HYPOXIS RADIX

Definition

Hypoxis Radix consists of the fresh or dried sliced corm of *Hypoxis hemerocallidea* Fisch. & C.A. Mey. (Hypoxidaceae)

Synonyms

H. rooperi S. Moore

Vernacular names

Inkomfe, ilabatheka (Z), moli kharatsa (S), African potato

Description

Macroscopical

Figure 1a: Live plant

Figure 1b: Corms

Perennial geophyte with a tuberous rootstock; **leaves** deciduous, in three distinct groups, strap shaped, up to 30cm long × 3.2 cm in width, folded from the midrib, distinctly ribbed, glabrous on the upper surface, softly pilose on the margin and lower surface; **flowers** (Oct-Jan) yellow, borne on slender villous pedicels; perianth segments ca. 20mm long and 15mm wide, bearing soft hairs on the margin and lower surface; calyx, developing fruit and bracts all villous.

Figure 2: Colour plate from FP5: 172

Microscopical

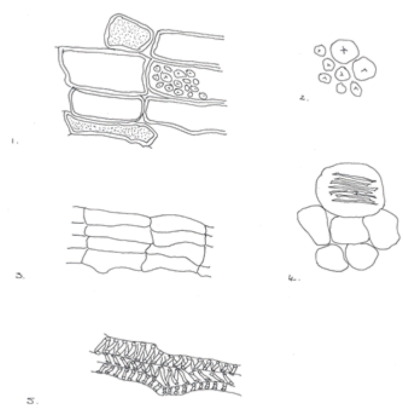

Figure 3: microscopical features

Characteristic features are: abundant thin walled pale brown cork tissue (3); numerous bundles of calcium oxalate raphides in the parenchyma cells of the central stele, individual needles up to 80µ long (4); the thick walled cells of the central stele containing numerous small round starch grains (1), mostly 7-15µ in diameter with occasional larger grains to 80µ in diameter, with cleft hilum (2); tannin idioblasts with red-brown contents becoming black-green with $FeCl_3$ in the stele parenchyma (1); the abundant very long thin reticulate vessels, 40-80µ in diameter, staining pink with phloroglucinol/HCl (5).

Crude drug

The corms usually seen in the marketplace are ca. 60mm in diameter but may be up to

25cm in diameter, bearing a ring of stout vertical bristles at the apex and a fringe of numerous secondary roots at the base; brown-black externally, bright yellow internally when freshly cut, darkening rapidly on exposure to air; exudes a sticky resinous yellow juice from the cut surface.

Geographical distribution

Common in grasslands of the Eastern Cape Province, KwaZulu/Natal, Mpumalanga, Northern Province, Gauteng, Swaziland and Lesotho.

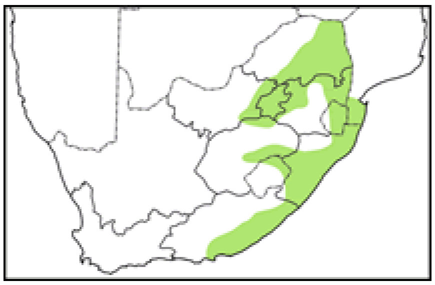

Figure 4: distribution map

Quality standards

Identity tests

Thin layer chromatography on silica gel using as solvent a mixture of toluene:diethyl ether:1.75M acetic acid (1:1:1). Reference compound cineole (0,1% in chloroform). Method according to Appendix 2a.
R_f values of major compounds: 0.23 (purple); 0.39 (mustard); 0.47 (purple); 0.78 (pink); cineole: 0.79 (blue-purple)

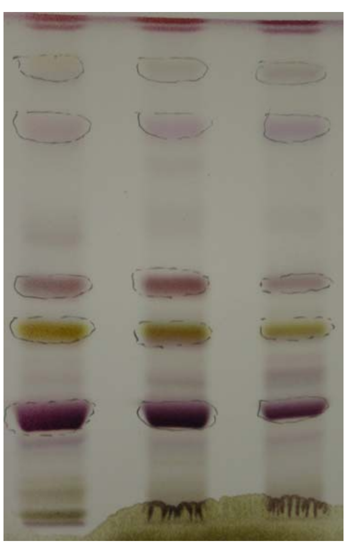

Figure 5: TLC plate

HPLC on C_{18} column, method according to Appendix 2b.

Major compounds:
Methanol extract: Retention times (mins): 6.56

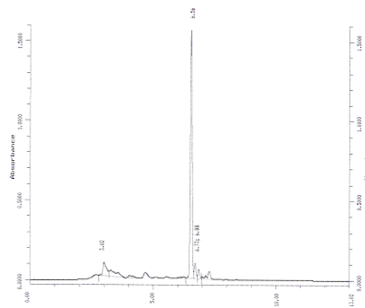

Figure 6: HPLC spectrum

Ethanol (70%) soluble extractive value (dried corm): not less than 31.0% (range: 31.07-36.10%)

Purity tests

Assay

Not yet available

Major chemical constituents

A major constituent of the corms of *Hypoxis hemerocallidea* as well other *Hypoxis* species is the pentenyne glycoside hypoxoside (figure 7), which on hydrolysis gives an aglycone with the trivial name of rooperol. Up to 4,5% of hypoxoside has been recorded in *H. hemerocallidea* corms, but the amount appears to vary seasonally[1]. The corms are reported to contain, in addition to hypoxoside, β-sitosterol, sterolins (sterol glycosides, up to 9mg/100g) and monoterpene glycosides[2,3]. The cytokinins

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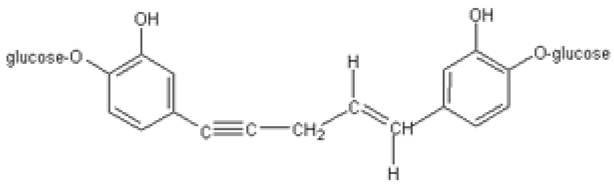
1 Drewes, S.E., Hall, A.J., Learmonth, R.A. and Upfold, U.J. (1984). Isolation of hypoxoside from *Hypoxis rooperi* and synthesis of (*E*)-1,5-*bis* (3',4'-dimethoxyphenyl) pent-4-en-1-yne. *Phytochemistry* **23(6)**: 1313-1316.

2 Pegel, K.H. (1973). Extraction of phytosterol glycosides from *Hypoxis* tubers. S.A.Patent ZA 7201855.

zeatin, zeatin riboside and zeatin glucoside have also been isolated from corms of this species[4].



hypoxoside

Figure 7: chemical constituents

Dosage forms

In traditional medical practice, an aqueous decoction is taken orally; fresh juice from the tuber is applied externally. As a patent remedy, tuber extracts are available in capsule and tablet form.

Medicinal uses

As traditional remedies, aqueous infusions are given to sickly children as a tonic, and to adults for dizziness and mental disorders, while fresh juice is applied to burn wounds [GR1, 12]. Following reports of its efficacy as a remedy for BPH (benign prostatic hyperplasia)[5]., *H. hemerocallidea* extracts have been used for some years in Europe for this purpose, bioactivity being ascribed to the sterol component. Additional claims, based on hypoxoside activity, have been made for its medical benefits in the treatment of cancer, HIV-AIDS and inflammation[6].

Note. A general immunomodulatory effect, attributable to phytosterols[7,8], is the basis of efficacy claims for the South African patent remedy, Moducare®, reputed to be derived from *Hypoxis hemerocallidea* but in fact manufactured from pine wood extracts. The latter are good sources of β-sitosterol and its glucoside, both of which are common in nature.

Pharmacology/bioactivity

Hypoxoside and its glycone rooperol have been shown to possess antimutagenic and cytotoxic properties [6.] Preliminary tests with hypoxoside indicated low or no toxicity following oral and intraperitoneal administration to mice (LD_{50} = 0 for 500mg/kg) and intravenous administration to rabbits (>100mg/kg). No foetotoxic or teratogenic effects were noted in mice following oral administration of up to 100mg/kg.

An *in vitro*/*in vivo* assessment of antineoplastic activity of Southern African plant species was unable to show cytotoxic activity in cell culture (CA-9KB) of ethanol:water (50:50) fresh leaf extracts, or antitumour activity of similar extracts in mice against Leuk-L1210 and Leuk-P388[9]. In an *in vitro/in vivo* study of 5-alpha reductase inhibitory activity of a tuber extract, no activity was demonstrated.[10]

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3 Wagner, H. and Wiesenauer, M. (1995). Phytotherapie: pp. 198-199. Gustav Fischer Verlag, Stuttgart.

4 Van Staden, J. (1981). Constituents of *Hypoxis rooperi*, a valuable medicinal plant in South Africa. *Deutsche Apotheke Zeitung* **33**: 460-464.

5 Pegel, K.H. (1984). B-sitosterol β-D-glucoside (sitosterolin) as the active agent in Harzol® and other phytopharmaka. *Extracta Urologica* **1**, suppl. 7: 105-111. (In German)

6 Albrecht, C. F. (1996). Hypoxoside as a putative non-toxic, multi-functional prodrug for the treatment of cancer, HIV-AIDS and inflammatory conditions. Proceedings of the 2nd IOCD International Symposium, Victoria Falls, Zimbabwe, 25-28 February 1996.

7 Bouic, P.J.D. (1998). Sterols and sterolins-the natural , non-toxic immunomodulators and their role in the control of rheumatoid arthritis. *Health Talk* 1998: 48-49.

8 Bouic, P.J.D. *et al.* (1996). Beta-sitosterol and beta-sitosterol glucoside stimulate human peripheral blood lymphocyte proliferation: implications for their use as an immunomodulatory vitamin combination. *International Journal of Immunopharmacology* **18(12)**: 693-700.

9 Charlson, A.J. (1980). Antineoplastic constituents of some Southern African plants. *Journal of Ethnopharmacology* **2(4)**: 323-335.

10 Rhodes, L. *et al.* (1993). Comparison of finasteride (Proscar), a 5-alpha reductase inhibitor, and various commercial plant extracts

A clinical assessment of the effects of whole plant extracts of *H. hemerocallidea* (randomised, placebo-controlled, double blind study involving 200 adult male patients with mild to moderate BPH) reported a statistically significant decrease in symptoms[11]. Peak flow rate was increased from 9.9 to 15.2 ml/sec and a decreased post void residual volume observed, compared with placebo (dose: 60.0mg/day; duration of trial: 6 months). An 18-month follow-up to the study showed that patients previously randomised to the placebo group, then later treated with the extract, had an improvement both in symptom scores and flow rates. The follow-up also showed that patients who had received *Hypoxis* extract for the first 6 months of the trial continued to improve during the subsequent 12-month period, irrespective of whether medication was continued or not.

Other clinical studies have demonstrated an improvement in symptoms associated with BPH in patients treated with *Hypoxis* extracts[12], [13], [14].

Whether the efficacy of *H. hemerocallidea* in the treatment of BPH is due to hypoxoside, sterols or the whole plant extract is not known at present. The efficacy of β-sitosterol in the treatment of BPH is however well-documented [5, 15], as is its immunomodulatory [7,8] and antimutagenic activity[16].

Contraindications

In view of the sterol content of this species, its use during pregnancy should be undertaken with caution.

Adverse reactions

Taken orally, this species is reputed to cause purging[GR1]

Precautions

No special precautions

Dosage

To be determined

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in *in vitro* and *in vivo* 5-alpha reductase inhibition. *Prostate* **22 (1)**: 43-51.

[11] Lowe, F.C. *et al.* (1998). A review of recent placebo-controlled trials utilising phytotherapeutic agents for the treatment of benign prostatic hyperplasia (BPH). *Prostate* **37(3)**: 187-193. (Review article)

[12] Buck, A.C. (1996). Phytotherapy for the prostate. *British Journal of Urology* **78(3)**: 325-336 (Review article).

[13] Muller-Christiansen, K. (1993). Besonderer Stellenwert der Phytopharmaka. *Therapiewoche* **43(26/27)**: 1490-1496. (German).

[14] Dreikorn, K. & Schonhofer, P.S. (1995). The place of phytotherapy in the treatment of Benign Prostatic Hyperplasia. *Urologe* **34(2)**: 119-129. (Review article-German)

[15] Berges, R.R. *et al.* (1995). Randomised, placebo-controlled, double blind clinical trial of β-sitosterol in patients with benign prostatic hyperplasia. *The Lancet* **345** (June 17):1529-1532.

[16] Merck & Co. Inc. (1989). The Merck Index 11th edition, Rahway, Massachusetts.