

WARBURGIA SALUTARIS CORTEX

Definition

Warburgia Salutaris Cortex consists of the dried bark of *Warburgia salutaris* (Bertol. f.) Chiov. (Canellaceae).

Synonyms

Warburgia breyeri Pott.
W. ugandensis Sprague
Chibaca salutaris Bertl. f.

Vernacular names

Pepper bark tree, isibaha (Z, V), sebaha (S); amazwecehlabayo (Z)



Figure 1: Fresh bark

Description

Macroscopical ^{GR25}

Slender, small to medium sized tree attaining a height of 5-10m; **leaves** aromatic, ovate-lanceolate, entire, alternate, glabrous, glossy dark green above, paler dull green on underside, 4.5-11 × 1-3cm; **flowers** (April) small, axillary, white to green-yellow, up to 7mm in diameter, borne singly or in few-flowered cymes; **fruit** a globose berry, up to 40mm in diameter, leathery, black when mature; **bark** rich brown, rough, peppery-aromatic.

Microscopical

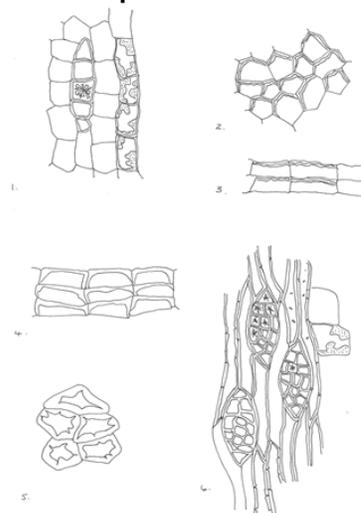


Figure 2: microscopical features

Characteristic features are: the abundant rosette aggregates (cluster crystals) of calcium oxalate up to 20µ in diameter, loose in the powdered drug or in cells of the medullary rays (1); the abundant groups of sclereids of the outer cortex (5), staining light pink with phloroglucinol/HCl; pale yellow-brown cork tissue (2+3); the oil cells of the parenchyma with red-brown contents (1); the abundant fibres (6).

Crude drug

Occurs in the marketplace as curved or channelled pieces up to 30cm long and 3-15mm in thickness; smooth grey-brown when young, showing numerous lenticels; rough-scaly when older, with a thick cork layer; grey-brown on the external surface; pale cream-brown to red-brown on the inner surface; breaking with a splintery fracture; odour aromatic; taste bitter and peppery.

Geographical distribution

This species has a restricted distribution in evergreen forests and wooded ravines of northern KwaZulu-Natal, Swaziland, Mpumalanga and the Northern Province (also Uganda and Kenya).



Figure 3: 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: 0,12 (purple); 0,33 (black); 0,53 (black); 0,64 (brown); 0,76 (purple); cineole: 0,76 (blue-purple)

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

Major compounds:

Methanol extract:

Retention times (mins): 7.14; 7.96; 10.13; 11.88

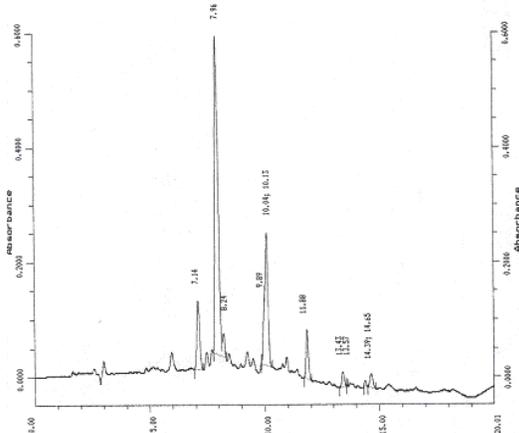


Figure 4: HPLC spectrum

Ethanol (70%) soluble extractive value: not less than 16.0 % (range: 15.94-23.04%)

Purity tests

Assay

Not yet available

Major chemical constituents

A number of drimane sesquiterpenes have been isolated from the stem bark of this and other *Warburgia* species. These dialdehydes include: warburganal^{1,2,3,4} (see a below) polygodial⁵, salutarisolid⁶, muzigadial^{7,8} (see b below), ugandensidial, isopolygodial⁶ and mukaadial⁶. Phytochemical tests in our laboratories indicated the presence of tannins. The sugar alcohol mannitol (3%) has been reported as present^{GR1}

¹ Kubo, I., Lee, Y-W., Pettei, M., Pilkiewicz, F. & Nakanishi, K. (1976). Potent army worm antifeedants from the East African *Warburgia* plants. *Journal of the Chemical Society, Chemical Communications* **24**: 1013-1014.

² Kubo, I., Miura, I., Lee, Y-W., Pettei, M., Pilkiewicz, F. & Nakanishi, K. (1977). Muzigadial and warburganal, potent antifungal, anti-yeast and African worm antifeedant agents. *Tetrahedron Letters* **52**: 4553-4556.

³ Kubo, I., Matsomoto, T., Kakooko, A.B. & Mbiru, N.K. (1983). *Chemistry Letters*: 979.

⁴ Mashimbye, M.J., Drewes, S.E., Appleton, C.C. and Cunningham, A.B. (1992). Observations on the molluscicidal properties of (-)-warburganal on the South African *Bulinus africanus* (Planorbidae). *Journal of Medical and Applied Malacology* **4**: 37-40.

⁵ Mashimbye, M.J. (1993). PhD thesis, University of Natal.

⁶ Mashimbye, M.J., Maumela, M.C. & Drewes, S.E. (1999). A drimane sesquiterpinoid lactone from *Warburgia salutaris*. *Phytochemistry* **51**: 435-438.

⁷ El-Feraly, F.S., McPhail, A.T. & Onan, K.D. (1978). *Journal of the Chemical Society, Chemical Communications* **1**: 75-76.

⁸ Rabe, T. & van Staden, J. (2000). Isolation of an antibacterial sesquiterpenoid from *Warburgia salutaris*. *Journal of Ethnopharmacology* **73**: 171-174.

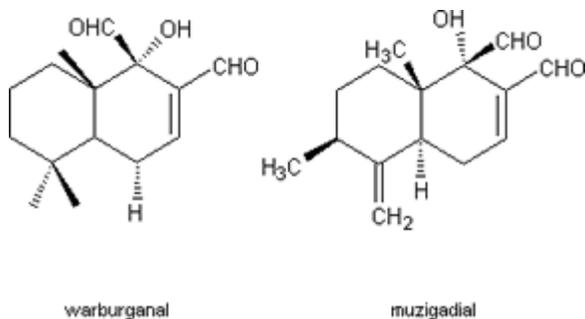


Figure 5: chemical constituents

Dosage forms

Powdered bark is taken orally (aqueous infusion), smoked, or mixed with fat and applied externally as an ointment.

Medicinal uses

This species is highly regarded as an expectorant for the treatment of dry cough and as a remedy for colds, chest infections, sinusitis, malaria, venereal diseases, stomach ulcers, toothache and dermatological disorders^{GR1 and 12}.

Pharmacology/bioactivity

The biological activity of drimane sesquiterpenoids is well documented and includes antimicrobial, insect antifeedant, cytotoxic, molluscicidal and skin irritant effects⁹. The antifungal and antibacterial activity of warburganal, polygodial and muzigadial against a range of organisms, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida utilis*, *Bacillus subtilis* and *Escherichia coli*, has been demonstrated⁹. Muzigadial was found to be the main antibacterial agent in the bark of *Warburgia salutaris*⁸, with an MIC of 12.5µg/ml against both *Staphylococcus aureus* and *Bacillus subtilis*. The MIC of neomycin, used as a control in this study, was 0.375µg/ml for the former organism and 0.2µg/ml for the latter.

Warburganal has been shown to have cytotoxic and haemolytic properties, and

⁹ Jansen, B.M.J. & de Groot, A. (1991). The occurrence and biological activity of drimane sesquiterpenoids. *Natural Products Reports* **8**: 309-318.

polygodial to enhance the activity of actinomycin D and rifampicin (papers cited in^{GR12}). Toxicity of inner bark extracts has been demonstrated in preliminary screening tests. (pers. comm. in^{GR12}). Both root and stem bark have been reported as ineffective in treating experimental malaria^{GR1}.

The results of an investigation of cytotoxicity and antiviral activity of 16 South African plant species¹⁰ showed that aqueous extracts of *Warburgia salutaris* were markedly cytotoxic, at all concentrations used, to HeLa, Vero, Jurkat E6.1, AA-2 and CEM-SS cells. These results are in agreement with findings cited above for warburganal. Similar extracts were shown to reduce infectivity of both Coxsackie B2 virus and HSV-1, at most dilutions tested. In direct *in vitro* cell culture antiviral assays, aqueous extracts were however not found to inhibit replication of either Coxsackie B2 virus or HSV-1.

Methanolic extracts of Kenyan bark collections were assessed *in vitro* for anti-giardiasis activity, but were found to be inactive against *Giardia lamblia* in the concentration used (1000ppm)¹¹.

Antibacterial activity of aqueous (conc. 1mg/ml) and methanolic extracts of South African dried barks was assessed *in vitro* against *Bacillus subtilis*, *Staphylococcus aureus* and *S. epidermidis*¹². The results were equivocal.

Aqueous extracts of South African dried leaf samples were assessed for *in vitro* molluscicidal activity against *Bulinus*

¹⁰ Treurnicht, F. T. (1997). An evaluation of the toxic and potential antiviral effects of some plants used by South Africans for medicinal purposes. MSc thesis, University of Stellenbosch.

¹¹ Johns, T., Faubert, G.M., Kokwaro, J.O., Mahunnah, R.L.A. and Kimanani, E.K. (1995). Anti-giardial activity of gastrointestinal remedies of the Luo of East Africa. *Journal of Ethnopharmacology* **46**(1): 17-23.

¹² Rabe, T. and van Staden, J. (1997). Antibacterial activity of South African plants used for medicinal purposes. *Journal of Ethnopharmacology* **56**: 81-87.

africanus and found to be active (LC₅₀: 2.483mg/ml).¹³

Contraindications

None known.

Adverse reactions

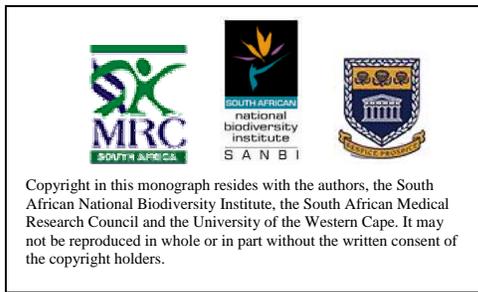
None reported for this species when used in the traditional manner. Skin irritation and contact dermatitis have however been demonstrated for individual drimanes e.g. warburganal and polygodial⁹.

Precautions

In view of reports of possible toxicity, this species should preferably be used only under the supervision of a competent traditional practitioner.

Dosage

To be determined.



¹³ Clark, T.E. and Appleton, C.C. (1997). Molluscicidal activity of *Apodytes dimidiata* E. Mey. ex Arn (Icacinaceae), *Gardenia thunbergii* L.f. (Rubiaceae) and *Warburgia salutaris* (Bertol. f.) Chiov. (Canellaceae) plants. *Journal of Ethnopharmacology* **56(1)**: 15-30.