PRUNUS AFRICANA CORTEX

**Definition**
Prunus Africana Cortex consists of the dried bark of Prunus africana (Hook. f.) Kalkm. (Rosaceae).

**Synonyms**
*Pygeum africanum* Hook. f.

**Vernacular names**
Bitter almond, African prune, red stinkwood, umkakase (Xh); umdumizulu, inyazangomelimnyama, umkhakhazi, inkokhokho, umlalume (Z); muchambati (Sh)

**Description**

**Macroscopical**

*Figure 1: Live plant*

Evergreen tree to 10-25m in height; leaves alternate, leathery, simple, elliptic, with deep pink petiole and midrib, margin finely crenate-serrate, 4-(8-10)-16 × 1.5-7cm, glabrous, dark green glossy above, paler green on underside; flowers (Mar-May) small, fragrant, white or cream, solitary or in axillary racemes; fruit (Nov-Mar) brown to purple, ellipsoid, very bitter, 8 ×12 mm. Freshly cut bark, crushed leaf and fruit all smell strongly of HCN.

**Microscopical**

Characteristic features are: the numerous rosette aggregates (cluster crystals) of calcium oxalate, up to 50µ in diameter, loose in the powdered drug or in cells of the parenchyma adjacent to fibre bundles, forming a crystal “sheath” (2+5); the abundant cork tissue with cells having deep red-brown contents (3+4); the yellow collenchyma of the outer cortex (1); the numerous sclereids, occurring singly or in groups in the parenchyma of the secondary phloem (7); individual sclereids often very large, up to 220µ in diameter, staining deep magenta-pink with phloroglucinol/HCl; the abundant thick-walled fibres occurring in bundles surrounding the medullary rays; individual fibres up to 50µ in diameter with narrow lumen (5); the occasional fragments of lichen, a single layer in thickness, pale green in colour (6).

**Crude drug**

*Figure 3: microscopical features*

Occurs as large, flat to slightly curved pieces, up to 50 cm long and 20mm in thickness; red-brown on the inner surface, grey-black, rough-corrugated, deeply square-fissured on the outer surface; heavy, dense textured, breaking with a short fracture; powdered drug deep red-brown in colour.

**Geographical distribution**

Moist evergreen forest of mountain mistbelt areas of the Eastern Cape Province, KwaZulu/Natal and Mpumalanga; often in riverine vegetation or on forest margins. Occurs throughout tropical Africa, in eastern Zimbabwe, Mozambique, Kenya, Uganda,
Prunus africana is listed in Appendix II of the Convention on International Trade in Endangered Species of Wild Flora and Fauna (CITES).

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. Rf values of major compounds: 0.27 (light purple); 0.35 (purple); 0.54 (brown); 0.72 (grey); cineole: 0.76 (blue-purple)

HPLC on C18 column, method according to Appendix 2b.

Major compounds:

Methanol extract:
Retention times (mins): 2.62; 3.61

Purity tests

Various qualitative and quantitative assays have been developed for major constituents of this species.

Major chemical constituents

The presence of the cyanogenic glycoside amygdalin in the bark, leaf and fruit of this species was documented by 1962GR1. Since then, a growing interest in the use of bark extracts to treat benign prostatic hyperplasia (BPH) has prompted numerous studies of

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bark secondary chemistry. These\textsuperscript{6, 7} have revealed the presence of:

1. phytosterols (e.g. $\beta$-sitosterol 15-18%, and its 3-O-glycoside, $\beta$-sitostenone, campesterol, daucosterol)
2. pentacyclic triterpenoids (mainly of theoleanolic and ursolic acid type)
3. long chain aliphatic alcohols (e.g. $n$-docosanol; $n$-tetracosanol)
4. long chain (C12-C22) fatty acids (e.g. palmitic acid)
5. \textit{trans}-ferulic acid esters of 2, 3 and 4.

\textbf{Figure 7: chemical constituents}

\textbf{Dosage forms}

In traditional practice, bark infusions are taken orally. In Europe, the lipid/sterol fraction, usually obtained by extraction of the bark with chloroform or dichloromethane, is taken orally. Tadenan\textsuperscript{®} is one such preparation.

\textbf{Medicinal uses}

Bark preparations are used by the Zulu people to treat intercostal pains\textsuperscript{GR 12} and elsewhere in Africa as a purgative and a remedy for stomach pains. In Europe, bark extracts are used in the treatment of BPH. Clinical data support its use for the relief of lower urinary tract symptoms of Stage 1 and 2 BPH (nocturia, polyuria and urinary retention) in cases where diagnosis of prostate cancer is negative\textsuperscript{6}.

\textbf{Pharmacology/bioactivity}

Standardised bark extract (lipid/sterol fraction) has been in clinical use in Europe since 1969. There have been numerous studies aimed at establishing both efficacy and precise mode of action; for a review of the current state of knowledge see references 6-8.

The beneficial effects noted in patients suffering from BPH following treatment with standardised bark extract include significant reduction in frequency of urination and residual urine volume and an increase in voided volume and flow rate, as compared with placebo. Reduction in oedema and inflammation as well as diminished histamine-induced vessel permeability have been demonstrated. These effects have been attributed to the presence of phytosterols (anti-inflammatory, antioestrogen), pentacyclic triterpenes (anti-oedema, immunostimulant) and ferulic acid esters (hypcholesterolaemic). It seems likely that several mechanisms are involved and that there may be synergism of the various secondary metabolites.

Although the etiology of BPH is not completely understood, it is thought that \textit{Prunus africana} bark sterols/lipids may act by some or all of the following mechanisms:

1. 5$\alpha$-reductase inhibition, preventing conversion of testosterone to dihydrotestosterone (DHT)
2. aromatase inhibition, preventing conversion of DHT to androstandiol and hence blocking the synthesis of oestrogen /oestradiol
3. blocking of leukotriene synthesis by inhibition of 5-lipoxygenase
4. reduction in oedema by inhibition of glucosyl transferase and $\beta$-glucuronidase

\textsuperscript{8} WHO (2002). Monographs on selected medicinal plants Volume 2 pp. 246-258.
Contraindications

Preparations of this species are contraindicated in cases of known allergy to members of Rosaceae, as well as during pregnancy, lactation and in children under the age of 12 years because of effects on androgen and oestrogen metabolism.

Adverse reactions

Lipophilic bark extracts appear to be well tolerated in humans. A few cases of minor and transient G-I side effects e.g. diarrhoea, nausea and gastric pain have been reported and single cases of constipation, dizziness and visual disturbance.

Precautions

A diagnosis of BPH is preferable before commencing treatment with standardised bark extract. Currently available evidence does not suggest carcinogenesis, mutagenesis or impairment of fertility associated with the use of *Prunus africana*.

Dosage

For the treatment of BPH, 100-200mg of standardised extract/day in divided doses.