Radix Harpagophyti

Definition
Radix Harpagophyti consists of the dried, tuberous, secondary roots of *Harpagophytum procumbens* DC. ex Meiss. (Pedaliaceae) (*1, 2*).

Synonyms
Harpagophytum burcherllii Decne (*3*).

Selected vernacular names
Afrikanische Teufelskralle, beesdubbeltjie, devil's claw, duiwelsklou, grapple plant, grapple vine, harpagophytum, kanako, khams, khuripe, legatapitse, sengaparele, Teufelskralle, Trampelklette, wood spider xwate (*3–8*).

Geographical distribution
Indigenous to the Kalahari desert and savannas of Angola, Botswana, Namibia and South Africa, being found southwards from central Botswana (*6, 7, 9–11*).

Description
Prostrate perennial mat-forming herb, up to 1.5 m across. Tuber up to 6 cm in diameter, bark yellowish-brown, longitudinally striated. Leaves pinnately lobed and clothed with glandular hairs, the underside densely pubescent. Flowers bright red, solitary, rising abruptly from the leaf axils; corolla pentamerous, tubular, pink-purple, up to 7 cm long; androecium of four stamens with one staminodium. Fruits characteristically large, hooked, claw-like, tardily dehiscent two-locular capsules, flattened at right angles to the septum, the edges bearing two rows of woody arms up to 8 cm long with recurved spines (*6, 12, 13*).

Plant material of interest: dried, tuberous, secondary roots
General appearance
Irregular thick, fan-shaped or rounded slices or roughly crushed discs of tuber, 2–4 cm and sometimes up to 6 cm in diameter, 2–5 mm thick,

greyish-brown to dark brown. Darker outer surface traversed by tortuous longitudinal wrinkles. Paler cut surface shows a dark cambial zone and xylem bundles distinctly aligned in radial rows. Central cylinder shows fine concentric striations. Seen under a lens, the cut surface presents yellow to brownish-red granules, longitudinally wrinkled; transverse surface yellowish-brown to brown, central region raised, fracture short (*1, 2*).

Organoleptic properties
Odour: none; taste: bitter (*1, 2*).

Microscopic characteristics
Several rows of large, thin-walled cork cells frequently with yellowish-brown contents; parenchymatous cortex with very occasional sclereids with reddish-brown contents, xylem arranged in concentric rings; reticulately thickened vessels, some with rounded perforations in the end walls (tracheidal vessels); abundant lignified parenchymatous cells associated with the vessels and in the small central pith (*1*).

Powdered plant material
Brownish-yellow with fragments of cork layer consisting of yellowish-brown, thin-walled cells; fragments of cortical parenchyma consisting of large, thin-walled cells, sometimes containing reddish-brown granular inclusions and isolated yellow droplets; fragments of reticulately thickened vessels and tracheidal vessels with associated lignified parenchyma from the central cylinder; small needles and crystals of calcium oxalate present in the parenchyma. May show rectangular or polygonal pitted sclereids with dark reddish-brown contents. Parenchyma turns green when treated with a solution of phloroglucinol in hydrochloric acid (*2*).

General identity tests
Macroscopic and microscopic examinations, and thin-layer chromatography for the presence of harpagoside (*1, 2*).

Purity tests
Microbiological
Tests for specific microorganisms and microbial contamination limits are as described in the WHO guidelines on quality control methods for medicinal plants (*14*).

Foreign organic matter
Not more than 2% (*1, 2*).

Total ash
Not more than 8% (*2*).

Acid-insoluble ash
Not more than 5% (*1*).

Water-soluble extractive
Not less than 50% (*1*).

Loss on drying
Not more than 12% (*2*).

Pesticide residues
The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (*15*). For other pesticides, see the *European pharmacopoeia* (*15*), and the WHO guidelines on quality control methods for medicinal plants (*14*) and pesticide residues (*16*).

Heavy metals
For maximum limits and analysis of heavy metals, consult the WHO guidelines on quality control methods for medicinal plants (*14*).

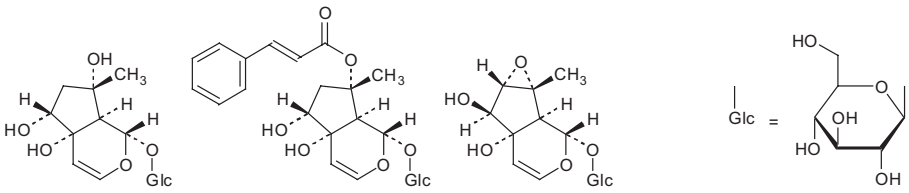
Radioactive residues
Where applicable, consult the WHO guidelines on quality control methods for medicinal plants (*14*) for the analysis of radioactive isotopes.

Other purity tests
Chemical, sulfated ash and alcohol-soluble extractive tests to be established in accordance with national requirements.

Chemical assays
Contains not less than 1.2% harpagoside as determined by high-performance liquid chromatography (*2*).

Major chemical constituents
The major active constituents are harpagoside and the related iridoid glycosides, harpagide and procumbide, which occur in lesser amounts. Total iridoid glycoside content 0.5–3.3% (*3, 7, 10, 11*). The structures of the major iridoid glycosides are presented below.

Medicinal uses
Uses supported by clinical data
Treatment of pain associated with rheumatic conditions (*17–24*).



Uses described in pharmacopoeias and well established documents
Treatment of loss of appetite and dyspeptic complaints; supportive treatment of degenerative rheumatism, painful arthrosis and tendonitis (*25*).

Uses described in traditional medicine
Treatment of allergies, boils, diabetes, liver disorders and sores (*8*).

Pharmacology

Experimental pharmacology

Anti-inflammatory and analgesic activity

A 60% ethanol extract of Radix Harpagophyti, 100.0 µg/ml, standardized to contain 2.9% harpagoside, inhibited the release of tumour necrosis factor-α (TNF-α) induced by the treatment of human monocytes with lipopolysaccharide (LPS) in vitro. However, treatment of the monocytes with harpagoside and harpagide, 10.0 µg/ml, isolated from the roots, had no effect on LPS-induced TNF-α release (*26*). Harpagoside, 10.0–100.0 µmol/l, reduced the synthesis of thromboxane B_2 in cells treated with calcium ionophore A23187 (*27*).

The results of studies assessing the anti-inflammatory activity of Radix Harpagophyti in animal models are conflicting. Intragastric administration of 20.0 mg/kg body weight (bw) of an aqueous or methanol extract of the root to rats inhibited oedema and inflammation in the granuloma pouch and carrageenan-induced footpad oedema tests (*28*). Intragastric administration of 20 mg/kg bw of a methanol extract of the root inhibited erythema induced by ultraviolet light in rats (*28*). Intragastric administration of 20.0 mg/kg bw of the same methanol extract to mice exhibited analgesic activity in the hot-plate test, but did not inhibit benzoquinone-induced writhing (*28*). Intraperitoneal pretreatment of rats with an aqueous extract of the roots reduced carrageenan-induced footpad oedema in a dose-dependent manner. Doses of 400 mg/kg bw and 1200 mg/kg bw reduced oedema by 43% and 64%, respectively, 3 hours after administration. The efficacy of the higher dose was similar to that of indometacin, 10 mg/kg bw (*29*). Intraperitoneal administration of 400.0 mg/kg bw of a

chloroform extract of the roots to mice with carrageenan-induced footpad oedema and inflammation reduced inflammation by 60.3% 5 hours after treatment (*30*).

Intraperitoneal administration of 200–400 mg/kg bw of an aqueous extract of the roots reduced carrageenan-induced footpad oedema in rats, but did not increase the reaction time of mice in the tail-flick hot-plate test. The anti-inflammatory activity of the highest dose was more efficient in rats than indometacin, 10.0 mg/kg bw. Treatment of the aqueous extract with 0.1 mol/l hydrochloric acid dramatically decreased the activity, suggesting that oral dosage forms should be enteric coated to protect the active principles from stomach acid. In the same study, harpagoside did not appear to be involved in the anti-inflammatory activity (*31*).

Intraperitoneal administration of 20.0 mg/kg bw of an aqueous extract of the roots to rats reduced formalin-induced arthritis. The effectiveness was comparable to that of phenylbutazone, 50.0 mg/kg bw. This study also demonstrated that intraperitoneal administration of 10–50 mg/kg bw of harpagoside to rats inhibits both formalin- and albumin-induced footpad oedema and formalin-induced arthritis (*32*).

Intragastric administration of 200.0 mg of an aqueous extract of the roots to rats inhibited formalin-induced footpad oedema (*33*). However, another study showed that intragastric administration of 1.0 g/kg bw of the powdered roots to rats did not inhibit carrageenan-induced footpad oedema or adjuvant-induced arthritis, as compared with other anti-inflammatory agents such as indometacin or acetylsalicyclic acid (*34*). Investigations of the antiphlogistic activity of harpagoside, harpagide and an aqueous extract of Radix Harpagophyti (doses not specified) indicated that all three substances had anti-inflammatory activity similar to that of phenylbutazone (*35*). In mice, intragastric administration of 100.0 mg/kg bw of harpagoside inhibited carrageenan-induced footpad oedema, and external application of 1.0 mg/ear reduced ear oedema induced by phorbol ester (*36*).

Intragastric administration of up to 100 times the recommended daily dose of powdered roots (6.0 g/kg bw) to rats did not reduce footpad oedema induced by carrageenan or *Mycobacterium butyricum*. Furthermore, the root preparation, 100.0 mg/ml, failed to inhibit prostaglandin synthase activity in vitro (*37*).

Antiarrhythmic activity

Intragastric administration of 100 mg/kg bw of an aqueous or methanol extract of the roots protected rats against ventricular arrhythmias induced by epinephrine-chloroform or calcium chloride (*38*). Intraperitoneal administration of 25 mg/kg bw of a methanol extract of the roots inhibited

cardiac arrhythmias induced by aconitine, epinephrine-chloroform or calcium chloride in fasted rats (*38*). Intragastric administration of 300–400 mg/kg bw of a methanol extract of the roots to normotensive rats reduced heart rate and arterial blood pressure (*38*). Other studies have demonstrated that lower doses of the extract have slight negative chronotropic and positive inotropic effects (*39*), whereas larger doses have a marked inotropic effect, with reductions in coronary blood flow. The inotropic effect is attributed to harpagide (*40*).

Clinical pharmacology

Antidyspeptic activity

A decoction of Radix Harpagophyti is one of the strongest bitter tonics known (*41*). Ingestion of a tea prepared from the root (dose not specified) over a period of several days led to an improvement in the symptoms of disorders of the upper part of the small intestine, which were accompanied by disturbances of choleresis and bile kinesis (*41*). It has been proposed that, because the root is very bitter, is a good stomachic and stimulates the appetite, it may also be useful for the treatment of dyspeptic complaints (*17, 42, 43*).

Anti-inflammatory and analgesic activity

A randomized double-blind comparison study, involving 46 patients with active osteoarthritis of the hip, assessed the effects of oral administration of 480 ng of an ethanol extract of the roots twice daily in the successive reduction of ibuprofen use for pain and the Western Ontario and McMaster Universities (WOMAC) arthrosis index. Patients received, in conjunction with the extract or placebo, 800.0 mg of ibuprofen daily for 8 weeks, then 400.0 mg daily for 8 weeks, then no ibuprofen. After 20 weeks of treatment, the WOMAC index decreased in the treatment group, with improvements in pain, stiffness and loss of function (*23*). In a randomized, double-blind clinical trial in 122 patients suffering from osteoarthritis of the knee and hip, the efficacy and tolerance of the roots and diacerein were compared. Patients received the roots as 6 capsules per day, each containing 435.0 mg of powdered roots or 100.0 mg of diacerein daily for 4 months. Assessments of pain and functional disability were made on a 10-cm horizontal visual analogue scale, and the severity of osteoarthritis was evaluated using the Lequesne functional index. There was a reduction in spontaneous pain and a progressive reduction in the Lequesne index in both groups. Fewer side-effects were observed in the group treated with the powdered roots (8.1%) than in the group receiving diacerein (26.7%) (*22*).

In a double-blind, placebo-controlled clinical trial, 50 patients with various arthroses were treated with 1200.0 mg of a hydroalcoholic extract of the roots, containing 1.5% iridoid glycosides, daily for 3-week courses. The severity of pain was assessed 10 days after completion of treatment. Each patient was given one to three courses of treatment. Compared with placebo, the extract produced a decrease in the severity of pain in individuals with a moderate pain level (*44*).

In an uncontrolled study involving 630 patients with arthrosis, 42–85% of the patients showed improvements after 6 months of daily oral treatment with 3.0–9.0 g of an aqueous extract of the roots containing 2.5% of iridoid glycosides (*45*). In an uncontrolled trial, the efficacy of an orally administered aqueous extract of the roots (as tablets) was assessed in 13 patients, 11 with arthritis and two with psoriatic arthropathy. Treatment of the patients for 6 weeks with 1.23 g daily did not reduce pain or inflammation in 12 patients, and one patient withdrew owing to side-effects (*46*). In an uncontrolled study, beneficial results were reported in 80% of 60 patients with chronic polyarthritis after treatment with subcutaneous lateral and medial injections of aqueous root extracts on both sides of the knee joint (*17*).

The efficacy of a standardized hydroalcoholic extract of the roots for the treatment of chronic back pain was assessed in a double-blind, randomized, placebo-controlled trial. The 197 patients were treated orally with 600.0 mg or 1200.0 mg of the extract (standardized to contain a total of 50–100 mg of harpagoside) or placebo daily for 4 weeks. A total of 183 patients completed the trial. Three, six and ten patients in the placebo, low-dose extract and high-dose extract groups, respectively, ($P = 0.027$) remained pain-free without the permitted pain medication (tramadol) for 5 days in the last week (*20*). A 4-week randomized double-blind, placebo-controlled clinical trial assessed the safety and efficacy of an ethanol extract of the roots in the treatment of acute attacks of pain in 118 patients with chronic back problems. Patients received two 400.0-mg tablets three times per day (equivalent to 6 g of roots containing 50.0 mg of harpagoside). Intake of a supplementary analgesic (tramadol) did not differ significantly between the placebo and the treatment group. However, further analysis revealed that nine out of 51 patients who received the extract were pain free at the end of the treatment period, compared to only one out of 54 in the placebo group (*18*). The efficacy of a dried ethanol extract of the roots was investigated in a 4-week, double-blind, placebo-controlled study in 118 patients with a history of chronic lower back pain. Patients were randomly assigned to receive two tablets of the extract or placebo three times per day. After 4 weeks of treatment, a reduction in the

Arhus low back pain index was observed in the treated patients compared with those receiving placebo (*19*). A randomized, placebo-controlled, double-blind study investigated the effects of an ethanol extract of the roots on sensory, motor and vascular mechanism of muscle pain in 65 patients with mild to moderate muscle tension or mild back, shoulder or neck pain. Patients received two doses of 480.0 mg of the extract or placebo daily for 4 weeks. At the end of the treatment period, a significant reduction in muscle pain as measured by a visual analogue scale ($P < 0.001$) was observed in the extract group. Muscle stiffness and ischaemia were also improved in this group, but no changes were found in antinociceptive muscle reflexes or surface electromyography (*24*).

Oral administration of powdered roots, four 500.0-mg capsules, standardized to contain 3% total iridoids, daily for 21 days to healthy volunteers did not statistically alter eicosanoid biosynthesis by the cyclooxygenase or 5-lipoxygenase pathways. The results indicated that in healthy humans Radix Hapagophyti did not inhibit arachidonic acid metabolism (*47*).

Adverse reactions

Mild and infrequent gastrointestinal symptoms were reported in clinical trials (*18, 20, 45*).

Contraindications

Radix Harpagophyti is contraindicated in gastric and duodenal ulcers, and cases of known hypersensitivity to the roots (*25*). Owing to a lack of safety data, Radix Harpagophyti should not be used during pregnancy and nursing.

Warnings

No information available.

Precautions

General

Patients with gallstones should consult a physician prior to using the roots (*25*).

Drug interactions

An extract of the roots did not inhibit the activity of cytochrome P450 isoform 3A4 in vitro, suggesting that Radix Harpagophyti would not interact with prescription drugs metabolized by this enzyme (*48*).

Pregnancy: non-teratogenic effects
See Contraindications.

Nursing mothers
See Contraindications.

Other precautions
No information available on precautions concerning drug and laboratory test interactions; carcinogenesis, mutagenesis, impairment of fertility; teratogenic effects during pregnancy; or paediatric use.

Dosage forms
Dried roots for decoctions and teas; powdered roots or extract in capsules, tablets, tinctures and ointments (*6, 7*). Store in a well closed container, protected from light (*2*).

Posology
(Unless otherwise indicated)
Daily dose: for loss of appetite 1.5 g of the roots in a decoction, 3 ml of tincture (1:10, 25% ethanol) (*25*); for painful arthrosis or tendonitis 1.5–3 g of the roots in a decoction, three times, 1–3 g of the roots or equivalent aqueous or hydroalcoholic extracts (*41*).

References
1. *British herbal pharmacopoeia*. Exeter, British Herbal Medicine Association. 1996.
2. *European pharmacopoeia*, 3rd ed., Suppl. 2001. Strasbourg, Council of Europe, 2000.
3. Hänsel R et al., eds. *Hagers handbuch der Pharmazeutischen Praxis. Bd 5, Drogen E–O*, 5th ed. [Hager's handbook of pharmaceutical practice. Vol. 5, Drugs E–O, 5th ed.] Berlin, Springer, 1993.
4. Hedberg I, Staugard F. *Traditional medicine in Botswana, traditional medicinal plants.* Gaborone, Ipeleng Publishers, 1989.
5. Van den Eynden V, Vernemmen P, Van Damme P. *The ethnobotany of the Topnaar*. University of Ghent/EEC, 1992.
6. Iwu MM. *Handbook of African medicinal plants*. Boca Raton, FL, CRC Press, 1993.
7. Bisset NG. *Herbal drugs and phytopharmaceuticals*. Boca Raton, FL, CRC Press, 1994.
8. Farnsworth NR, ed. *NAPRALERT database.* Chicago, IL, University of Illinois at Chicago, 9 February 2001 production (an online database available

directly through the University of Illinois at Chicago or through the Scientific and Technical Network (STN) of Chemical Abstracts Services).
9. Czygan FC. *Harpagophytum* – Teufelskralle. [*Harpagophytum* – devil's claw.] *Zeitschrift für Phytotherapie*, 1987, 8:17–20.
10. Bruneton J. *Pharmacognosy, phytochemistry, medicinal plants*. Paris, Lavoisier Publishing, 1995.
11. Eich J, Schmidt M, Betti G. HPLC analysis of iridoid compounds of *Harpagophytum* taxa: Quality control of pharmaceutical drug material. *Pharmaceutical and Pharmacological Letters*, 1998, 8:75–78.
12. Dyer RA. *The genera of southern African flowering plants. Vol. I*. Pretoria, Botanical Research Institute, 1975.
13. Betti GJR. *Harpagophytum procumbens* DC. Complexe d'éspèces. Description comparative du développement végétatif. Origine, prévention et conséquences de la confusion entre éspèces. [*Harpagophytum procumbens* DC. Species complex. Comparative description of vegetative development. Origin, prevention and consequences of the confusion between species.] *Revista Italiana*, 1994, Special issue, February.
14. *Quality control methods for medicinal plant materials.* Geneva, World Health Organization, 1998.
15. *European pharmacopoeia*, 3rd ed. Strasbourg, Council of Europe, 1996.
16. *Guidelines for predicting dietary intake of pesticide residues*, 2nd rev. ed. Geneva, World Health Organization, 1997 (WHO/FSF/FOS/97.7; available from Food Safety, World Health Organization, 1211 Geneva 27, Switzerland).
17. Schmidt S. Rheumatherapie mit *Harpagophytum.* [Treatment of rheumatism with *Harpagophytum.*] *Therapiewoche*, 1972, 13:1072–1075.
18. Chrubasik S et al. Effectiveness of *Harpagophytum procumbens* in treatment of acute low back pain. *Phytomedicine*, 1996, 3:1–10.
19. Stange CF, Schultz J. Treatment of low back pain with *Harpagophytum procumbens* (Burch.) De Candolle ("devil's claw"). *Erfahrungsheilkunde*, 1997, 6:330–335.
20. Chrubasik S et al. Effectiveness of *Harpagophytum* extract WS 1531 in the treatment of exacerbation of low back pain: a randomized, placebo-controlled, double-blind study. *European Journal of Anaesthesiology*, 1999, 16:118–129.
21. Wegener T. Therapie degenerativer Erkrankungen des Bewegungsapparates mit sudafrikanischer Teufelskralle (*Harpagophytum procumbens* D.C.). [Treatment of degenerative diseases of the locomotor system with south African devil's claw (*Harpagophytum procumbens* D.C.).] *Wiener Medizinische Wochenschrift*, 1999, 149:254–257.
22. Chantre P et al. Efficacy and tolerance of *Harpagophytum procumbens* versus diacerhein in the treatment of osteoarthritis. *Phytomedicine*, 2000, 7:177–183.
23. Frerick H, Biller A, Schmidt U. Stufenschema bei coxarthrose. [Graded approach to the treatment of coxarthrosis.] *Der Kassenarzt*, 2001, 5:34–41.

24. Göbel H et al. Harpagophytum-Extrakt LI174 (Teufelskralle) bei der Behandlung unspezifischer Rückenschemerzen. Effekte auf die sensible, motorische und vaskuläre Muskelreagibilität. [Harpagophytum-extract LI174 (devil's claw) for the treatment of non-specific back pain. Effects on sensory, motor and vascular muscle responsiveness.] *Schmerz*, 2001, 15:10–18.
25. Blumenthal M et al., eds. *The complete German Commission E monographs*. Austin, TX, American Botanical Council, 1998.
26. Fiebich et al. Inhibition of TNF-alpha synthesis in LPS-stimulated primary human monocytes by *Hargophytum* extract SteiHap 69. *Phytomedicine*, 2001, 8:28–30.
27. Tippler B et al. *Harpagophytum procumbens*: Wirkung von Extrakten auf die Eicosanoidbiosynthese in Ionophor A23187-stimuliertem menschlichem Vollblut. [*Harpagophytum procumbens*: Effect of extracts on eicosanoid biosynthesis in ionophore A23187-stimulated whole blood.] In: Loew D, Rietbrock N, eds. *Phytopharmaka II: Forschung und klinische Anwendung*. [Phytopharmacological drugs II. Research and clinical use.] Darmstadt, Steinkopff, 1996:95–100.
28. Erdös A et al. Beitrag zur Pharmakologie und Toxicologie verschiedener Extracte, sowie des Harpagosids aus *Harpagophytum procumbens* DC. [Contribution to the pharmacology and toxicology of different extracts as well as the harpagosid from *Harpagophytum procumbens* DC.] *Planta Medica*, 1978, 34:97–101.
29. Baghdikian B et al. An analytical study, anti-inflammatory and analgesic effects of *Harpagophytum procumbens* and *Harpagophytum zeyheri. Planta Medica*, 1997, 63:171–176.
30. Mañez S et al. Selected extracts from medicinal plants as antiinflammatory agents. *Planta Medica*, 1990, 56:656.
31. Lanhers MC et al. Anti-inflammatory and analgesic effects of an aqueous extract of *Harpagophytum procumbens. Planta Medica*, 1992, 58:117–123.
32. Eichler VO, Koch C. Über die antiphlogistische, analgetische und spasmolytische Wirksamkeit von Harpagosid, einem Glykosid aus der Wurzel von *Harpagophytum procumbens*. [On the antiphlogistic, analgesic and spasmolytic action of harpagoside, a glycoside from the roots of *Harpagophytum procumbens* DC.] *Arzneimittelforschung*, 1970, 20:107–109.
33. Zorn B. Über die antiarthritische Wirkung der *Harpagophytum*-Wurzel. [On the anti-arthritic effect of *Harpagophytum* roots.] *Zeitschrift für Rheumaforschung*, 1958, 17:134–138.
34. McLeod DW, Revell P, Robinson BV. Investigations of *Harpagophytum procumbens* (devil's claw) in the treatment of experimental inflammation and arthritis in the rat. *British Journal of Pharmacology*, 1979, 66:140P–141P.
35. Sticher O. Plant mono-, di- and sesquiterpenoids with pharmacological and therapeutic activity. In: Wagner H, Wolff P, eds. *New natural products with pharmacological, biological or therapeutic activity.* Berlin, Springer, 1977:137–176.

36. Recio M et al. Structural considerations on the iridoids as anti-inflammatory agents. *Planta Medica*, 1994, 60:232–234.
37. Whitehouse LW, Znamirowska M, Paul CJ. Devil's claw (*Harpagophytum procumbens*): no evidence for anti-inflammatory activity in the treatment of arthritic disease. *Canadian Medical Association Journal*, 1983, 129:249–251.
38. Circosta C et al. A drug used in traditional medicine: *Harpagophytum procumbens* DC. II. Cardiovascular activity. *Journal of Ethnopharmacology*, 1984, 11:259–274.
39. Occhiuto F et al. A drug used in traditional medicine: *Harpagophytum procumbens* DC. IV. Effects on some isolated muscle preparations. *Journal of Ethnopharmacology*, 1985, 13:201–208.
40. Costa de Pasquale R et al. A drug used in traditional medicine: *Harpagophytum procumbens* DC. III. Effects on hyperkinetic ventricular arrhythmias by reperfusion. *Journal of Ethnopharmacology*, 1985, 13:193–199.
41. Weiss RF, Fintelmann V, eds. *Herbal medicine*, 2nd ed. Stuttgart, Thieme, 2000.
42. Czygan FC et al. Pharmazeutische-biologische Untersuchungen der Gattung *Harpagophytum* (Bruch.) DC ex Meissn. 1. Mitteilung: phytochemische Standardisierung von Tubern Harpagophyti. [Pharmaceutical-biological studies of the genus *Harpagophytum*. Part 1. Phytochemical standardization of tubera harpagophyti.] *Deutsche Apotheker Zeitung*, 1977, 117:1431.
43. Jaspersen-Schib R. Harpagophyti radix: est-ce vraiment une drogue miracle? [Radix Hargophyti: is it really a miracle drug?] *Journal Suisse de Pharmacie*, 1989, 11:265–270.
44. Lecomte A, Costa JP. *Harpagophytum* dans l'arthrose. [*Harpagophytum* in arthrosis.] *Le Magazine*, 1992, 15:27–30.
45. Belaiche P. Étude clinique de 630 cas d'arthrose traités par le nebulisat aqueux d'*Harpagophytum procumbens.* [Clinical study of 630 cases of arthrosis treated with an aqueous spray of *Harpagophytum procumbens*.] *Phytotherapie*, 1982, 1:22–28.
46. Grahame R, Robinson BV. Devil's claw (*Harpagophytum procumbens*): pharmacological and clinical studies. *Annals of Rheumatic Diseases*, 1981, 40:632.
47. Moussard C et al. A drug used in traditional medicine, *Harpagophytum procumbens:* no evidence for NSAID-like effect on whole blood eicosanoid production in humans. *Prostaglandins, leukotrienes and essential fatty acids*, 1992, 46:283–286.
48. Budzinski JW et al. An in vitro evaluation of human cytochrome P450 3A4 inhibition by selected commercial herbal extracts and tinctures. *Phytomedicine*, 2000, 7:273–282.
49. Frerick H, Biller A, Schmidt U. Stufenschema bei coxarthrose. [Graded approach to the treatment of coxarthrosis.] *Der Kassenarzt*, 2001, 5:34–41.