- Where the paper was located:
 - Medline by searching both PubMed
- Full text access:
 - BMC Complementary and Alternative Medicine (BioMed Central - open access to all articles,

Search Strategy – Review Article

Appendix 1 Highly sensitive search strategy for randomized controlled trial searches using PUBMED

(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR (clinical trial [tw]) OR ((singl* [tw] ORdoubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR (latin square [tw]) OR placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR cross-over studies [mh] OR control* [tw] OR prospectiv* [tw] or volunteer* [tw]) NOT (animal [mh] NOT human [mh])

Search Strategy – Review Article

Appendix 2 PUBMED search strategy

(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR (clinical trial [tw]) OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR (latin square [tw]) OR placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR cross-over studies [mh] OR control* [tw] OR prospectiv* [tw] or volunteer* [tw]) NOT (animal [mh] NOT human [mh]) AND ("harpagophytum procumbens" OR (devil's AND claw)) AND (pain OR "musculoskeletal pain" OR "muscle pain" OR "skeletal pain" OR "bone pain" OR "joint pain" OR "extremity pain" OR myalgia OR osteoarthritis OR "rheumatoid arthritis" OR arthrosis OR "low back pain" OR lumbago OR "back pain") NOT review

Primary Paper

Harpagophytum procumbens for
osteoarthritis and low back pain: a
systematic review.

Gagnier JJ, Chrubasik S, Manheimer E

BMC Complement Altern Med. 2004 Sep 15;4:13.

Type of study: Review

Study Design: Varies, see inclusion criteria

Introduction

- Natives in the steppes of South and Southwest Africa use the secondary root tubers of *Harpagophytum procumbens* for the treatment of various diseases, including musculoskeletal complaints.
- For more than half a century, various preparations have been continuously used in Europe and have become an established traditional treatment for rheumatic complaints.
- The monograph of the European Scientific Cooperative on Phytotherapy (ESCOP) recommends it for painful osteoarthritis and relief of low back pain in a dosage equivalent of up to nine grams of crude plant material and over a treatment period of at least two to three months.
- It has been suggested that the plant material should contain not less than 1.2% of the constituent harpagoside, an iridoid glycoside.

Introduction

- Pharmacological studies indicate that in various animal models, the extract is more effective than its marker compound harpagoside. However, a number of contradictory findings make it difficult to draw definitive conclusions on the analgesic and anti-inflammatory effects.
- Recent in-vitro studies indicate that preparations may interact with the inflammatory cascade, including the cytokines.
- A significant decrease in stimulated production of matrix-degrading enzymes has recently been shown in isolated chondrocytes and a dose-dependent weak elastase inhibition.

The objective of the review was to determine the effectiveness of *Harpagophytum* preparations in the treatment of musculoskeletal pain.

Inclusion criteria for considering studies for this review

Types of studies: Randomized controlled trials (RCTs), quasi-randomized controlled trials, and controlled clinical trials (CCTs) with no language restriction.

Types of participants: Adults suffering from pain in the musculoskeletal system due to osteoarthritis or low back pain.

Types of interventions: Studies utilizing preparations of *Harpagophytum procumbens* were included. Preparations may differ in the solvent (water, alcohol) used to prepare the extract (if not crude powdered plant material is used), the drug extract ratio, and the galenic application form. They also differ in the content of the active principles (the sum of active ingredients) and in the quantity of the co-active marker compound harpagoside.

Types of outcome measures:

Primary outcome: pain (e.g. visual analogue scale, visual rating scale, pain component of the disease-specific Arhus Low Back Pain Index, component pain of the Western Ontario MacMaster (WOMAC) instrument).

Secondary outcomes: number of pain-free patients (defined as being pain-free on at least five days in the last treatment week without taking any rescue medication see above), functional indices (e.g. Lequesne index, finger-ground distance), and generic outcome measures [global assessments, health assessment questionnaire (HAQ)] or the consumption of additional analgesic treatment.

Methodological quality of controlled trials of *Harpagophytum procumbens* - 12 studies included in the review

Were eligibility criteria specified?

Was randomization appropriate?

Was treatment allocation concealed?

Were groups similar at baseline regarding important prognostic indicators?

Were outcome measure(s) and the control interventions explicitly described?

Were co-interventions avoided or comparable?

Were the outcome measures relevant?

Were adverse events described?

Were drop-outs described?

Was the sample size based on *a priori* power calculation?

Did the study include intention-to-treat analysis? AND/OR

Were point estimates and measures of variability presented for the POM?

Was the timing of outcomes appropriate?

Results

Study	Sample Size	Condition; mean age (range)	Harpagophytum Intervention / control	Outcome measures and effects	Adverse effects	Reviewer's Overall Conclusions
Schrüffler 1980 (Germany)	50	Osteoarthritis; 51 years	2500 mg/ day, (harpagoside less than 30 mg per day) / Phenylbutazone for 4 weeks	mean pain improvements: H 80%, Phenylbutazone 72%; physical impairment: H n = 1, Phenylbutazone n = 5; morning stiffness: H n = 2, Phenylbutazone n = 5	0 H vs 4 Phenylbutazone	H better than Phenylbutazone
Lecomte and Costa 1992 (France)	89	Osteoarthritis; (55-75) years	2000 mg/day (Harpagoside content estimated indirectly as 60 mg per day) / placebo for 60 days	mean pain improvement: H 38%, P 25% p < .05; finger-ground distance modified Schober test (cm) mean improvement: H 16%, P 6% p < .05	none for either group	H better than placebo
Biller 2002 (Germany)	78	Osteoarthritis; not stated	4500 mg/day, (harpagoside content estimated at < 30 mg per day) / placebo for 20 weeks	responders: H 90%, P 80% p-value not stated; mean consumption of ibuprofen: H .1, P .5 tablets	not stated	H better than placebo
Chantre et al. 2000 (France)	122	Osteoarthritis; 62 years	4500 mg / day, (57 mg harpagoside per day) / Diacerhein for 16 weeks	difference after 16 weeks between groups as measured by Lequesne functional index: less than 10 mm NS (intention-to-treat analysis with not all possible confounders considered)	10 H vs 21 Diacerhein	H not worse than diacerhein
Frerick et al. 2001 (Germany)	46	Osteoarthritis; 59 years	4500 mg/day, (< 30 mg harpagoside per day) / placebo for 20 weeks	responders: H 71%, P 41% p=.041; WOMAC component pain NS (type of statistical analysis not stated)	8 H vs 7 P	H better than placebo
Chrubasik et al. 1996b (Germany)	118	Back pain; 54 years	4500 mg/day, (50 mg harpagoside per day) / placebo for 4 weeks	mean tramadol consumption: H 99 ± 157 mg, P 102 ± 250 mg p =.44; number of pain-free patients at 4th week: H 9 P 1 p=.008; percentage change Arhus component pain: H 34%, P 6% p=.016 (per protocol analysis)	4 H vs 10 P	not on primary outcome measure

Results

Study	Sample Size	Condition; mean age (range)	Harpagophytum Intervention / control	Outcome measures and effects	Adverse effects	Reviewer's Overall Conclusions
Chrubasik et al. 1997 (Germany)	102	Back pain; 49 years	4500 mg/day, (30 mg harpagoside per day) / conventionally treating physicians administering oral NSAIDs, physical exercises, or paravertebral injections for 6 weeks	number of pain-free patients 4th week: H 16, C 12 NS; number of pain free patients 6th week: H 20, C 23 NS; percentage change Arhus component pain after four weeks: H 23%, C 22% p=.95; after 6 weeks H 33%, C 38% p=.38	5 H vs 0 C	H not worse than C
Chrubasik et al. 1999 (Germany)	197	Back pain; 56 years	4500 and 9000 mg/day, (50 and 100 mg harpagoside per day) / placebo for 4 weeks	number of pain-free patients: H-100 18%, H-50 9%, P 5% p=.027; percentage change Arhus component pain: H-100 vs H-50 vs P NS (intention-to-treat analysis)	10 P, 18 H-50, 17 H-100	H better than placebo
Chrubasik et al. 2003a (Germany)	88	Back pain; 62 years	4500 mg/day, (60 mg harpagoside per day) / Rofecoxib for 6 weeks	number of pain-free patients: H 22%, Rofecoxib 11% NS; percentage change Arhus component pain: H 30%, Rofecoxib 29% (intention-to-treat analysis)	14 H, 14 Rofecoxib	H not worse than Rofecoxib
Schmelz and Hämmerle 1999 (Germany)	100	Mixed pain; not stated	4500 mg/day, (30 mg harpagoside per day) / placebo for 30 days	free of low back pain: H n = 4, P n = 2; free of other pain: H n = 5, P n = 0 (confounders not considered)	not stated	H better than placebo
Guyader 1984 (France)	50	Mixed pain; 64 years	Harpagoside content estimated indirectly as <20 mg harpagoside per day / placebo for 1-3 'cycles' of 21 days each	mean pain improvements: H 72%, P 65% (confounders not considered)	6 H vs 3 P	H better than placebo
Goebel et al. 2001 (Germany)	65	Mixed pain; 28 years	4500 mg/day, (< 30 mg harpagoside per day) / placebo for 28 days		4 H vs 2 P	H better than placebo

Conclusions

- There is limited evidence for an ethanolic *Harpagophytum* extract containing less than <30 mg harpagoside per day in the treatment of knee and hip osteoarthritis.
- There is moderate evidence of effectiveness for
 - The use of a *Harpagophytum* powder at 60 mg harpagoside in the treatment of osteoarthritis of the spine, hip and knee;
 - The use of an aqueous *Harpagophytum* extract at a daily dose of 100 mg harpagoside in the treatment of acute exacerbations of chronic non-specific low back pain; and,
 - The use of an aqueous extract of *Harpagophytum procumbens* at 60 mg harpagoside being non-inferior to 12.5 mg rofecoxib per day for chronic non-specific low back pain (NSLBP) in the short term.
- Strong evidence exists for the use of an aqueous *Harpagophytum* extract at a daily dose equivalent of 50 mg harpagoside in the treatment of acute exacerbations of chronic NSLBP.

Discussion

Potential bias or problems with the study	No apparent bias. From the paper, “One individual (SC) was an author of several original trials included in this systematic review. This did not appear to influence the content of this paper.”
Is this study Valid?	Yes. Grading of inclusion criteria seemed to be fair and adequate.
What are the results?	There is a moderate amount of evidence concerning the effectiveness of the use of a <i>Harpagophytum</i> powder at 60 mg harpagoside in the treatment of osteoarthritis of the hip
Impact Statement Are these results applicable to Chiropractic Practice?	In patients exploring alternative therapy for osteoarthritis, there is a moderate amount of evidence that the use of Devil’s Claw appears to be an effective therapy towards improving clinical outcomes in patients with osteoarthritis.

Discussion

- Additional literature reviews on the topic of hip osteoarthritis treatment, particularly medical interventions, were found and posted on Blackboard.

Discussion Questions

- Did you see any flaws or bias with this review?
- Do you agree with the impact statement?
 - Why or Why Not?
- How would you treat the patient?
- Do you feel this topic is applicable and important to the chiropractic profession?

Additional Information

- About Devil's Claw

<http://altmedicine.about.com/od/herbsupplementguide/a/DevilsClaw.htm>

- Possible drug interactions with Devil's Claw

http://altmedicine.about.com/od/druginteractions/p/devils_claw_int.htm