DEVIL'S CLAW

Harpagophytum procumbens (Burch.) DC. ex Meisn.

Family

Pedaliaceae (Sesame family).

Parts Used

Root.

Description

Devil's claw grows in the Kalahari region of southern Africa including Namibia, Botswana, South Africa, Angola and to a lesser extent, Zambia, Zimbabwe and Mozambique. It is a weedy, perennial tuberous plant with visually striking fruits, some say diabolical (the other common name is wood spider). The botanical name Harpagophytum is derived from the Greek 'harpago' which translates to 'the grappling hook' named after the fruits which have numerous characteristically long protrusions with sharp, grapple like, hooks as well as two straight thorns on the upper surface. The common names devil's claw and grapple plant are also derived from this. Procumbens means prostrate or lying down after the creeping stems which grow along the ground and are up to two metres long. They sprout annually from the persistent primary tubers which can extend up to two metres deep. The flowers and leaves emerge from the ground after the first rains during the active growing season but die in the winter months or during periods of drought. The flowers are tubular and typically have violet lobes with a light-yellow throat but sometimes they are purely yellow or purely violet while the leaves are blueish green and usually irregularly divided into several lobes. The flowers are pollinated by bees during the one day that they are open. To enable survival during long severe dry periods the plant forms potato like, water storing, secondary tubers which

branch off horizontally from the primary tubers. They can be 25 centimetres with a diameter of six centimetres. It is these secondary tubers that are harvested for their medicinal properties. Initially this species was considered a nuisance by livestock farmers as the fruit can cripple an animal if lodged on its feet but this also aids seed dispersal. Like Velcro the fruit becomes entangled in the wool, tails or feet of animals and subsequently deposited in sandy soils. This seed dispersal method leads some to state that the name devil's claw originates from the bedevilled dance that animals do to get rid of the fruit trapped in their hooves. The seeds are released slowly from the mature fruit, have a high degree of dormancy (possibly an adaptation to drought) and low respiration rate, and it is estimated that it can remain viable in the seed bank for more than 20 years.[1,2]

Traditional Use

Devil's claw is a 'celebrity' among arthritis natural remedies being approved by German Commission E for the treatment of degenerative diseases of the musculoskeletal system. There is a lack of written historical records but some of the ethnobotanical uses of devil's claw, in addition to the common use to treat arthritis and pain, include fever, type 2 diabetes, urinary tract infections, asthma, dyspepsia, diarrhoea, constipation, postpartum pain, sprains, sores, ulcers and boils, as an appetite stimulant and as an important tonic in infectious diseases including tuberculosis, colds and influenza (including in children). It is commonly used for general body aches, especially muscle and joint aches and pains in the elderly. The San of Botswana say most old people use it for painful muscles and joints, taking it daily on a long-term basis. In 1820 devil's claw was collected and described by European scientists. However it was only much later that a German trader named G.H. Mehnert learnt of the medicinal properties from the San and Nama people in Namibia and made these uses known in the early 1900s, with large-scale export starting in 1962. It is now one of the most highly commercialised indigenous traditional medicines from Africa, with bulk exports mainly to Europe. The use of devil's claw was prominent amongst the indigenous San and Khoi people of southern Africa and its use was further adopted into the traditional knowledge systems of immigrating Bantu speakers. Devil's claw is used for a wide variety of health conditions in the form of infusions, decoctions, tinctures, powders and extracts. Small doses of the plant extract are used to relieve menstrual cramps whereas higher doses assist in expelling retained placentas. The dry, powdered secondary tuber is used directly as a wound dressing and it can also be mixed with animal fat to make a wound and burn healing ointment. The Topnaar people of Namibia drink a decoction of the secondary tubers, or chew them, to relieve stomach and postpartum pains. Before digging up the secondary tubers a needle or a button is put in the soil to 'buy the tubers from the earth'. An infusion is taken for the relief of fevers, as a bitter tonic and for unspecified 'blood diseases.' The dried and powdered secondary tuber is administered to pregnant women in a dose of about 250mg three times a day to relieve pain and this is continued in a lower dose after delivery. However other tribes, such as the Molapo community in the central Kalahari, believe it will cause abortion or stillbirth. Fresh secondary tuber is made into an ointment and applied to the abdomen of women who anticipate a difficult birth. The ointment is also applied to various skin lesions including sores, ulcers, boils and cancerous growths. An infusion can be taken orally especially for rheumatism and for treating liver, kidney, pancreas and stomach ailments. The Herero cut the tuber into small pieces, cover it with cold water and allow it to steep. Two tablespoons of this cold infusion is taken daily for treating cough, diarrhoea, constipation, as well as syphilis and gonorrhoea in both women and men. If the tea is taken too often, or if it is too concentrated, diarrhoea results. A decoction of pieces of the secondary tuber is taken for pain. Africans, and people of mixed descent, emphasise that Europeans use the plant too intensively and this can be damaging to health. San uses of devil's claw were recorded on an ethnobotanical field trip to Botswana during January 1998. In summary the San in Molapo do not make a distinction between the medicinal value of the primary tubers or the secondary tubers. Either, or both, are used fresh or dried, chewed directly or made into hot or cold infusions. Only small amounts are used. A single dose is estimated to represent approximately 100 to 200mg. This dose can be swallowed directly, or made into a tea, and can be taken daily on a chronic basis. No adverse

effects are known. Devil's claw is taken orally to treat any venereal disease and is also taken to treat intermittent abdominal pain suggestive of peptic ulceration. It is regarded as the best plant of all to treat menstrual cramps by the Molapo community and it is taken orally to expel a retained placenta immediately after childbirth although it is not their preferred plant for this purpose. Small amounts are used to initiate labour if there is delayed onset of labour, and during labour it is taken to ease labour pains. It is taken to help expel the placenta in the third stage of labour (time between complete delivery of the infant and the placenta) and for treating pain after giving birth.[3,4,5]

Sustainability

The three largest producers of wildcrafted devil's claw are Namibia, Botswana and South Africa. In 2002, the peak year of export, 1018 tonnes of dried tubers were exported from southern Africa representing the harvest of millions of plants. In 2001 sales in Germany were estimated at 30 million euros accounting for 74% of the prescriptions for rheumatism. Harvest has improved income levels in marginalised communities but it has also raised questions of sustainability. Indigenous communities used devil's claw for subsistence and had developed traditional knowledge systems of using it sustainably. When commercial exploitation and international trade on the product surpassed the subsistence use the traditional knowledge systems, which were in place to ensure its sustainable use, became inadequate. As a result of this the populations of the plant became threatened in the wild. In 2000 recommendations were made to the Convention on the International Trade in Endangered Species (CITES) to add devil's claw to Appendix II. Appendix II contains species that, although not threatened with extinction now, might become so unless trade in them is strictly regulated. If you want to trade in Appendix II species to/from Australia you will generally need both a CITES export and import permit issued by CITES management authorities. In 2004 the proposal was formally withdrawn due to the efforts of the range states to address sustainability issues. Devil's claw remains off the list as of September 2018. Replacing wild collection with cultivation has generated a debate on the positive and negative effects on harvester income and rural farmers. Successful cultivation efforts have involved micropropagation techniques and growing the plant without water or fertilisers. The governments of the main range states are working with local communities to develop policies and regulations to protect the species and to determine a sustainable harvest.[6]

Around 2400 to 2800 harvesters are registered in South Africa and the harvesting is considered sustainable with 1620 plants harvested per person per season on average equating to 3,504,060 in the 2003 to 2004 season. In Namibia wildcrafting of devil's claw is the livelihood of many rural communities with between 10,000 and 15,000 people relying on this income. The increased demand for this medicinal plant brings greater opportunities for primary producers but also strains the natural resource. Secondary tubers are normally harvested for medicinal use but care must be taken to cover the primary tubers and not damage them as this may lead to death of the plant. It has been reported that the plant requires a four year rotational harvesting period and that regeneration requires that the primary tuber be left totally undisturbed during harvesting. Cultivation of devil's claw remains a challenge due to low germination rates and plants propagated by cuttings fail to produce primary tubers. However several techniques have been proposed to culture it. Wildcrafting by knowledgeable harvesters protected the species but increased demand, and therefore financial motivation, has caused over harvesting by more (less knowledgeable) harvesters with significant effects on the devil's claw resource base. Controlled harvesting by way of permits has protected the species to some extent.[7,8]

Constituents

Iridoid glycosides (the bitter harpagoside, procumboside, harpagide, procumbide, 8-p-coumaroylharpagide); phenylpropanoids (acteoside and isoacteoside); acetyl phenolic glycosides (6-acetylacteoside, 2,6-diacetylacteoside); harpagoquinones; diterpenes (ferruginol); pagoside; cinnamic acid; caffeic acid; amino acids; flavonoids; phytosterols and carbohydrates (stachyose). It is worthy to mention that the whole plant extracts seem to have

a better therapeutic effect than those obtained from isolated parts. Despite the exhaustive isolation of the various constituents the exact mechanisms of action remain elusive but it has been suggested that the efficacy of devil's claw is dependent on synergistic or antagonistic interactions of the ratios of the four compounds 8-p-coumaroylharpagide, harpagide, harpagoside and verbascoside. In addition other constituents such as sugars, polyphenols and their derivatives may also have medicinal effects. European Pharmacopoeias recommend that devil's claw contains not less than 1.2% of harpagoside, calculated with reference to the dried drug.[9,10,11,12,13]

Actions

Anti-inflammatory, analgesic, antirheumatic, chondroprotective, antioxidant, bitter tonic, antimicrobial.

Pharmacological Activity

Investigations of the biological activities of devil's claw have provided scientific support for many of the traditional uses including pain, arthritis, diabetes, labour and convulsions. Reviews of the clinical trials on devil's claw provide supporting evidence for safety relative to pharmaceutical non-steroidal anti-inflammatory drugs, and efficacy in treating pain and inflammation in arthritis and lower back pain. However the methodological quality of many of the existing clinical trials is poor and further high quality clinical investigations are necessary to provide definitive clinical evidence of safety and efficacy.[14]

Anti-inflammatory Activity

In 1957 scientists showed that subcutaneous injection and oral ingestion of an infusion of devil's claw caused significant reduction in the swelling of arthritic joints of rats with induced arthritis. It was concluded that it contained a potent anti-inflammatory or antirheumatic substance and subsequent tests were undertaken in 1970 to determine whether the isolated constituent, harpagoside, yielded the same results. The results were positive but the whole plant extract showed better activity. Since then numerous studies have been undertaken to prove *in vitro* and *in vivo* anti-inflammatory activity although there is conflicting evidence.[15,16]

It has been postulated that the efficacy of devil's claw in reducing pain and inflammation associated with rheumatoid arthritis and osteoarthritis can be explained by its ability to block the production of inflammatory mediators such as prostaglandin (PG) E2. However some reports on the anti-inflammatory effect are inconsistent and differences have widely been attributed to the extraction procedure, geographical source of the crude drug and the fractions of constituents.[17]

In preclinical studies devil's claw influences the synthesis and release of pro-inflammatory factors, inhibiting transcription factor activator protein 1 (AP-1) activity and cytokine expression such as TNF-α and interleukin 6 (IL-6) at certain concentrations. Researchers have observed that devil's claw's effectiveness is not only based on its harpagosides but also on synergistic activity with other compounds.[18]

Clinical trials of devil's claw for the treatment of low back pain typically have tested oral doses ranging from 2000 to 4500mg daily, in two or three divided doses for four to 20 weeks. Animal studies of the anti-inflammatory and analgesic activities of devil's claw have reported conflicting results. Activity appears to differ depending on the route of administration of devil's claw, and the model of inflammation, whether acute or subacute. Also studies have assessed the effects of different preparations of devil's claw (e.g. aqueous extracts and ethanolic extracts) and it is important to consider this when interpreting the results.[19]

Clinical studies on devil's claw often lack a control group making it difficult to properly evaluate the effects of the tested herb. However use of a control group was a requirement for inclusion in a large 2016 Cochrane review on the efficiency of various plant based medicinal drugs for treatment of lower back pain.[20] Devil's claw appeared to reduce pain more than placebo but the evidence was reported to be of moderate quality only. Another potential problem is the quality of the preparations used in various trials. Chemical contents and anti-inflammatory effects documented by an ex vivo porcine skin model proved to be variable when six commercial devil's claw derived products were analysed.[21]

An earlier 2014 Cochrane Review to determine the effectiveness of herbal medicine for lower back pain found that daily doses of devil's claw, standardised to 50mg or 100mg harpagoside, may be better than placebo for short term improvements in pain and may reduce use of rescue medication (two trials, 315 participants, low quality evidence). Another devil's claw trial demonstrated relative equivalence to 12.5mg per day of rofecoxib (Vioxx) but was of very low quality (one trial, 88 participants, very low quality). Although devil's claw seemed to reduce pain more than placebo the researchers concluded that evidence was of moderate quality at best and suggested additional, well designed large trials are needed to test devil's claw against standard treatments. The authors included 14 randomised controlled trials (2050 participants) in the review.[22]

A clinical study with 259 patients suffering from rheumatic disorders showed that after eight weeks of ingesting devil's claw tablets 960mg (480mg twice daily) a significant improvement was documented based on patient assessments of global pain, stiffness and function. There was also significant reductions in mean pain scores for hand, wrist, elbow, shoulder, hip, knee and back pain. Quality of life scores significantly increased and more than 60% of patients either reduced or stopped concomitant pain medication.[23]

A randomised double-blind study compared the effects of treatment with devil's claw 2610mg/day with diacerein (100mg/day), a slow acting drug for osteoarthritis. The study involved 122 people with osteoarthritis of the hip and/or knee and was conducted over four months. It found that both treatment groups showed similar considerable improvements in symptoms of osteoarthritis however those receiving devil's claw required fewer rescue analgesics.[24]

As mentioned above the anti-inflammatory effects of devil's claw have been studied however the mechanism of action is not elucidated. A 2013 *in vitro* study has shown that devil's claw acts either by preventing oxidative stress or loss of cell viability. Thus, the previously reported anti-inflammatory effect of devil's claw could also be attributed to its antioxidant activity. It is known that excess of reactive oxygen and nitrogen species may contribute to increasing tissue damage due to inflammation. All tested extracts of devil's claw inhibited lipid peroxidation in a concentration dependent manner.[25]

An earlier 2012 preclinical study indicated that a standardised ethanolic devil's claw extract inhibits induction of pro-inflammatory gene expression possibly by blocking the AP-1 pathway. The researchers claim this is evidence of a possible mechanism of action for this anti-inflammatory herb. The devil's claw extract dose dependently inhibited the release of TNFα as well as that of interleukin (IL)-6, IL-1β and prostaglandin E2 (PGE2).[26]

The ability of the major active components in devil's claw (harpagoside, harpagide, 8-coumaroylharpagide and verbascoside) to inhibit the expression of COX-2 following administration to animal skin was investigated recently. These compounds are believed to interact either synergistically or antagonistically in modulating the enzymes responsible for inducing inflammation. An ethanol soluble extract of devil's claw and two of the pure compounds tested showed promising activity. The data suggests that the efficacy of devil's claw is dependent upon the ratios of the compounds present, which is inconsistent with some current official monograph specifications based solely on harpagoside content.[27]

An earlier study also suggested that the activity of the total extract is higher than that of pure harpagoside which was only inhibitory at concentrations between 0.3 and 1mg/mL.[28]

Fourteen clinical trials were reviewed to assess the efficacy and effectiveness of devil's claw in osteoarthritis. A review of the literature on devil's claw and osteoarthritis from 1966 to 2006 was performed using multiple search databases, monographs and citation tracking. Many of the published trials lacked certain important methodological quality criteria. However the data from the higher quality studies suggests that devil's claw appeared effective in the reduction of the main clinical symptom of pain.[29]

Devil's claw has shown chondroprotective activity. *In vitro* data suggests that devil's claw inhibits not only inflammatory mediators but also mediators of cartilage destruction such as matrix metalloproteinases (MMPs). Inflammatory articular cartilage diseases such as arthritis and

osteoarthritis are characterised by a loss of articular cartilage due to an imbalance between synthesis and degradation of the extracellular cartilage matrix. These diseases are accompanied by an increased induction of cytokines such as interleukin 1beta (IL-1beta) and tumour necrosis factor alpha (TNF-alpha). The increased release of cytokines leads to an enhanced production of matrix-degrading enzymes such as the MMPs. In this study the direct antirheumatic effects of devil's claw on the production of MMPs in stimulated human chondrocytes were examined. The capability of the herb to suppress the MMP production via the inhibition of the synthesis of inflammatory cytokines could explain its therapeutic effect in arthritic inflammations.[30]

Analgesic Activity

Devil's claw acted synergistically with morphine in resolving two typical symptoms of neuropathic pain in rats. The 2016 study investigated the advantage of co-administration of a subanalgesic dose of morphine preceded by a low dose of devil's claw. The results support the strategy of using an adjuvant drug to improve opioid analgesic efficacy.[31]

The results of a 2014 *in vivo* study suggest that devil's claw extracts have potential analgesic effects in acute postoperative pain and chronic neuropathic pain in rats. The experiments showed that rats treated with 300mg/kg of devil's claw extract had reduced ultrasonic vocalisations (animal behavioural sounds) at six hours and 24 hours after a surgical incision in the foot.[32]

Antidiabetic Activity

A study investigating the antidiabetic effect of devil's claw in induced diabetic rats returned positive results. Dose dependent, significant reductions in the blood glucose concentration of both fasted normal and fasted diabetic rats were observed.[33]

Anticancer Activity

Tumour regression has been documented in two patients with follicular lymphoma who were taking devil's claw. Whether these regressions were causally related to the intervention or were coincidental is uncertain, but the timing of the intervention points to a treatment effect. Both patients were taking 500mg of devil's claw daily and one patient was also taking Essiac (a herbal tea including burdock root, Indian rhubarb root, sheep sorrel and slippery elm). CT scan images at baseline and follow-up (10 and 11 months later) provided objective evidence of regression of the tumours. Spontaneous regression in low grade lymphoma has been reported in seven of 44 patients not taking herbal medicines or COX-2 inhibitors. However the timing of the response in these two patients suggested a possible therapeutic benefit.[34]

Central Nervous System Activity

One study showed that devil's claw can markedly delay the onset, as well as reduce the average duration, of convulsion in mice. Although not conclusive it seems that the extract produces its anticonvulsant activity by enhancing GABAergic neurotransmission and/or facilitating GABAergic action in the brain. This lends pharmacological support to the suggested traditional uses of devil's claw in the treatment, management and/or control of epilepsy and childhood convulsions in some rural communities of South Africa.[35]

Uterotonic Activity

Experimental evidence obtained in an *in vitro* study indicates that devil's claw possesses contractile, uterotonic action on the mammalian uterus. This finding suggests that it should be contraindicated in pregnancy. However the findings of the laboratory animal study lend pharmacological credence to the suggested traditional obstetric uses of the plant's secondary root extract for induction or acceleration of labour, as well as for expelling retained placentas in pregnant women in some rural communities of southern Africa.[36]

Appetite Modulating Activity

Devil's claw has been used as an appetite modulator but most evidence is anecdotal and no clear scientific studies relating to appetite modulation have been done. Ghrelin is a stomach derived peptide that has been identified as the only circulating hunger hormone that exerts a potent appetite stimulant effect via activation of its receptor, the growth hormone secretagogue receptor (GHS-R1a). Hence the ghrelinergic system represents a promising target to treat obesity and obesity related diseases. A 2014 study analysed the GHS-R1a receptor activating potential of devil's claw

and its effect on food intake ***in vivo***. A significant appetite stimulant effect was observed in mice following peripheral administration of devil's claw.[37]

Antimicrobial Activity

Devil's claw has been shown to be effective against a panel of bacteria in an ***in vitro*** study.[38]

Indications

- Rheumatic and arthritic conditions including muscle pain such as degenerative rheumatoid arthritis, osteoarthritis and tendonitis
- Mild digestive disorders such as bloating, flatulence, dyspepsia and loss of appetite
- Traditionally used in small amounts to relieve menstrual and labour pain

Energetics

Cold, pungent.

Use in Pregnancy

Not recommended.

Contraindications

Use cautiously in patients with gastric and duodenal ulcers, gallstones or acute diarrhoea as devil's claw may cause gastric irritation.

Drug Interactions

Combination may be beneficial with non-steroidal anti-inflammatory drugs (NSAIDs). Caution with warfarin and acid-reducing drugs (such as H_2 antagonists and proton pump inhibitors).

Administration and Dosage

Liquid Extract:	1:1
Alcohol:	25%
Weekly Dosage:[39]	20 to 40mL

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