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**LIST OF REFERENCES SUPPORTING THE ASSESSMENT REPORT ON:**

**Harpagophyti radix**  
***Harpagophytum procumbens* DC. and/or *Harpagophytum zeyheri* Decne, radix**  
**(devil's claw root)**

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Baghdikian B., Lanhers M.C., Fleurentin J., Ollivier E., Maillard C., Balansard G., Mortier F. An analytical study, anti-inflammatory and analgesic effects of *Harpagophytum procumbens* and *Harpagophytum zeyheri*. *Planta Med* **1997**, 63: 171-176.

Baghdikian B., Guiraud-Dauriac H., Ollivier E., N'Guyen A., Dumenil G., Balansard G. Formation of nitrogen-containing metabolites from the main iridoids of *Harpagophytum procumbens* and *H. zeyheri* by human intestinal bacteria. *Planta Med* **1999**, 65: 164-166.

Bhattacharya A., Bhattacharya S.K. Anti-oxidant activity of *Harpagophytum procumbens* (Devil's claw). *Brit J Phyt* **1998**, 5: 68-71.

Bisset N.G., editor (translated from Wichtl M, editor. Teedrogen). *Harpagophyti radix*. In: *Herbal Drugs and Phytopharmaceuticals*. Stuttgart, Medpharm, Boca Raton-London, CRC Press **1994**, 248-250.

Blumenthal M, Goldberg A, Brinckmann J, eds. *Herbal Medicine, Expanded Commission E Monographs*. American Botanical Council Austin, Texas. **2000**.

Boje K., Lechtenberg M., Nahrstedt A. New and known iridoid- and phenylethanoid glycosides from *Harpagophytum procumbens* and their *in vitro* inhibition of human leukocyte elastase. *Planta Med* **2003**, 69: 820-825.

Braun H., Frohne D. *Harpagophytum procumbens* DC. Teufelskralle. In: *Heilpflanzen-Lexikon für Ärzte und Apotheker*, 5<sup>th</sup> ed. Stuttgart, Gustav Fisher **1987**, 129.

*British Herbal Compendium* **1992**, 1: 78-80.

Chantre P., Cappelaere A., Leblan D., Guédon D., Vandermander J. and Fournie B. Efficacy and tolerance of *Harpagophytum procumbens* versus Diacerhein in treatment of osteoarthritis. *Phytomedicine* **2000**, 7(3):177-183.

Chrubasik S., Zimpfer Ch., Schütt U., Ziegler R. Effectiveness of *Harpagophytum procumbens* in treatment of acute low back pain. *Phytomedicine* **1996**, 3: 1-10.

Chrubasik S., Schmidt A., Junck H., Pfisterer M. Wirksamkeit und Wirtschaftlichkeit von Teufelskrallenwurzelextrakt bei Rückenschmerzen: erste Ergebnisse einer therapeutischen Kohortenstudie. *Forsch Komplementärmed* **1997**, 4: 332-336

- Chrubasik S., Junck H., Breitschwerdt H., Conradt Ch. and Zappe H. Effectiveness of *Harpagophytum* extract WS 1531 in the treatment of exacerbation of low back pain: a randomized, placebo-controlled, double-blind study. *Eur J Anaesth* **1999**, 16: 118-129.
- Chrubasik S., Künzel O., Tanner J., Conradt C., Black A. and Pollak S., Comparison of outcome measures during treatment with the proprietary *Harpagophytum* Extract Doloteffin® in patients with pain in the lower back, knee or hip. *Phytomedicine* **2002**, 9: 181-194.
- Chrubasik S., Model A., Black A. and Pollak S. A randomized double-blind pilot study comparing Doloteffin® and Vioxx® in the treatment of low back pain. *Rheumatology* **2003**, 2: 141-148.
- Chrubasik S., Künzel O., Tanner J., Conradt C. and Black A. A 1-year follow-up after a pilot study with Doloteffin® for low back pain. *Phytomedicine* **2005**, 12: 1-9.
- Chrubasik S., Chrubasik C., Kunzel O., Black A. Patient-perceived benefit during one year of treatment with Doloteffin. *Phytomedicine* **2007**, 14: 371-376.
- Circosta C., Occhiuto F., Ragusa S., Trovato A., Tumino G., Briguglio F., de Pasquale A. A drug used in traditional medicine: *Harpagophytum procumbens* DC. II. Cardiovascular activity. *J Ethnopharmacol* **1984**, 11: 259-274.
- Czygan F-C. *Harpagophytum* – Teufelskralle. *Z Phytotherapie* **1987**, 8: 17-20.
- de Pasquale R. C., Busa G., Circosta C., Lauk L., Ragusa S., Ficarra P., Occhiuto F. A drug used in traditional medicine : *Harpagophytum procumbens* DC. III. Effects on hyperkinetic ventricular arrhythmias by reperfusion. *J Ethnopharmacol* **1985**, 13: 193-199.
- Engel S., Rivoltan (Li 174) zur Behandlung von Patienten mit degenerativen Erkrankungen des Bewegungsapparates. *Deutsche Apotheker Zeitung*. **2000**, 140: 1369.
- Eichler O., Koch C. Antiphlogistic, analgesic and spasmolytic effect of harpagoside, a glycoside from the root of *Harpagophytum procumbens* DC. *Arzneimittelforsch* **1970**, 20: 107-109.
- Erdös A., Fontaine R., Friehe H., Durand R., Pöppinghaus Th. Beitrag zur Pharmakologie und Toxikologie verschiedener Extrakte, sowie des Harpagosids aus *Harpagophytum procumbens* DC. *Planta Med* **1978**, 34: 97-108.
- ESCOP. *Harpagophyti* radix (Devil's Claw root). In: ESCOP Monographs, 2<sup>nd</sup> ed. **2003**.
- Fiebich B.L., Heinrich M., Hiller K.O., Kammerer N. Inhibition of TNF- $\alpha$  synthesis in LPS-stimulated primary human monocytes by *Harpagophytum* extract SteiHap 69. *Phytomedicine* **2001**, 8: 28-30.
- Frerick H., Biller A., Schmidt U. Stufenschema bei Coxarthrose. *Der Kassenarzt* **2001**, 5: 34-41.
- Gagnier J. J., Chrubasik S. and Manheimer E. *Harpagophytum procumbens* for osteoarthritis and low back pain: a systematic review. *BMC Complem Altern Med* **2004**, 4:13.
- Göbel H., Heize A., Ingewersen M., Niederberger U., Gerber D. *Harpagophytum*-Extrakt LI 174 (Teufelskralle) bei der Behandlung unspezifischer Rückenschmerzen. *Schmerz* **2001**, 15: 10-8.
- Hänsel R., Keller K., Rimpler H., Schneider G., editors. *Harpagophytum*. In: Hagers Handbuch des Pharmazeutischen Praxis, 5<sup>th</sup> ed. Volume 5: Drogen E – O. Berlin: Springer-Verlag **1993**, 384-390.
- Heck A.M., DeWitt B.A., Lukes A.L. Potential interactions between alternative therapies and warfarin. *Am J Health Syst Pharm*. **2000**, 57(13): 1221-1227.
- Izzo A.A., Di Carlo G., Borrelli F., Ernst E. Cardiovascular pharmacotherapy and herbal medicines: the risk of drug interaction. *Int J Cardiol*. **2005**, 98(1):1-14.
- Jadot G. Lecomte A. Activité anti-inflammatoire d'*Harpagophytum procumbens* DC. *Lyon médit. Méd Méd Sud-Est* **1992**, XXVIII: 29-31.

- Jang M.H., Lim S., Han S.M., Park H.J., Shin I., Kim J.W., Kim N.J., Lee J.S., Kim K.A., Kim C.J. *Harpagophytum procumbens* suppresses lipopolysaccharide-stimulated expressions of cyclooxygenase-2 and inducible nitric oxide synthase in fibroblast cell line L929. *J Pharmacol Sci* **2003**, 93: 367-371.
- Kundu J.K., Mossanda K.S., Na H.K., Surh Y.J. Inhibitory effects of the extracts of *Sutherlandia frutescens* (L.) R. Br. and *Harpagophytum procumbens* DC. on phorbol ester-induced COX-2 expression in mouse skin: AP-1 and CREB as potential upstream targets. *Cancer Lett* **2005**, 218: 21-31.
- Lanthers M.C., Fleurentin J., Mortier F., Vinche A., Younos C. Anti-inflammatory and analgesic effects of an aqueous extract of *Harpagophytum procumbens*. *Planta Med* **1992**, 58: 117-123.
- Laudahn D. and Walper A. Efficacy and tolerance of *Harpagophytum* Extract LI 174 in patients with chronic non-radicular back pain. *Phytother Res* **2001**, 15: 621-624.
- Leblan D., Chantre P. and Fournie B. *Harpagophytum procumbens* in the treatment of knee and hip osteoarthritis. Four-month results of a prospective, multicenter, double-blind trial *versus* Diacerhein. *Joint Bone Spine* **2000**, 67: 462-467.
- Lienert A., Ruetten S., Kuhn M., Wartenberg-Demand A. A randomised, active-controlled, mono-centric study of the herbal drug, Devil's claw (*Harpagophytum procumbens*) (ALLYA® tablets), Voltaren® and Vioxx® indicates equal efficacy in the treatment of patients with unspecific lumbar pain. Meeting abstract. 54. Jahrestagung der Norddeutschen Orthopädenvereinigung e.V. Hamburg **2005**, 616- 618.
- Loew D., Möllerfeld J., Schrödter A., Puttkammer S., Kaszkin M. Investigations on the pharmacokinetic properties of *Harpagophytum* extracts and their effects on eicosanoid biosynthesis *in vitro* and *ex vivo*. *Clin Pharmacol Ther* **2001**, 69: 356-364.
- Müller B., Deitelhoff P., Petrowicz O. *Harpagophytum procumbens* ist effizient bei degenerativen Erkrankungen des Bewegungsapparates. *Natura Med* **2000**, 15: 21-29
- McLeod D.W., Revell P., Robinson B.V. Investigations of *Harpagophytum procumbens* (Devil's Claw) in the treatment of experimental inflammation and arthritis in the rat. *Brit J Pharmacol* **1979**, 66: 140-141.
- Recio M.C., Giner R.M., Manez S., Rios J.L. Structural considerations on the iridoids as anti-inflammatory agents. *Planta Med* **1994**, 60: 232-234.
- Ribbat J.M., Schakau D. Behandlung chronisch aktivierter Schmerzen am Bewegungsapparat. *Natura Med* **2001**, 16: 23-30.
- Salvemini D., Misko T.P., Masferrer J.L., Seibert K., Currie M.G., Needleman P. Nitric oxide activates cyclooxygenase enzymes. *Proc Natl Acad Sci USA* **1993**, 90: 7240-7244.
- Schendel U.M., Arthrose-Therapie : Verträglich geht es auch. Studie mit Teufelskrallenextrakt. *Der Kassernarzt* **2001**, 29/30: 36-39.
- Schilcher H. Teufelskralle. In: Kleines Heilkräuter-Lexikon, 4<sup>th</sup> ed. Weil der Stadt: Haedeker **1999**, 187-188.
- Schmelz H., Hämmerle H. D., Springorum H.W. Analgetische Wirkung eines Teufelskrallenwurzel-Extraktes bei verschiedenen chronisch-degenerativen Gelenkerkrankungen. Hippokrates Verlag Stuttgart **1997**, 86-89.
- Schmidt A., Berghol U., Schmidt E. Therapie der unspezifischen Lumbalgie mit Teufelskrallenwurzelextrakt – Ergebnisse einer Klinischen Studie. Effectiveness of *Harpagophytum procumbens* in treatment of unspecific low back pain. *Phys Med Rehab Kuror* **2005**, 15: 317-321.
- Soulimani R., Younos C., Mortier F., Derrieu C. The role of stomachal digestion the pharmacological activity of plant extracts, using as example extracts of *Harpagophytum procumbens*. *Can J Physiol Pharmacol* **1994**, 72: 1532-1536.

van Haelen M. Aspects botaniques, constitution chimique et activité pharmacologique d'*Harpagophytum procumbens*. *Phytotherapy* **1983**, 5: 7-13.

Wegener T., Lüpke N.P. Treatment of patients with arthrosis of hip or knee with an aqueous extract of Devil's Claw (*Harpagophytum procumbens* DC). *Phytother. Res.* **2003**, 17: 1165-1172

Weiss R.F. *Harpagophytum procumbens*, Teufelskralle. In: *Lehrbuch der Phytotherapie*, 7<sup>th</sup> ed. Stuttgart, Hippokrates **1991**, 86: 340-342.

Whitehouse W.L., Znamirowska M., Paul C.J. Devil's Claw (*Harpagophytum procumbens*): no evidence for anti-inflammatory activity in the treatment of arthritic disease. *Can Med Assoc J* **1983**, 129: 249-251.

Zimmermann W. Pflanzliche Bitterstoffe in der Gastroenterologie. *Z Allgemeinmed* **1976**, 54: 1178-1184.

Supersedes