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Review on plants with CNS-effects used in traditional South African medicine against mental diseases

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ABSTRACT

The majority of the population in South Africa use traditional health care to treat various mental conditions. In this review, we present ethnobotanical information on plants used by the traditional healers in South Africa to treat mental illnesses, specifically epilepsy, depression, age-related dementia and debilitative mental disorders. Details of the recent scientific studies conducted on some of these plants are reviewed.

Extracts of *Searsia chirindensis*, *Cotelydon orbiculata* and *Leonotis leonurus* have shown *in vivo* anti-convulsant activity. Extracts from *Searsia dentata* and *Searsia pyroides* showed spontaneous epileptiform discharge in mouse cortical slices, and acted as NMDA-receptor antagonists. Apigenin, amentoflavone and agathisflavone with affinity to the benzodiazepine site on the $GABA_A$-receptor were isolated from *Searsia pyroides*. Naringenin with affinity to the $GABA_A$-benzodiazepine receptor was isolated from *Mentha aquatica*.

Agapanthus campanulatus, *Boophone disticha*, *Mondia whitei* and *Xysmalobium undulatum* exhibited antidepressant-like activity in three *in vivo* models for depression. Amaryllidaceae alkaloids with activity to the serotonin transporter were isolated from *Boophone disticha*. The alkaloid mesembrine, which act as a serotonin reuptake inhibitor, was isolated from *Sceletium tortuosum*.

Investigations of plants used to treat age-related dementia and debilitative mental disorders lead to the isolation of a number of Amaryllidaceae alkaloids with acetylcholinesterase inhibitory activity from *Boophone disticha* and *Crinum* species. Extracts of *Mentha aquatica*, *Gasteria croucheri*, *Ruta graveolens* and *Scotia brachypetala* inhibited MAO-B. Naringenin was isolated from *Mentha aquatica* as a MAO inhibitor.

Only a small number of the more than 300 southern African plant species reported to treat or affect the CNS have been scientifically evaluated. Very few of the active compounds have been isolated and identified.

1. Introduction

Currently in South Africa a dual healthcare system exists: one based on traditional medicine and another based on Western medical practice. The use of traditional medicine in South Africa is widespread where it is estimated that as high as 80% of the black population consult traditional healers. The more available traditional healthcare system offers a cheap, individualized and culturally appropriate alternative to the costly allopathic system. The state healthcare system with 8000 doctors including 18 neurologists provides aid for 85% of the population (approximately 38 million people) whereas 15% of the population (approximately 7 million people) is covered by private healthcare system with 12,000 doctors including 55 neurologists (Eastman, 2005). The number of traditional healers, on the other hand, outnumbers the allopathic doctors by at least 10 to 1 (Morris, 2001).

Traditional practice may include psychological, spiritual and cultural elements, as well as a medical element. This review deals with the medical element, namely the plants traditional healers use in their treatments. In this paper we will review plants used in South African traditional medicine in these categories of indications: epilepsy and convulsions, depression, age-related dementia and debilitative mental disorders.

Abbreviations: ACh, acetylcholine; AChE, acetylcholinesterase; AD, Alzheimer's disease; AIDS, acquired immune deficiency syndrome; BIC, bicuculline; BuChE, butyrylcholinesterase; CNS, central nervous system; DAT, dopamine transporter; DOPA, dopamine; GABA, γ-aminobutyric acid; HIV, Human immunodeficiency virus; MAO, monoamine oxidase; MAOI, monoamine oxidase inhibitor; NAT, noradrenalin transporter; NMDA, *N*-methyl-D-aspartic acid; PD, Parkinson's disease; PIC, picrotoxin; PTZ, pentylenetetrazole; SERT, serotonin transporter; SSRI, serotonin reuptake inhibitor.

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Table 1
Southern African plants traditionally used for sedative, anticonvulsant and epilepsy treatments

Family *Species* Colloquial name – meaning[1]	Traditional use, ethnobotanical information and known active constituents
Adiantaceae (Pteridaceae)	
Pellaea calomelanos (Swartz) Link	Taken as an infusion or smoked to treat convulsions in Zimbabwe (Gelfand et al., 1985). The Kwena and Kgatla administer milk decoctions of rhizome to frightened children at night (Hutchings et al., 1996) presumably to calm them
Alliaceae	
Tulbaghia alliaceae L.f. Ishaladi lezinyoka	Rhizome infusion is administered as enemas for fits in the Eastern Cape of South Africa (formerly the Transkei) (Hutchings et al., 1996). The Zulu name, *ishaladi lezinyoka* means 'garlic/shallots of the snakes', the plant parts smell of garlic and is used by Zulu as a snake repellent (Hutchings et al., 1996)
Tulbaghia violaceae Harv. Syn: *Omentaria cepacea* Salisb., *T. cepacea* L.f. Isihaqa (Z) *haqa* (v) surround, encircle, enclose	In Transkei the bulb is rubbed on the body as protection from evil spirits before ritual dancing by diviners (Hutchings et al., 1996). Leaves are rubbed on the head of restless young children (Batten and Bokelmann, 1966) presumably to calm them
Amaryllidaceae	
Boophone disticha (L.f.) Herb. Syn: *B. longepedicellata* Pax Incotho, incwadi (Z)	Weak decoctions of bulb scales given to sedate violent, psychotic patents (van Wyk and Gericke, 2000). Traditional healers and patients in South Africa drink bulb infusions to induce hallucinations for divinatory purposes, and also as a medicine to treat mental illness (Sobiecki, 2002)
Anacardiaceae	
Lannea discolor (Sond.) Engl. *Lannea schweinfurthii* (Engl.) Engl.	The Luvale of Zambia use the leaves to prevent fits (Watt and Breyer-Brandwijk, 1962) The roots are covered with a dense layer of very fine root hairs, that are reportedly used as a sedative snuff, and the smoke of the burned roots is inhaled as a sedative (van Wyk and Gericke, 2000)
Searsia chirindensis (Baker f.) Moffett Syn: *Rhus chirindensis* Bak. f.	Bark is used to strengthen the body, stimulate circulation and for rheumatism (Pujol, 1990), bark decoctions are traditionally administered for mental disturbances in Transkei (Hutchings et al., 1996). Stembark aqueous extract (100–800 mg/kg i.p.) significantly delayed ($p < 0.05$–0.001) the onset of, and antagonized pentylenetetrazole-induced seizures (Ojewole, 2008c). The plant's stem-bark aqueous extract (100–800 mg/kg i.p.) also profoundly antagonized picrotoxin-induced seizures, but only weakly antagonized bicuculline-induced seizures (Ojewole, 2008c). The aqueous and ethanolic extracts of the leaves and roots did not show any activity in the $GABA_A$-benzodiazepine receptor assay (Risa et al., 2004a,b)
Searsia natalensis (Bernh. ex Krauss) F.A. Barkley Syn: *Rhus natalensis* Bernh. ex krauss	Roots are used to treat fits in children (Watt and Breyer-Brandwijk, 1962)
Searsia pyroides (Burch.) Moffett Syn: *Rhus pyroides* Burch.	In Zimbabwe the roots are use in infusions to treat delirium (Gelfand et al., 1985). Two biflavonoids, agathisflavone and amentoflavone (K_i of 28 and 37 nM, respectively), with activity in the 3H-Ro 15–1788 (flumazenil) binding assay, for $GABA_A$-benzodiazepine receptor binding activity, were isolated from the ethanol extract of the leaves from *Rhus pyroides*. Extracts of *Rhus dentata* and *Rhus pentheri* were not as active as the extract from *Rhus pyroides*; both were found to contain apigenin and agathisflavone (Svenningsen et al., 2006)
Annonaceae	
Artabotrys brachypetalus Benth. Mukosvo (Sh)	Root infusions are drunk to treat convulsions in Malawi (Gelfand et al., 1985; Sobiecki, 2002). *Artabotrys* spp. Is used in Madagascar as a stimulant (Githens, 1949; Sobiecki, 2002)
Apiaceae	
Alepidea amatymbica Eckl. and Zeyh. Ikathazo (Z) *khathazo* (*n*) a kind of herb used as a remedy (Dent and Nyembezi, 1999)	Smoking the roots reportedly results in mild sedation and vivid dreams (van Wyk et al., 1997). Antihypertensive, antimicrobial and diuretic effects have been indicated in tests on animals (van Wyk et al., 1997). The dry rhizome and roots are smoked, or powdered and taken as a snuff by diviners and healers to assist in divination and communication with ancestors (Hutchings et al., 1996; van Wyk et al., 1997)
Arctopus echinatus L.	Watt (1967) mentions *Arctopus echinatus* as being administered, together with potassium nitrate, for epilepsy. He states that in this form it may cause drowsiness. This plant was held in great esteem as a "comfort to the sick", hence the Afrikaans vernacular name *sieketroos* (Pappe, 1847, 1857). It is thought to have been adopted from the Khoi-San by the Early Cape Settlers (Pappe, 1847, 1857). Their resinous roots are chemically similar to those of *Alepidea amatymbica* Eckl. and Zeyh. (*ikhathazo* in Zulu), a well-known Zulu and Sotho medicinal plant, with an equally rich ethnobotanical history (van Wyk et al., 1997; van Wyk and Gericke, 2000; Magee et al., 2007)