

Devil's Claw - Finally Available in Switzerland for the Treatment of Rheumatic Symptoms

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Botany

Devil's Claw (*Harpagophytum procumbens*) is a member of the sesame family (Pedaliaceae) (1) and is mostly found in the savannah of the Kalahari Desert in South Africa and Namibia (2). The lignifying fruit consists of long branched arms with small barbs, which is why it is called devil's claw.

The extract is derived from the secondary tubers. These start in the primary root and grow up to 2 m deep and 1.5 m laterally (Figure 1).

Cultivation

The devil's claw is an extremely sensitive plant, which makes its commercial cultivation very difficult. To ensure that enough high quality extract is available to prepare the extract, Bioforce AG has carried out a collaborative research project with Münster University and further companies. The objective of this program was to ensure the distribution, cultivation and continuity of the harvest of devil's claw, as the drug now mostly comes from wild collections and the long-term survival of the plant is endangered.

The Kalahari Desert is the main area of distribution of the devil's claw and the limiting factor for plant growth here is water. Rain is rare and unpredictable.

Underground water is difficult to reach and is not regularly regenerated. Because of this situation, the local farmers have developed their own culture system, which generates enough water without irrigation. This is known as the "water harvesting system". In this system, 5 m wide strips of natural vegetation are fully removed, thus reducing water losses by transpiration. Between the vegetation-free strips, there are 7 m wide naturally overgrown strips, which prevent wind erosion.

Wind erosion is further reduced by rotating the strips every 200 m by 90°.

A study of underground water shows that substantially more moisture is available in the vegetation-free strips than in the overgrown strips. The devil's claw is grown in the vegetation-free strips. With the "water harvesting system", the yield could be raised by up to 10-fold.



Figure 1: Picture of an unearthed *Harpagophytum* plant with the primary and secondary roots. The extract is produced from the secondary roots (tubers).

History

The San, the aboriginal inhabitants of southern Africa, have been living as hunters and collectors for more than 20.000 years. The devil's claw is one of their most important medicinal plants. The San's living space and culture are now under severe threat and their traditional way of life is now only found in a few small areas in the Kalahari.

According to various sources, the Swiss botanist Augustin-Pyrame de Candolle in about 1845 was the first botanist to describe and record *Harpagophytum* (3), although people were apparently not clear about the plant's medicinal properties at this time. The devil's claw is particularly well known in the German speaking area, through G.H. Mehnert, who was stationed to the home guard in the former German South West Africa (Namibia) in 1904, where he later became a farmer. He observed and documented how the local population used the plant. Later, in the 1950s, his family sent samples of devil's claw for analysis to the pharmacists Volk and Dr.

Tunmann PD in Würzburg and to Professor Zorn in Jena. At almost the same time, Prof. O.H. Volk of Würzburg University introduced the plant to Europe. Since then, the plant has been established as a medicinal plant, at least in Germany (4).

Traditional use

South African aborigines use the devil's claw for rheumatic diseases, to increase appetite, for digestive symptoms, as laxative, for fever, to treat skin injuries, to alleviate pain (5,6,7) and for asthma (8). Devil's claw has been used in European folk medicine since the middle of the last century, mostly for the treatment of dyspeptic symptoms, liver, gall bladder, kidney and bladder disease and for rheumatic illness (9, 10).

Current use

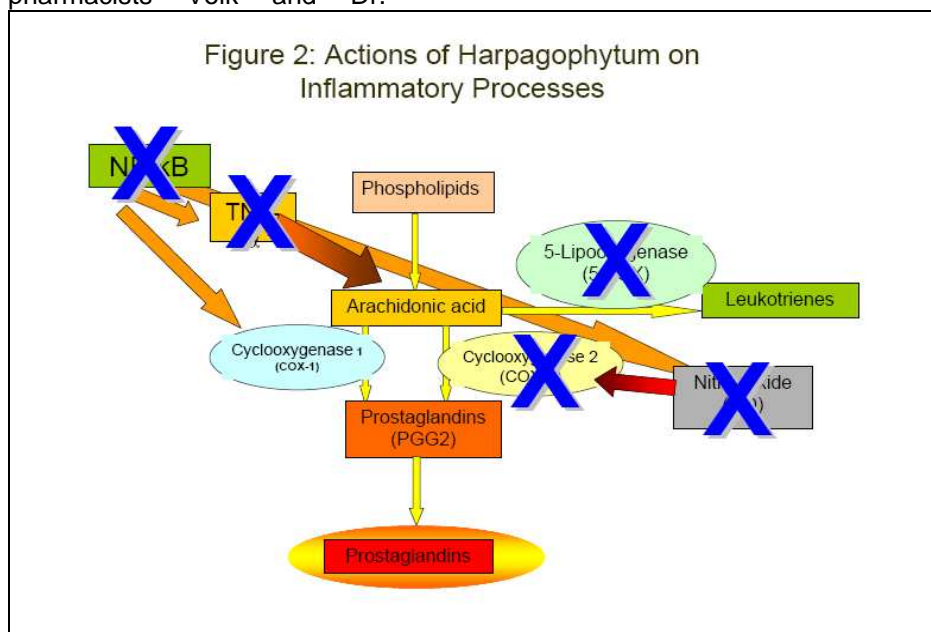
The current ESCOP monograph recommends devil's claw preparations for the symptomatic treatment of painful arthrosis, back pain, lack of appetite and dyspepsia. The recommended dosage for rheumatic symptoms is 2-5 g

drug or an equivalent quantity of extract for 2-3 months (11). In Switzerland, two products are currently approved for the supportive treatment for diseases linked to the wear of the locomotor system (e.g. arthroses).

Pharmacology

The main components of the secondary tubers of the devil's claw are iridoid glycosides, which make up about 3%. The main component of the latter is harpagoside, followed by procumbide, harpagide and 8-para-cumaroyl-harpagide.

Other relevant compounds are flavones, such as kempferol and luteolin, 2-phenylethanol derivatives, such as acteoside, and water soluble substances, such as stachyose, raffinose and their breakdown products (12, 13). Several experimental studies have measured analgesic, anti-inflammatory, anti-oedema and anti-arthritic activities; most of these detected low to intermediate levels of activity (Figure 2).



There remains however the principle problem with Harpagophytum that no main mechanism of action has been identified for anti-inflammatory or analgesic activity. It is therefore assumed that the inhibition of several mechanisms involved in inflammation, coupled to improved digestion triggered by the bitter constituents of Harpagophytum, lead to alleviation of the rheumatic symptoms or inflamed state.

Efficacy

The efficacy of devil's claw extracts has been investigated in 7 studies in comparison to placebo, in 2 studies in comparison to standard treatment and in 5 open uncontrolled studies.

Efficacy of Devil's Claw versus Placebo

The trials found that Harpagophytum exhibits good analgesic and anti-inflammatory activity in the treatment of patients with mild to intermediate back symptoms or with arthrosis of the knee or hip joints. One example is the trial with 65 patients with mild to intermediate pain (on the VAS scale) or muscular tension in the shoulders, back of the neck and/or the back (14). After 4 weeks of treatment with placebo or 2x480 mg Harpagophytum extract (extraction medium 60 % ethanol), there was significant improvement in muscular pain in the active treatment group in comparison to placebo ($p < 0.001$) and a significant reduction in stiffness ($p < 0.001$) (Figure 3).

Another placebo-controlled trial was performed to

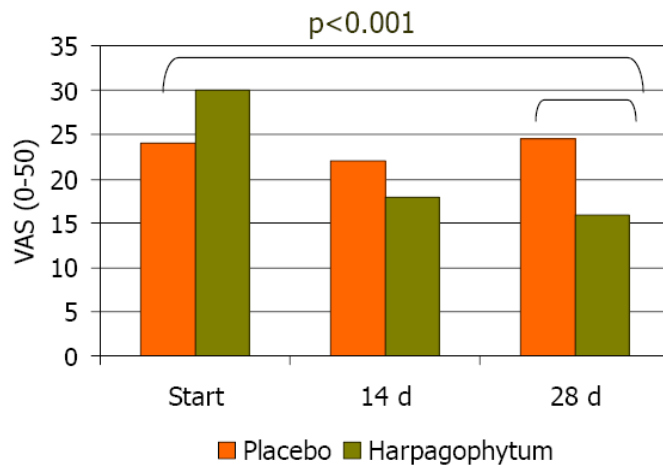


Figure 3 : Intensity of muscular pain (0-50) after 4 weeks 2x480mg Harpagophytum or placebo

investigate the analgesic activity of devil's claw extract in 100 patients with various rheumatic symptoms (active arthritis, chronic lumbago and soft tissue rheumatism) (15). The patients were given 2 tablets of devil's claw extract (corresponding to 4.92 g drug) or placebo three times daily for 30 days. At the start of the trial, 31 patients in the active drug group reported intense pain and 15 intermediate pain, in comparison with 26 and 24 patients, respectively, in the control group. At the end of the trial, 15 patients with the active treatment were free of pain, in comparison with only 3 in the placebo group.

Efficacy of Devil's Claw versus Standard Therapy

Devil's claw extract was compared in a randomised double blind multicentre trial with diacerhein – a traditional antirheumatic medicine in France and Italy. 122 patients with gonarthrosis or coxarthrosis were administered either a devil's claw preparation (n = 62) or standard therapy (n = 60) for 4 months. Pain intensity was measured with the VAS scale, the Lequesne Index and the

requirement for emergency medication (diclofenac and/or paracetamol). The patients treated with devil's claw needed significantly less emergency medication than the patients in the control group. The pain intensity and the Lequesne Index were reduced to comparable degrees in the two test groups (16).

In addition, a pilot trial was performed in which patients with back pain were administered either 2.4 g devil's claw extract or 12.5 mg rofecoxib daily. The improvement after 6 weeks of treatment was equal in the two groups (17).

Another trial, with a complex design, showed that 2x480 mg Harpagophytum is equivalent to 800 mg ibuprofen for the treatment of knee and hip joint arthrosis over 20 weeks (18).

Open Trial with A.Vogel Rheumatism Tablets

In an open clinical trial, 259 patients with mild to intermediate rheumatic symptoms in at least one joint or body site were treated for 8 weeks with 2x1 A.Vogel

Rheumatism Tablets (each with 480 mg devil's claw extract). After completion of the treatment, 30 % of the patients taking analgesics for their rheumatic symptoms could totally discontinue this medication and 52 % could reduce the dose (Figure 4).

therapy for patients with mild to intermediate rheumatic symptoms and is very well accepted by the patients (19).

Tolerability

All clinical trials with devil's claw (drug and extract) have found good to very good tolerability - even with long-term use. Reports of side effects have

Notes on the use of Devil's Claw

In contrast to NSAIDs, devil's claw preparations act slowly. They must therefore be administered for 2-4 weeks before the initial activity is evident. Devil's claw is therefore unsuitable for the treatment of acute pain or inflammation, but should be taken as basic therapy for chronic states.

If devil's claw preparations are used as basic therapy, it is usually possible for the patient to reduce the dosage of synthetic analgesics and thus to decrease the risk of gastrointestinal side effects. If the patient responds, the therapy can be taken for an extended period free of risk. Interactions with other drugs have not been observed. Patients who notice no effect after 2-3 months should see a doctor.

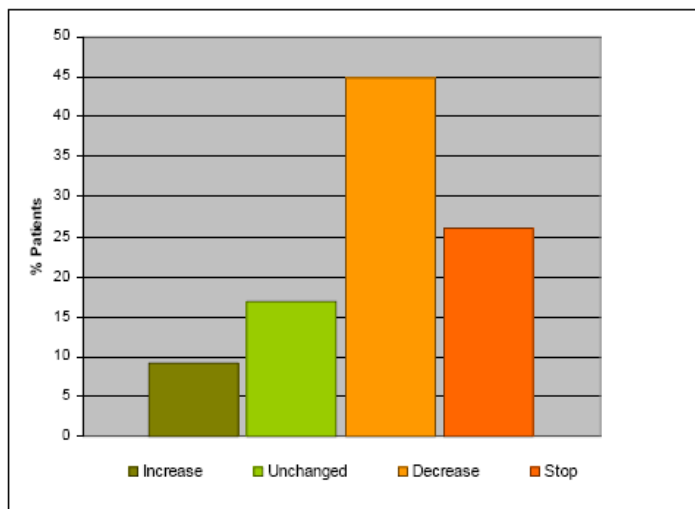


Figure 4: Effects on concomitant synthetic pain medication after 8 weeks of treatment (n=154)

The severity of the pain for each painful joint or body site was determined with a visual analogue scale (VAS), on a scale from 0 (no symptoms) to 10 (most intense symptoms). There were significant decreases in the pain in the individual joints, ranging from 36 to 58 %, with 37 % for back pain ($p < 0.05$).

In most cases, the doctor and patient rated the efficacy as very good or good (54%). The tolerability was rated as very good in 87 % of cases. The overwhelming majority at the conclusion would definitely (74.3 %) or possibly (12.6 %) take the tablet again. The trial demonstrates that A.Vogel Rheumatism Tablets are an active and well tolerated basic

been rare. The most frequent adverse events were gastrointestinal symptoms.

It is important that the gastrointestinal symptoms come from the bitter constituents, so that they stimulate digestion. The side effects are reversible and not comparable to those with NSAIDs, which are caused by damage to the gastric mucous membrane. Devil's claw should therefore only be taken with food and not on an empty stomach.

Now that Harpagophytum preparations are (finally!) available in Switzerland, doctors and patients will be able to use this proven, well tolerated and safe medicinal plant for the treatment of rheumatic symptoms.

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