

Chapter 9

Antidepressant Plant Species from the Portuguese-Speaking African Countries (PALOP)

Generosa Teixeira, Eurico S. Martins, and Luís Catarino

Abstract The Portuguese-speaking African countries belong to the sub-Saharan region and are known by the acronym PALOP. As in other African countries, the traditional medicine is an important element in their cultural patrimony and the value of those ancestral practices is recognized.

The access to the biological resources from developing countries became easier but also the awareness to its preservation as well as the alert to the need of covering the insufficient scientific data on the safety, efficacy, and quality of traditional medicines.

We have done a research on the available information about medicinal plants commonly used for treatment of depression in the PALOP. The ethnobotanical data were firstly obtained through a review conducted on several works on the medicinal flora of these countries and their neighbors and information contained in the herbarium labels.

The plants with more reliable information as antidepressants were *Bacopa monnieri* (Scrophulariaceae), *Boophone disticha* (Amaryllidaceae), *Centella asiatica* (Apiaceae), *Cissampelos* genus (Menispermaceae), *Griffonia simplicifolia* (Fabaceae), *Mondia whitei* (Apocynaceae), *Palisota hirsuta* (Commelinaceae), *Securidaca longepedunculata* (Polygalaceae), and *Xysmalobium undulatum* (Apocynaceae). For these plants, we combined the data gathered on bioecology and uses with their chemical compounds and their reported pharmacological activity.

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These seem to be plants with psychotropic effects, potentially active and to which modern pharmacology can appeal. Further studies are needed to completely elucidate the chemical groups responsible for the reported antidepressant effect, and additional research is necessary therefore to confirm the exact mechanisms involved in this central nervous system pathology.

Keywords Medicinal plants • Phytotherapy • Ethnopharmacology • Depression • Ethnobotany • Portuguese-speaking African countries (PALOP)

9.1 Introduction

9.1.1 *The Portuguese-Speaking African Countries*

In Africa, there are five countries in which Portuguese is the official language: Angola, Cape Verde, Guinea-Bissau, Mozambique, and São Tome and Principe. All of them were Portuguese colonies and acquired their independence in 1974 and 1975.

The Portuguese-speaking countries in Africa are also known as PALOP—*Países Africanos de Língua Oficial Portuguesa* (formed in 1992)—and besides the official language, they also share a long common history and a strong cultural identity.

The PALOP occupy different geographic regions in the African continent: Cape Verde and Guinea-Bissau are located in Western Africa, Sao Tome and Principe and Angola in Middle (Central) Africa, and Mozambique in Eastern Africa (Fig. 9.1). Two of them, Cape Verde and Sao Tome and Principe, are small archipelagos, while others are among the largest, in the case of Angola, the 7th largest country in the African continent (UN Statistics Division 2006).

These countries show a huge cultural and ethnical diversity. In Angola, Guinea-Bissau, and Mozambique, a large number of ethnical groups coexist, each one with its beliefs, practices, and ways of nature appropriation. In Cape Verde and Guinea-Bissau, Creole emerged as the vehicular language, while, in the remaining PALOP, Portuguese is the vehicular language.

In terms of natural resources, these five countries show huge differences. Some are among the poorest countries in the world, showing a high reliance on foreign aid, and their economy is dependent on such assistance. To exacerbate this situation, after the independence, some experienced periods of strong political instability, as in Guinea-Bissau, and others were even devastated by for a very long time civil wars, as in Angola and Mozambique.

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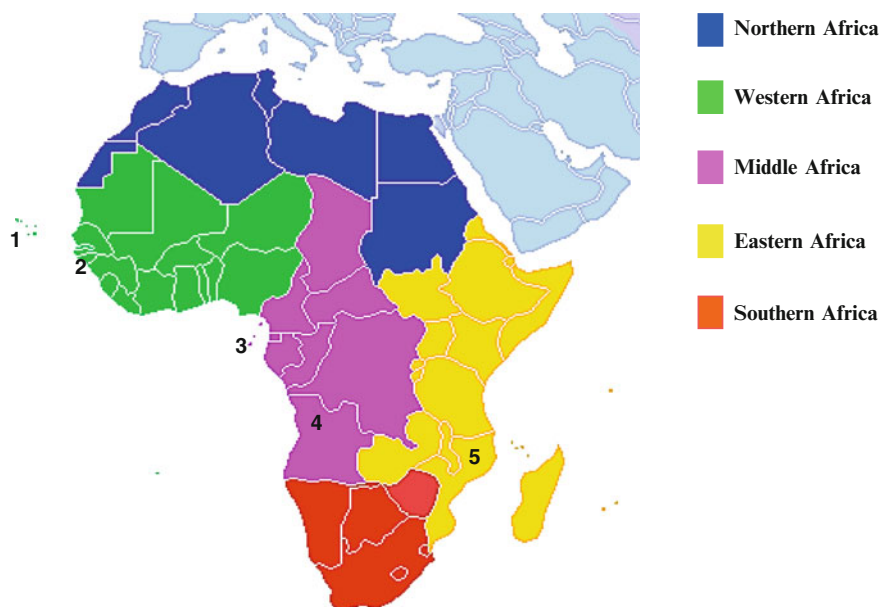


Fig. 9.1 Geographical location of PALOP in Africa, according to the subdivisions of the UN (UN Statistics Division, 2006). 1, Cape Verde; 2, Guinea-Bissau; 3, Sao Tome and Principe; 4, Angola; 5, Mozambique

9.1.1.1 Health Services

In most African cultures, the disease is an adversity imposed upon people by strange forces, and its cure is closely related with rituals and mystic practices, with the intervention of a native healer and so the therapy might not be attributed to the use of a medicine itself.

In spite of the progress made, as regards to basic care in most of African countries, the health status of the population continues to be a major challenge, since there is a high incidence of disease and the health-care system remains weak and fragmented (WHO 2009).

As with other sub-Saharan African countries, the PALOP show some sociodemographic asymmetries, high levels of poverty, poor schooling, and geographic population isolation, which do not contribute to the improvement of people's quality of life. Those asymmetries are in part due to migration flows and cause even deep social inequalities and serious infrastructural problems. In addition, they generate troubles on the inequality of access to the health services, also leading to the worsening of infectious disease transmission and to the absence of prevention and treatment of non-transmitted diseases (WHO 2008). Most of these countries have not yet met material conditions or know-how to improve the living status of their people, with basic sanitation, health, and education systems being yet under low implementation. The inadequacy of financial and human resources for those

areas and the difficulties in the formation and maintenance of qualified technicians also compelled the dependence on foreign aid. The geographical distribution of human resources is a well-known problem (WHO 2008). In fact, the health systems of the PALOP do not have a sufficient number of health professionals, some showing a professional density lower than the African average not only in rural areas but also in the major population centers (Martins 2010; WHO 2008, 2010).

9.1.1.2 African Traditional Medicine

According to the WHO, “traditional medicine is the total combination of knowledge and practices, used for the diagnosis, prevention and elimination of physical, mental and social diseases, which may be based on past experience and on observation handed down from generation to generation, on oral or written form” (WHO 2001).

Traditional medicine, or ethnomedicine, plays a central role in the health of a large part of the world’s population, since 80 % of the population depends on traditional medicine for primary health care (WHO 2011a). In Africa, the culture, political instability, and socioeconomic problems combined with isolation, basic needs of survival, and the asymmetries previously mentioned led or perpetuated the underdevelopment of many regions. This compelled the population to deal with traditional medicine and local healers as the first and only source of health care (Agostinho and Silva 2013; Carvalho 2013; Diniz and Martins 2005). The traditional healers provide a popular and accessible service, especially in the rural areas across the African continent where the sanitary situation is characterized by a lack of qualified health workers, medicines, and equipment. So, the traditional medicine is an important element in the cultural patrimony and remains the main resource for the majority of people for treating health problems, particularly in rural areas (Romeiras et al. 2012; Rukangira 2001).

An African indigenous system of health is composed of three essential parts: the active medicinal substance, which may be plants, soil, or animals or animal parts; the spiritual forces, the gods and God; and the human spirit, which includes the healer and the patient. The functions of the traditional medicine practitioner are not limited to the diagnosis of diseases and the prescription of drugs. It is the medicine practitioner who provides the needed answers to the adversities imposed on the community by outside forces that are beyond the comprehension of ordinary people. These forces include curses, charms, evil spirits, aggrieved ancestors, witches, and the gods (Iwu 2014). It is the belief among most Africans that a herbal prescription from a medicine man could cure an indicated illness not necessarily because the plant has a demonstrable pharmacological activity per se, but because there is life-giving potency in every creature that the medicinal plants possess and also the acquired properties imparted to the plant through invocations, incantations, and rituals. The African medicinal agents consist of two main groups: (1) those using rituals, sacrifices, and other religious acts as part of the process of treatment of diseases and (2) those using plant extracts, herbs, seeds, roots, leaves, juices, liquids, powders, bones, minerals, and other substances that are supposed to have organic

effects directly on the patient. Some of the procedures and rituals, and even the very plants used, may lack any overt value, but they are psychologically vital and play a great role in healing the sick and helping the afflicted.

After the Alma-Ata Conference, in 1978, the WHO suggested to the African governments the promotion and integration of traditional medicines in the primary health care, providing a source of affordable health care to local communities (WHO 1978). From these resolutions, the African traditional medicine began to achieve prominence, although it varies greatly from region to region (WHO 2001). In 2001 in Lusaka, the African Unity Organization declared the period 2001–2010 as the “Decade of African Traditional Medicine.” During the presentation of the results of this first decade, it was renewed in the second “Decade of African Traditional Medicine” from 2011 to 2020 (WHO 2011b). In 2003, the African Union (ex-African Unity Organization), meeting in Mozambique, created the “African Traditional Medicine Day” to be celebrated on 31st of August, each year being devoted to a specific theme. Subsequently, some countries have instituted the “Traditional Medicine Week.” In both cases, during the celebrations, there are several activities such as debates, symposiums, and cultural presentations, in order to enhance the traditional medicine (WHO 2011b).

In the course of these actions, traditional medicine has been recognized and also associated to a less dependence on foreign aid by reducing the reliance on expensive imported medicines. There were other achievements like an update on the knowledge about the African flora, with the emergence of research institutions in some African countries, though those activities were initially more related with the harvesting and taxonomy of plants and less with the information and study about their traditional uses. The guidelines for the protection of intellectual property rights and of the traditional medicine knowledge were established and the first steps toward the creation of an *African Herbal Pharmacopoeia* were given. With all this, the access to the biological resources from developing countries became easier but also the awareness to its preservation as well as the alert to the need of covering the insufficient scientific data on the safety, efficacy, and quality of traditional medicines (WHO 2011b). Indeed the problem begins in the fact that most of traditional medicinal plants are traded in local open markets, with few conditions, like lack of storage facilities and trading infrastructures which affects the final product quality (Stafford et al. 2005).

9.1.2 Depression: A Mental Disorder

The mental disorders are usually neglected, but they occur in all societies and affect hundreds of millions of people, women and men, at all stages of life, among rich and poor, both in urban and rural communities. If not treated, beyond the personal and family suffering, they lead to significant economic and social difficulties which affect society as a whole.

In most African societies, mental illness is seen as the clearest manifestation of the disturbed equilibrium of life. These diseases can be traced to a broken taboo, a contravened societal norm, or witchcraft. It is indeed futile to prescribe herbs and tranquilizers without first making a proper diagnosis of the causative factors responsible for the illness (Iwu 2014).

Despite the introduction of a number of antidepressant drugs with different pharmacological activities, depression continues to be a major medical problem. Even in industrialized countries, only a minority of people suffering from depression seeks or receives treatment. Part of the explanation lies in the symptoms themselves. Feelings of worthlessness, excessive guilt, and lack of motivation deter individuals from seeking help. In addition, such individuals are unlikely to appreciate the potential benefits of treatment. The integration of mental health services in primary care is the most viable way of ensuring that people have access to mental health care when they need it. Personal and social costs of the disease are very high. After anxiety, depression is the most common psychiatric disorder. It is estimated that about 10 % of people who consulted a doctor thinking that they have a physical problem actually suffer from depression. Those born in the last decades of the twentieth century seem to have a higher incidence of depression than previous generations (IOM 2010).

9.1.2.1 Antidepressant Drugs and Medicinal Plants as Alternative Therapy

There are several types of currently available antidepressant drugs, such as selective serotonin reuptake inhibitors, tricyclic antidepressants, monoamine oxidase inhibitors, and psychostimulants. They all act on the nervous system and are often associated with several side effects. They have to be taken regularly for at least 4–6 weeks before they begin to work and are often associated with several side effects. The chances that any given antidepressant will work for a particular person are approximately 60–70 % (Nestler et al. 2002; Wong and Licinio 2001). Therefore, the identification of new therapeutic alternatives for the treatment of depression still becomes necessary.

The more traditional and less industrialized societies are based on the knowledge of the living world surrounding them and depend on the sustainable exploitation of the natural resources, for their food needs, housing, and medicine, among others. The importance of these ancestral practices is recognized (WHO 2011b) and its search also has substantially increased in Western countries, as it grows the demand for alternative methodologies against diseases, partly resulting from technological development and also of the complex way of life on those societies (WHO 2011b; Calixto 2005; Rates 2001).

Plants synthesize a variety of chemical compounds that are at the base of its medicinal and pharmaceutical importance. For a long time, the pharmaceutical industry uses raw materials of vegetable origin which were originally known and developed from the study of its traditional uses (Oliver-Bever 1986). These compounds

can have a particular biological and pharmacological activity. In other cases, the isolated compounds from plants are used as chemical experimental models for the hemi-synthesis or complete synthesis of more effective and less toxic drugs, as well as many other applications in the pharmaceutical area. About 25 % of conventional medicines are originated directly or indirectly from plants (Cos et al. 2006). The available African natural resources are synonymous of abundant natural products, many of which possess known medicinal properties and as such its potential is enormous (Kuate 2013).

The therapeutic action of a plant depends on its chemical composition. It is important to ascertain if the plants from different geographical zones have the same chemical composition and so the same biological activity, as different ecological conditions might affect the biosynthetic pathways. In traditional medicine, local uses might differ for the same plant and this requires an accurate analysis of the associated biological and chemical data (Iwu 2014; Kuate 2013; Oliver-Bever 1986).

There are medicinal plants with psychotropic effects, potentially active and to which modern pharmacology can appeal, although the clinical use of medicines with antidepressant action obtained from plants is still limited (Iwu 2014; Kumar 2006; Zhang 2004).

9.2 Methods

Literature search was performed using electronic databases including ScienceDirect, Web of Science, Scopus, SciELO, PubMed, and Google Scholar. Keywords such as “alternative medicine, ethnomedicinal uses, pharmacological properties, mental disorders, depression, African plants, and antidepressant properties” were used. In addition, relevant information was also searched on the Internet, and publications containing original data and an adequate detailed description of methodology were considered, like academic dissertations, including Ph.D. and master’s theses, and ethnobotanical works. We obtained free original articles where possible and also hand-searched for cross-referenced articles and books. Searches were restricted to English, French, and Portuguese language publications but no restrictions on year of publication were applied.

According to the literature survey, we have tried to combine the ethnomedicinal data collected about the plants with antidepressant activity with their chemical compounds and their reported pharmacological activities.

The search was done on the available information about medicinal plants commonly used for treatment of depression in the PALOP. As the explicit information on the traditional use for this condition is scarce, the ethnobotanical data were firstly obtained through a review conducted on several published works on the medicinal flora of these countries and secondly on the plants used in the neighboring sub-Saharan African countries and also belonging to the flora of the PALOP.

9.3 Conclusions

There is a consensus about plants as an important source of phytochemicals, potentially beneficial health agents. Those benefits are far from being fully exploited. Plants are used in different traditional medicine systems, but there is a vast amount of research still to be conducted to scientifically validate their traditional uses, that is, the search for the phytochemical constituents which are responsible for a certain biological activity. Many ethnomedicinal uses of plants from various sources are documented and compared, concentrating merely on the gross effects induced by herbal preparations. Relevant scientific studies on the plant's pharmacological properties and scientific literature for the reported constituents from the plant, which can scientifically validate the plant's traditional uses and pharmacological properties, are still out of focus. Ethnomedicinal studies are published every year without any discussion of the chemical constituents of the medicinal plants reported and scientific validations of their traditional medicinal uses. It is believed that a new approach on natural products can prove more valuable in not only identifying which diseases it may be beneficial but also contain associated chemical and biological data, which could lead to the discovery of new drugs. In this particular case, further studies are needed to completely elucidate the chemical groups responsible for the antidepressant effect of plant extracts, and further experiments are necessary therefore to confirm the exact mechanisms involved in this central nervous system pathology.

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9.5 *Bacopa monnieri* (L.) Pennell

9.5.1 *Scrophulariaceae*

1) *Synonyms:*

Bacopa monniera (L.) Wettst.; *Gratiola monniera* L.; *Lysimachia monnieri* L.; *Monniera africana* Pers.

2) *Common names:*

Water hyssop (Eng.)

Hysope d'eau (Fr.)

3) *Photograph of the species (Fig. 9.2)*

Fig. 9.2 *Bacopa monnieri* (L.) Pennell. Detail of leaves and flower (original photo taken by L. Allain)



4) *Description of the species:*

A) **Habitat, world distribution, and PALOP distribution:**

The genus *Bacopa* includes over 100 species of aquatic herbs distributed throughout the warmer regions of the tropics and subtropics (Philcox 1990). *B. monnieri* is native to Asia, mainly tropical Asia, and Africa and is a small sprawling herb common in fresh and brackish waters, found growing in wet pastures and margins of ponds and in rice fields as well. In some situations, it might be considered as an invasive species (<http://www.issg.org/database/species/ecology.asp?si=1784>; <http://www.iucnredlist.org/details/164168/0>).

In PALOP, it can be found in Mozambique (<http://www.iucnredlist.org/details/164168/0>).

B) **Morphology of the plant:**

Annual herb, creeping, glandular-punctate, glabrous, often rooting at the nodes, sometimes in flooded fields or swamps; stem usually simple, rarely branched. Leaves opposite, sessile, 10–15 × 5–7 mm, obovate to spatulate, obtuse at the apex, cuneate at the base, entire or rarely crenulate toward the apex, glandular-punctate. Flowers axillary, solitary, pedicellate, bracteate, hermaphrodite, irregular; pedicels up to 25 mm long at fruiting, always exceeding the leaves; bracts 2–3 mm long; calyx 5-partite, the lateral lobes narrow, oblong, the posterior one 4–6 × 3–4 mm, broadly ovate, the anterior ca. 5 × 2.5 mm, ovate; corolla 6–7.5 mm long, bilabiate, upper lip bilobed, lower trilobed; stamens 4, didynamous, included. Fruit, a capsule 2–2.5 mm long, ovoid; seeds small, numerous (Philcox 1990).

C) **Conservation status:**

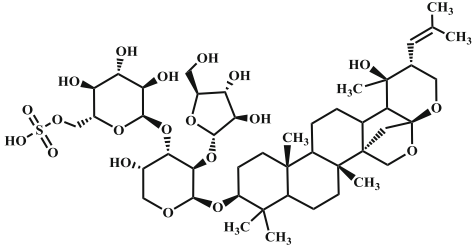
There are no known conservation measures (<http://www.iucnredlist.org/details/164168/0>).

D) **Medicinal parts:**

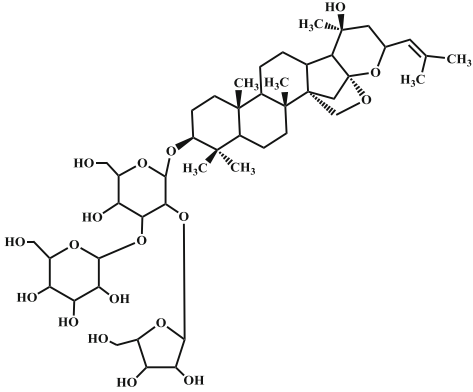
Aerial parts.

E) **Chemical composition:**

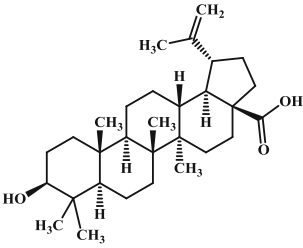
B. monnieri contain **alkaloids** (brahmine, nicotine, and herpestine) and **triterpenoid saponins** known as bacosides which comprise a group of 12 known analogs (Sivaramakrishna et al. 2006). Other saponins called bacopasides (I–XII), dammarane-type triterpenoid saponins also with biological interest, have been identified in the extract of the whole plant of *B. monnieri* (Garay et al. 2009). This extract also contained **betulinic acid**, **D-mannitol**, **Stigmastanol**, **β -sitosterol**, and **stigmasterol** (Al-Snafi 2013).



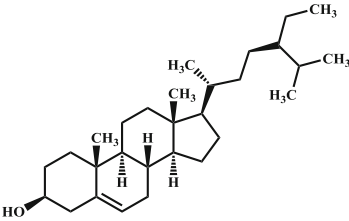
Bacopaside I



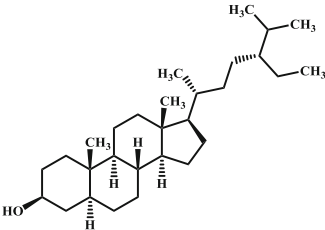
Bacoside A3



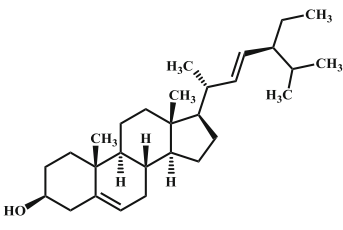
Betulinic acid



beta-Sitosterol



Stigmasterol



Stigmasterol

5) *Major ethnomedicinal uses.*

There are references to the traditional use of *B. monnieri* for centuries (<http://www.iucnredlist.org/details/164168/0>; Al-Snafi 2013), to treat nervous disorders; as a brain tonic to enhance memory development, learning, and concentration; and to provide relief to patients with anxiety; it is also used for digestive complaints, for skin disorders, and as an antiepileptic, antipyretic, and analgesic. Other references mentioned its use as aphrodisiac and against snakebites (<http://www.ars-grin.gov/cgi-bin/npgs/html/taxon.pl?102292>).

6) *Pharmacology and bioactivities:*

The most important effects of the plant, plant extracts, and isolated triterpenoid saponins are on cognition and memory functions, their anxiolytic effects, and their role in management of convulsive disorders (Russo and Borrelli 2005; Kumar 2006). The extracts and isolated bacosides and bacopasides have been investigated extensively for their neuropharmacological effects. Singh et al. (1996) suggest an involvement of the GABAergic system in the mediation of CNS effects. The mechanism of action reported in various preclinical studies indicating a cognitive enhancing effect is still uncertain. Its multiple active constituents make its pharmacology complex (Russo and Borrelli 2005; Gomes et al. 2009). It is noteworthy that dammarane-type triterpenoid saponins are major constituents of a number of reputed herbal drugs, including ginseng (Russo and Borrelli 2005).

Later studies with some of the bacosides and bacopasides isolated from the whole plant of *B. monnieri* showed antidepressant activity when tested on common in vivo assays, like forced swimming test (FST) and tail suspension test (TST) in mice (Zhou et al. 2007). The methanolic extract from the whole plant of *B. monnieri* and different fractions were also evaluated for their antidepressant activity in the same in vivo rodent models of depression. These results showed that the methanolic extract, EtOAc fraction, and *n*-BuOH fraction significantly reduced the immobility times in mice after being administered orally for five consecutive days and was comparable to that of imipramine, a tricyclic antidepressant (Sairam et al. 2002; Shen et al. 2009). A similar outcome was obtained with a hydroethanolic extraction and an *n*-butanolic extract of *B. monnieri* aerial parts (Abbas et al. 2011). These authors mentioned that the antidepressant effect was comparable to fluoxetine, a selective serotonin reuptake inhibitor. In another study, *n*-butanolic extract of *B. monnieri* potentiated yohimbine in mice. Yohimbine is an inhibitor of the presynaptic α -adrenergic receptors, and its potentiation induced by *B. monnieri* indicated the involvement of noradrenaline in the mediation of antidepressant actions of *B. monnieri* (Abbas et al. 2011).

7) *Precautions and side effects:*

According to Singh and Dharwan (in Al-Snafi 2013), contraindications and adverse effects of *B. monnieri* are not known.

8) **Dosage:**

According to the monograph of *B. monnieri* (Alternative Medicine Review 2004, in Al-Snafi, 2013), for *B. monnieri* extracts standardized to 20 % bacosides A and B, the dosage is 200–400 mg daily in divided doses for adults and 100–200 mg daily in divided doses for children.

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9.7 *Boophone disticha* (L.f.) Herb

9.7.1 (*Amaryllidaceae*)

1) Synonyms:

Amaryllis disticha L.f.

2) Common names:

Moz: Tchindzondzonzozo, (Tete).

Windball, poison bulb, sore-eye flower (Eng.).

3) Photograph of the species (Fig. 9.3)



Fig. 9.3 *Boophone disticha* (L.f.) Herb., inflorescence, in Mozambique (Torre, 13123, IICT Herbarium collection)

4) Description of the species:

A) Habitat, world distribution, and PALOP distribution:

Occurs in tropical and subtropical regions, from East Africa to South Africa. In PALOP, it can be found in Angola and Mozambique.

B) Morphology of the plant:

Bulbous plant with distichous leaves. Bulb up to 25 cm in diameter partially exposed above ground. Leaves developing after the flowers, sessile, up to 50 cm long and 1.5–4.2 cm wide, narrowly oblanceolate, prominently nerved, rigid, glaucous, the younger ones with a toothed cartilaginous margin. Scape 5–25 cm long, solid, with a large globose inflorescence subtended by two bracts 4–9 × 1–4 cm. Flowers up to 200, pink to purple, bisexual, regular, sweet-scented; pedicels 3–8.2 cm long at anthesis, up to 32 cm in fruit, angular; perianth with a 3–12-mm-long funnel-shaped tube and 6 identical segments 20–30 × 2–4 mm in two series of 3; stamens 6 with filaments 23–48 mm long and anthers yellow about 3 mm long; ovary inferior, 3-locular; style slender, exserted, up to 45 mm long. Fruit a 3-angled elongate capsule up to 4 cm long, with irregular dehiscence and a single pale fleshy globose seed (Zimudzi et al. 2008).

C) Conservation status:

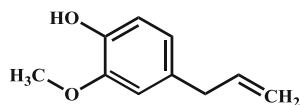
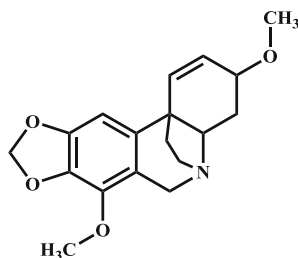
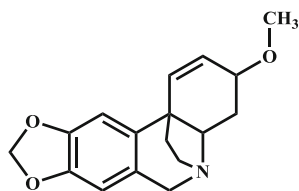
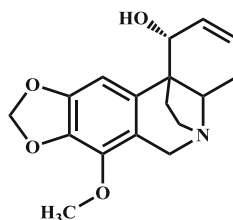
B. disticha has been classified as “threatened” or “near threatened” because of unsustainable harvesting and as a consequence of large parts of its habitat have been destroyed for cultures (Williams et al. 2013). Sustainable harvesting is impossible since the plant is destroyed when bulbs are removed. As it is a slow-growing plant, its intensive culture is not attractive and discourages cultivators. In South Africa, the species is protected by environmental legislation and may not be harvested without permission (<https://www.botanicalsociety.org.za/ProjectsAndActivities/Downloadable%20articles/FW07%20Boophone%20Gifbol.pdf>; Williams et al. 2008).

D) Medicinal parts:

Bulbs and leaves.

E) Chemical composition:

The foremost compounds identified in bulbs and leaves are **eugenol**, an aromatic, volatile oil, smelling of cloves and having analgesic properties, and the **toxic alkaloids** buphandrin (=buphanidine), buphanamine, buphenine, undulatine, buphanisine, and nerbowdine.

**Eugenol****Buphandrin****Buphanisine****Buphanamine**

5) Major ethnomedicinal uses:

B. disticha bulb is very toxic and there are many documented deaths from its use, although it is easily found in local markets. Traditional healers use the bulb to treat pain and wounds, as the outer covering of the bulb is applied to boils and abscesses. Fresh leaves are used to stop bleeding of wounds and bulb infusions for anxiety, depression, and age-related dementia (Risa et al. 2004). There have been unsubstantiated reports of *B. disticha* being consumed recreationally for its hallucinogenic properties when taken in relatively small doses (<http://www.plantzafrica.com/plantab/boophdist.htm>).

6) Pharmacological studies:

B. disticha showed high activity both in aqueous and ethanolic extracts of leaves and bulbs (Nielsen et al. 2004). Amaryllidaceae alkaloids are reported to exhibit several biological activities, including on the central nervous system (Lewis 1990; Elgorashi et al. 2006). Investigations on plants used to treat age-related dementia and debilitating mental disorders lead to the isolation of several compounds through bioassay-guided fractionations. In *B. disticha* bulb scale extracts, the identification of the alkaloids buphanamine, buphanadrine, buphanisine, and distichamine was achieved (Sandager et al. 2005; Neergaard et al. 2009; Nair and van Staden 2014). The first two alkaloids showed affinity for SERT (Sandager et al. 2005) and have a chemical structure, the benzo-1,3-dioxole moiety, similar to a number of the available clinically used selective serotonin reuptake inhibitor (SSRI) drugs, which could explain their activity (Stafford et al. 2008).

Pedersen et al. (2008) employed a rat model for depression to show that ethanolic extracts from *B. disticha* bulbs inhibited the serotonin transporter (SERT), noradrenaline transporter (NAT), as well as the dopamine transporter (DAT), all of which are believed to be involved in the pathophysiology of depression. The same bulb extracts were also investigated for in vivo antidepressant-like effects in animal models for depression that employed the forced swim test (FST) in both mice and rats and the tail suspension test (TST) in mice. The extracts exhibited antidepressant-like effects in those in vivo animal models (Pedersen et al. 2008).

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9.9 *Centella asiatica* (L.) Urb

9.9.1 (*Apiaceae*)

1) Synonyms:

Hydrocotyle asiatica L.; *H. thunbergiana* Spreng.; *H. pallida* DC.

2) Common names:

STP: Olha d'atô.

Angola: Mafoibale (muila).

Asiatic or Indian pennywort, wild violet, and tiger herb (Eng.).

3) Photograph of the species (Fig. 9.4)

4) Description of the species:

A) Habitat, world distribution, and PALOP distribution:

Species occurring throughout tropical and subtropical regions of the world, native to Southeast Asian countries. In Africa, it is recorded from Central and Southern Africa. Among countries belonging to PALOP, this species can be found in Guinea-Bissau, Sao Tome and Principe, Angola, and Mozambique.

B) Morphology of the species:

Creeping perennial herb rooting at the nodes. Leaves alternate, simple, solitary or in groups of up to 5; petiole very variable, 2–20 cm long, glabrous or sometimes densely hairy when young; lamina 1–7 cm wide, reniform to almost circular with a deep basal sinus, margin crenate, pubescent or glabrous, with venation radiate and reticulate. Flowers 2–8 in subcapitate umbels, bisexual, subtending by two ovate bracts; peduncles 0.5–5 cm long, glabrous to hirsute; pedicels usually obsolete; calyx null; petals 5, dark crimson to greenish-white, sometimes tinged with purple, orbicular with a slender inflexed point; stamens 5, free; ovary inferior, 2-celled; styles 2, short, divergent. Fruit dry, laterally flattened, 3–3.5 mm long and 3.5–4 mm wide, orbicular to ellipsoid, deeply constricted at the commissure, dividing at maturity into two 1-seeded mericarps supported by an entire carpophore; mericarps with 5 primary ribs prominent when ripe, under which is present a small oil canal (Cannon 1978).



Fig. 9.4 *Centella asiatica* (L.) Urb., from Mozambique (LISC Herbarium specimen, Torre 2602)

C) Conservation status:

The species is common throughout its regions. It has no known major threats and it is considered of least concern. No conservation actions are required. (<http://www.iucnredlist.org/details/168725/0>).

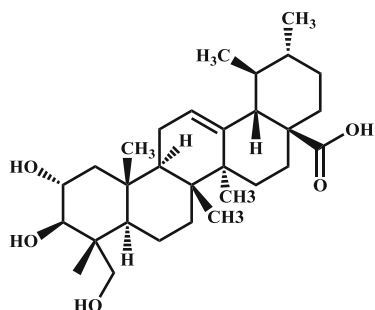
D) Medicinal parts:

Aerial parts.

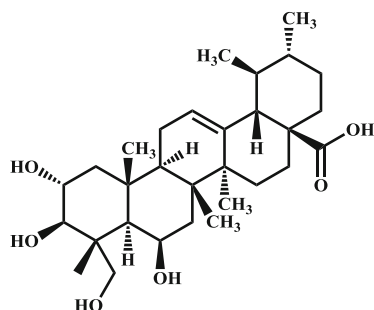
F) Chemical composition:

Different chemical groups can be found in *C. asiatica*; standing out are large amounts of **triterpene saponosides** and their glycosides; the major ones are asiatic acid, madecassic acid, and asiaticosides and madecosides (Singh and Rastogi 1969; James and Dubery 2009; Hashim et al. 2011). **Monoterpene and sesquiterpene derivatives**, the most prominent being α -pinene, β -pinene, and bisabolene, have also been identified in this species,

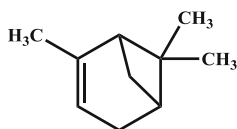
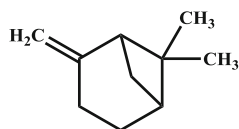
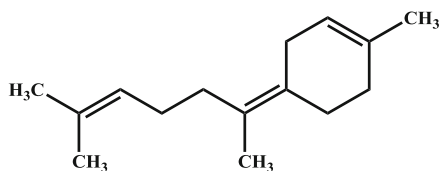
as well as **steroids**, like stigmasterol and β -sitosterol; several **flavonoid derivatives**, like quercetin and kaempferol derivatives; **phenolic acids**; and **polysaccharides** (Jahan et al. 2012; Orhan 2012). According to the *African Herbal Pharmacopoeia* (2010), the chemical composition of the plant varies with its geographical distribution.



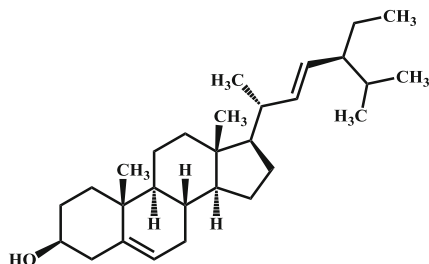
Asiatic acid



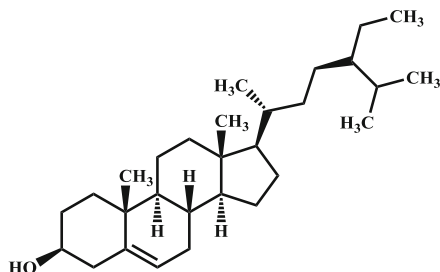
Madecassic acid

 α -Pinene β -Pinene

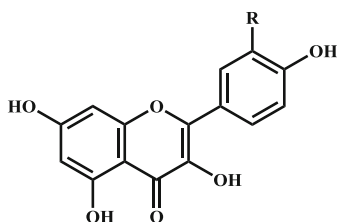
Bisabolene



Stigmasterol



Beta-Sitosterol



R=OH: Quercetin

R=H: Kaempferol

5) Major ethnomedicinal uses:

In Asia, *C. asiatica* is used as a vegetable, cooked or raw in salads and in curries. It has a long history of utilization in Ayurvedic and Chinese traditional medicines. The major ethnomedicinal uses of *C. asiatica* appear to be related to gastrointestinal disorders, skin wound healing and eczema, and memory enhancement or serving as nerve stimulant (Jahan et al. 2012). Among other uses, it is applied as a medicine for inflammation, cardiac tonic, depurative, febrifuge, hypotensive, nervine, sedative, astringent, stimulant, and cosmetic (Jahan et al. 2012; Orhan 2012). Monographs of the plant can be found in the *European Pharmacopoeia* and World Health Organization.

6) Pharmacological studies:

C. asiatica is a reputed medicinal plant due to its various pharmacological effects. It has uses in traditional African medicine, traditional Chinese medicine, and the Ayurvedic system of medicine (Jahan et al. 2012). A number of studies describe the protective effect of the plant extracts against several degenerative diseases of central nervous system, including Alzheimer's (Mukherjee et al. 2007) and Parkinson's diseases (Khan 2007; Awad et al. 2007). Soumyanath et al. (2012) used in vivo and in vitro standard tests to evaluate the cognitive effects of the aqueous extract of *C. asiatica*. These authors found that *C. asiatica* attenuated the behavioral abnormalities in a mouse model of Alzheimer's disease. In vitro, the same water extract protected some types of human neuroblastoma cells (SH-SY5Y cells and MC65) from toxicity induced by exogenously added and endogenously generated β -amyloid. The water extract did not show anticholinesterase activity or protect neurons from oxidative damage and glutamate toxicity, mechanisms of current Alzheimer's disease therapies. The combination of data from these in vivo and in vitro studies supports the *C. asiatica* potential for conferring clinical benefits in Alzheimer's disease. The water extract is rich in phenolic compounds and does not contain asiatic acid, a known *C. asiatica* neuroprotective triterpene. In this way, the aqueous extract of *C. asiatica* may offer a unique therapeutic mechanism and novel active compound of potential relevance to the treatment of this degenerative disease (Soumyanath et al. 2012).

Moreover, *C. asiatica* extracts have been found to have imipramine-like antidepressant effect (imipramine=tricyclic antidepressant) and significant anti-stress activity comparable to diazepam, a benzodiazepine (Sarma et al. 1998). In another study, trained rats treated with extracts of *C. asiatica* showed dose-dependent conditioned avoidance comparable to chlorpromazine, a drug used to treat schizophrenia. It has been suggested that the extract causes impairment of muscular coordination and has a tranquilizing effect (Arora et al. 2002).

Antidepressant activity of *C. asiatica* was evaluated using its triterpenic fraction in cortex, hippocampus, and thalamus regions of rat brains by determining the corticosterone levels (Chen et al. 2003 in Orhan 2012). The triterpenic fraction created a momentous diminution in corticosterone level and a notable increase in amount of monoamine-related neurotransmitters. This *C. asiatica* effect is generally attributed to the mentioned major triterpene saponosides,

asiatic and madecassic acids, as well as to their heterosides. Liang et al. (2008) studied the potential antidepressant properties of the triterpene heteroside asiaticoside using valuable mice models to evaluate the antidepressant-like activity, and the results suggested that asiaticoside may have antidepressant-like action and the regulation of $\alpha 2$ -adrenergic receptor may be the major mechanism of this model, although the authors refer that further experiments evaluating the levels of noradrenaline and serotonin in different brain regions are still necessary to confirm this hypothesis.

7) **Precautions and side effects:**

C. asiatica has been used in traditional Indian Ayurvedic and Chinese medicines for decades. In pharmaceutical industries, it has shown good efficacy, performance, and safety, with low toxicity. According to WHO monographs (<http://apps.who.int/medicinedocs/pdf/s2200e/s2200e.pdf>), allergic contact dermatitis has been associated with topical application, but these reactions may be due to other ingredients in such preparations. Possible skin carcinogen in rodents after repeated topical application is also mentioned, but further experimentation is needed to substantiate this claim.

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9.11 *Cissampelos* Genus

9.11.1 (*Menispermaceae*)

Cissampelos mucronata A. Rich., *Cissampelos owariensis* P. Beauv. ex DC., *Cissampelos pareira* L. var. *orbiculata* (D.C.) Miq.

1) **Synonyms:**

Cissampelos pareira L. = *Cissampelos madagascariensis* Miers.

2) **Common names:**

Angola: enhati, enyati, nhati (muila).

GB: cauce-edjambaran (felupe); inétulo (mandinga); noferbalo, nopelebaló (fula); oreja di sandjo (criolo).

Moz: nacadindi (macua); sissi (Tete); chipomba-folia (mateuè).

Hairy heartleaf; heart-leaved vine (Eng.) (isto encontrei para *C. mucronata* in Fl Zimbab).

3) **Photograph of *Cissampelos mucronata*** (Fig. 9.5)

4) **Description of the genus:**

A) **Habitat, world distribution, and PALOP distribution:**

This genus is widely distributed throughout the tropics (Troupin, 1960). In PALOPs, some species can be found in Guinea-Bissau, Angola, and Mozambique (*C. mucronata* and *C. owariensis* (Semwal et al. 2014) and *C. pareira* var. *orbiculata* (Troupin 1960)).

B) **Morphology of *C. mucronata*:**

Twining liana with stem somewhat woody at the base and leafy stems puberulous or pubescent. Leaves alternate, simple, subpeltate, or clearly peltate; petiole up to 7 cm long, usually inserted 1–4 mm from the base of

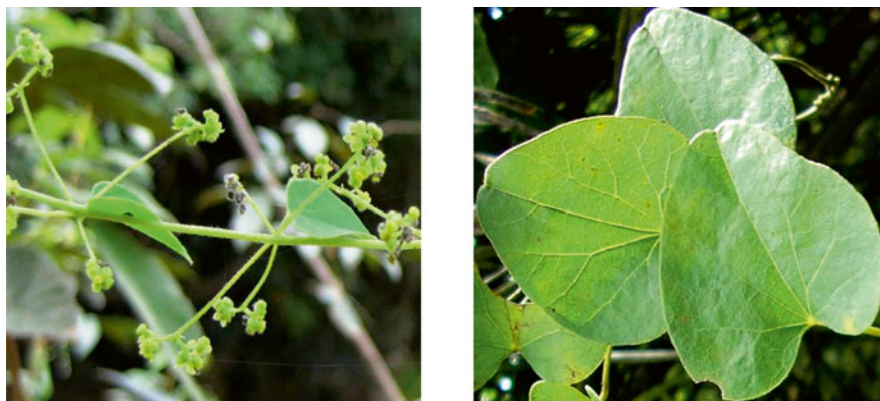


Fig. 9.5 *Cissampelos mucronata* A. Rich., from Guinea-Bissau, detail of inflorescences and leaves (original photos taken by L. Catarino)

the lamina, pubescent; lamina 2–12×2–12 cm, broadly cordate to ovate or orbicular, obtusely or emarginately mucronate or rarely acuminate at the apex, truncate to deeply cordate at the base, entire, membranous to papery, sparsely hairy above, puberulous to tomentose beneath, with 3–7 nerves from the base; stipules absent. Male flowers in solitary or paired axillary corymbose cymes up to 4 cm long, arranged in axils of bracts along an axis up to 10 cm long; sepals 4–5, ovate or obovate, 1.2–1.5×0.5 mm, keeled, hairy outside; petals united in a cup; stamens connate in a 4-locular synandrium. Female flowers in 5–9-flowered cymes arranged in axillary false racemes 5–10 cm long; bracts up to 1.5 cm in diameter, suborbicular to kidney-shaped, pubescent to tomentose; sepals usually 1, as in male flowers; petals 1, obtriangular to kidney shaped, ca. 1.5×2 mm; ovary superior, hairy with a thick 3-lobed style. Fruit a drupe 4–6×3–4 mm, curved, pubescent, 1-seeded; seed horseshoe-shaped tuberculate (Troupin 1960).

C) Conservation status:

Not threatened.

D) Medicinal parts:

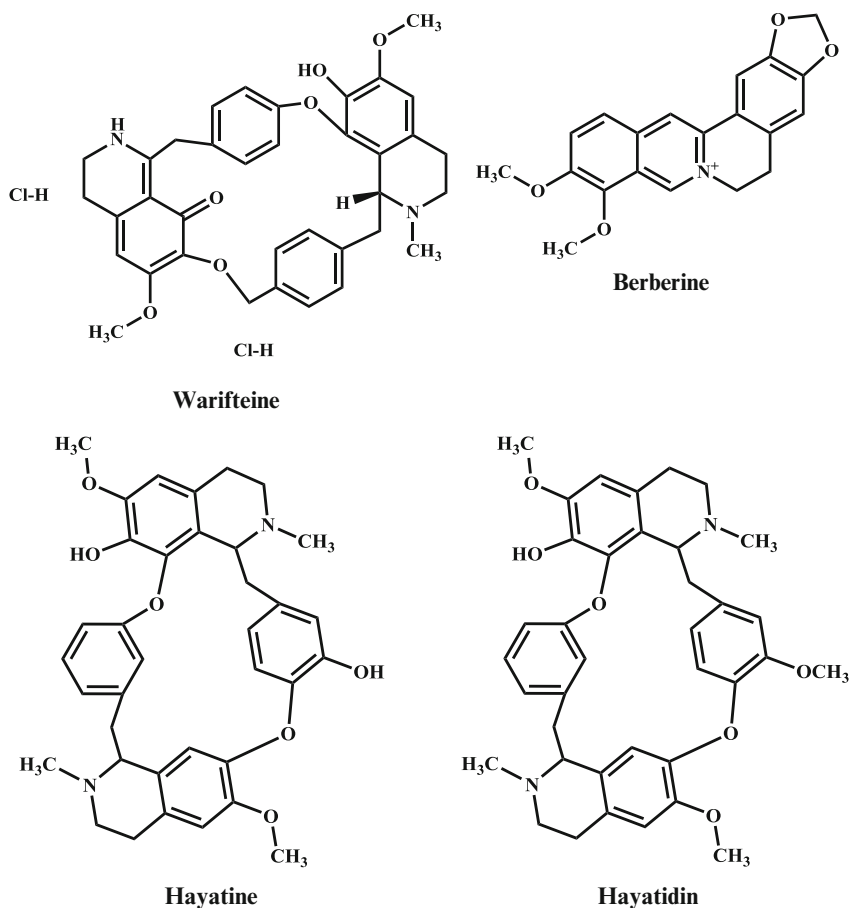
Roots (tuberous roots) and leaves.

E) Chemical composition:

The **alkaloids** are the major chemical group reported in the genus *Cissampelos*. Most of the compounds were isolated from the roots of different species, including *C. pareira*, *C. owariensis*, and *C. mucronata*, and these include the **alkaloids** warifteine, methyl warifteine, berberine, hayatine, and hayatidin (Semwal et al. 2014).

In addition also **flavonoids** like quercetin and **saturated fatty acids, polysaccharides**, and **pectins** were isolated in roots and aerial parts of *Cissampelos* species (Semwal et al. 2014). Some authors remember that there are chemical

variations in *Cissampelos*, and the plant organ, the developmental stage, the time of harvesting, and the geographical distribution must be taken into account for chemotaxonomic purposes (de Wet et al. 2011).



5) Major ethnomedicinal uses:

Cissampelos species have a wide geographical distribution and vast traditional uses, being used because of both therapeutic and toxic properties. The roots of *C. owariensis* and *C. pareira* (which are often confused) are used as an emmenagogue, abortifacient, antipyretic, and diuretic (Oliver-Bever 1986). Roots and leaves are traditionally applied to asthma, cough, fever, arthritis, obesity, dysentery, snakebite, jaundice, blood pressure, and skin-related problems (Semwal et al. 2014). Iwu (2014) also mentions the use of aerial parts of *C. owariensis* against diarrhea, dysentery, colic, intestinal worms, and digestive complaints and as a tonic for amnesia and psychosis. In various parts of the world, some of *Cissampelos* species are used for arrow poison (Oliver-Bever 1986).

6) Pharmacological studies:

Some of the quinoline structure alkaloids isolated from different *Cissampelos* populations are known by its pronounced antipsychotic bioactivity and showed promising anti-allergic, immunosuppressive, antidepressant, anticancer, vasodilatory, and muscle-relaxant activities (Oliver-Bever 1986; Semwal et al. 2014). The total tertiary alkaloid fraction (containing warifteine) from *C. sympodialis* demonstrated an antidepressant effect in depression models, forced swimming test (FST), and reserpine test (Mendonca-Netto et al. 2008). The hydroalcoholic leaf extract of *C. sympodialis* (also containing warifteine) exhibited antidepressant effects together with antioxidant activity in the FST in mice (Zhang 2004). The ethanolic leaf extract was found to potentiate the toxicity of pentylenetetrazol, a convulsant drug, in mice. It also reduced the immobility period in the FST in mice and reversed the degree of catalepsy induced by reserpine in rats, an imipramine-like antidepressant effect (Almeida et al. 1998). The extracts of aerial parts of *C. owariensis* seem to have an effect against degenerative diseases of central nervous system, including Alzheimer's disease, as the methanolic extract showed activity against both acetylcholinesterase and butyrylcholinesterase (Elufioye et al. 2010). On the contrary, Hage et al. (2010), in order to select plants for the treatment of Alzheimer's disease, did not observe any effect on the production of β -amyloid peptide by n-hexane, dichloromethane, ethyl acetate, and water extracts of *C. owariensis*.

The ethanolic root extract of *C. mucronata* showed sedative activity in mice as it reduced ephedrine-induced spontaneous motor activity in rats and prolonged pentobarbitone sleeping time in mice (Akah et al. 2002).

Although these plants are used in different traditional medicine systems, there is a vast amount of research still to be conducted to validate their traditional use (Semwal et al. 2014).

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9.13 *Griffonia simplicifolia* (Vahl ex DC.) Baill

9.13.1 (*Fabaceae*)

1) Synonyms:

Bandeiraea simplicifolia (Vahl ex DC.) Benth.; *Schotia simplicifolia* Vahl ex DC.

2) Common local names:

Griffonia (Eng.)

3) Photograph of the species (Fig. 9.6)

4) Description of the species:

A) Habitat, world distribution, and PALOP distribution:

G. simplicifolia is native to West-Central Africa. It is usually found associated with termite hills and along the margins of primary forest and old farms (Iwu 2014). This species is found in Guinea-Bissau and Sao Tome and Principe (African Herbal Pharmacopoeia 2010).

B) Morphology of the species:

Liana or shrub with glabrous shining branches. Leaves alternate, simple, with petiole up to 1.5 cm long and lamina 6–12 × 3–6 cm, ovate, rounded to shortly acuminate at the apex, rounded to cordate at the base, entire, glabrous, 3-nerved from the base with reticulum prominent on both sides;



Fig. 9.6 *Griffonia simplicifolia* (Vahl ex DC.) Baill., from Gabon (LISC Herbarium specimen, Le Testu 1926)

stipules minute, triangular. Flowers bisexual in axillary racemes 5–20 cm long; bracts and bracteoles minute, triangular, persistent; pedicels 3–4 mm long; calyx-tube 12–15 mm long, grayish tomentose, curved, gradually dilating and abruptly enlarged and ending in 5 obtuse lobes; petals 5, subequal, 10–12 mm long, elliptic, long-clawed, fleshy, sparsely short-hairy or glabrous, greenish; stamens 10, free with filaments up to 2 cm long, pubescent; ovary superior, ca. 4 mm long, stiped. Fruit an obliquely ovoid pod ca. 8×4 cm, leathery, blackish, with a stipe 1–1.5 cm long; seeds 1–4, orbicular, ca. 18×6×5 mm, glabrous (Aubréville 1968; Bosch 2008).

C) **Conservation status:**

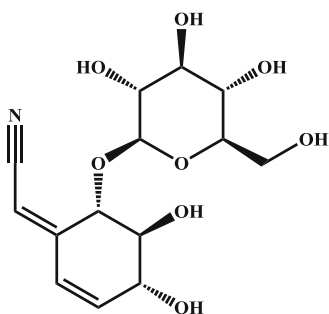
G. simplicifolia is reported as a common species, but the high commercial value of its seeds is a serious threat to the reduction of populations. Sustainable harvesting needs to be implemented (Kumar et al. 2010) since cuttings and seed germination gave poor results (Iwu 2014).

D) **Medicinal parts:**

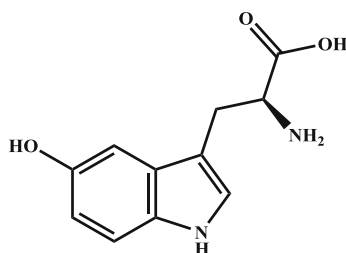
Roots, stems, and leaves.

E) **Chemical composition:**

In *G. simplicifolia* leaves, a **volatile oil** and **coumarins** have been isolated; a **cyanoglucoside** (lithospermoxide = griffonin) was also isolated in this species roots (Kumar et al. 2010). Several **indole derivatives** were also isolated in the whole plant, among them stands out 5-hydroxy-L-tryptophan, known as 5-HTP (African Herbal Pharmacopoeia 2010), a natural occurring and highly absorbable type of aromatic amino acid and a direct precursor to serotonin. *G. simplicifolia* seeds have the richest 5-hydroxytryptophan content, but a similar composition is found in the seeds of the other species of *Griffonia*. *G. simplicifolia* seed extract is either a gray-white powder or pale brown crystals containing 95–98 % of 5-hydroxytryptophan (Kumar et al. 2010). **Lectins**, with insecticidal properties, were also isolated in *G. simplicifolia* seeds (Kumar et al. 2010).



Griffonin



5-Hydroxy-L-tryptophan

5) **Major ethnomedicinal uses:**

The roots, stems, and leaves are used in chewing, a popular means of tooth cleaning, and aiding wound healing. A decoction of aerial parts is taken to stop vomiting; to treat gonorrhea, stomach problems, and congestion of the pelvis (African Herbal Pharmacopoeia 2010); and for mental disorders (Iwu 2014). Young leaves are eaten as an aphrodisiac (African Herbal Pharmacopoeia 2010). An extract from the powdered roots is used to treat sickle-cell anemia (African Herbal Pharmacopoeia 2010; Iwu 2014). The leaves are highly valued as animal feed and are said to stimulate reproduction (Iwu 2014).

6) Pharmacological studies:

G. simplicifolia is considered as a natural alternative for the antidepressant Prozac (fluoxetine, an SSRI), since 5-HTP is the precursor in the biosynthesis of the neurotransmitter serotonin within the central nervous system. 5-HTP crosses the blood-brain barrier (BBB) easily and is completely transformed into serotonin by 5-hydroxytryptophan decarboxylase, which is found in the nervous and liver tissues (Birdsall 1998; www.linnea-worldwide.com/download/5htp.pdf). Other neurotransmitters and CNS chemicals, such as melatonin, dopamine, norepinephrine, and β -endorphin, have also been shown to increase following oral administration of 5-HTP (Kumar et al. 2010). The use of 5-HTP has also been beneficial in the treatment of other low levels of serotonin situations, like in the treatment of fibromyalgia, insomnia, chronic headaches (Nicolodi and Sicuteri 1996; Birdsall 1998), and obesity (Cangiano et al. 1992).

Most studies on 5-HTP use in depression treatment were done 30–40 years ago, between the 1970s and 1990s, when there was a great interest in the serotonin hypothesis of depression (Iovieno et al. 2011). Kumar et al. (2010) mentioned studies following patients with different types of depression, unipolar and bipolar depression and severe depression. In the treatment of severe depression, when comparing the use of 5-HTP to selective serotonin reuptake inhibitor (SSRI) drugs, like fluoxetine, it was found that this indole derivative was at least as effective as the synthetic drugs, but with fewer side effects (Kumar et al. 2010).

After the introduction and approval of other SSRIs, the research on 5-HTP became less compelling to investigators, and since *G. simplicifolia* and 5-HTP are naturally occurring and cannot be patented as a pharmaceutical drug, industry has no profit incentive to market this natural compound (Kumar et al. 2010; Iovieno et al. 2011). So far there are no published reports comparing 5-HTP against newer antidepressants such as SSRIs (Turner et al. 2006; Iovieno et al. 2011). Results from the previous clinical studies and safety reports suggest that 5-HTP supplementation may have at least some antidepressant efficacy and generally good tolerability and may deserve to be evaluated in more rigorous studies in order to conclusively establish its effectiveness, both as monotherapy and as augmentation (Das et al. 2004; Turner et al. 2006; Iovieno et al. 2011).

7) Precautions and side effects:

Some patients initially may feel mild nausea after taking 5-HTP (African Herbal Pharmacopoeia 2010).

8) Dosage:

Initially 50 mg of 5-HTP 3 times a day, at mealtimes; after 2 weeks, the dose can duplicate, 100 mg keeping takes, i.e., three times a day, at mealtimes (African Herbal Pharmacopoeia 2010).

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9.15 *Mondia whitei* (Hook. f.) Skeels

9.15.1 (*Apocynaceae*)

1) Synonyms:

Chlorocodon whitei Hook. f.

2) Common names:

GB: Lacadje (Fula); ngaru (mandinga).

Angola: mudondo.

White's ginger, tonic root (Eng.).



Fig. 9.7 *Mondia whitei* (Hook. f.) Skeels, flower, in Mozambique (Torre and Correia 17386, IICT Herbarium collection)

3) Photograph of the species (Fig. 9.7)

4) Description of the species:

A) Habitat, world distribution, and PALOP distribution:

Native to Africa, considered endemic in almost all African regions with the exception of the northern part of the continent, from sea level to 1800 m. It is found in the PALOP countries Guinea-Bissau, Angola, and Mozambique.

B) Morphology of the species:

Large liana with white latex and aromatic roots. Leaves opposite with petiole 2–7 cm long and lamina ovate to suborbicular, 10–20×6–14 cm, acuminate at apex, obtuse to cordate at base; interpetiolar stipules frill-like. Flowers with unpleasant odor, in lax axillary panicles, 10–20 in each panicle; peduncles 2–4 cm long; pedicels more or less 1 cm long; sepals 5, ovate, 2–3×1–2 mm, acute with fimbriate margin; corolla coriaceous, glabrous with tube 2–3 mm long, lobes 5, obliquely ovate, 9–11×4–6 mm, outside greenish, inside violet, maroon, mauve or reddish. Corona with 5 tri-segmented lobes, lateral ones flaplike, 1–2 mm long, greenish or creamy yellow, central one ligulate or corniculate, 5–8 mm long, darker colored. Fruit with two narrowly ovoid follicles 8–12×2–4 cm; seeds obliquely ovoid, 8–10 mm long with a 20–25-mm-long tuft of silky hairs. Species known from tropical Africa and Southern Africa, including Mozambique (Venter 2012).

C) Conservation status:

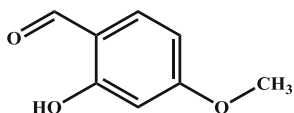
In West Africa, the plant is cultivated but in other regions it is seriously threatened by overharvesting (Iwu 2014).

D) Medicinal parts:

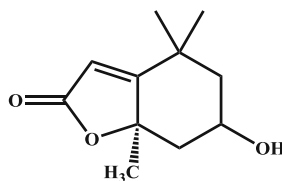
Roots, leaves, and flowers.

E) Chemical composition:

In *M. whitei* root and leaf extracts, **terpenes**, **flavonoids**, **coumarins**, **coumarinolignan**, as well as chlorinated coumarinolignan, **reducing sugars**, and **tannins** were detected. No alkaloids were found. The main compounds identified were both non-nitrogenous compounds: 2-hydroxy-4-methoxybenzaldehyde (Kubo and Kinst-Hori 1999) and monoterpene-lactone loliolide (Neergaard et al. 2010). Nutritional analysis indicated that *M. whitei* is rich in **minerals** and **vitamins** (Lamidi and Bourobou 2010; Iwu 2014).



2-Hydroxy-4-methoxybenzaldehyde



(-)-Loliolide

5) Major ethnomedicinal uses:

M. whitei root infusion is popularly used as aphrodisiac and in the treatment of male erectile dysfunction (African Herbal Pharmacopoeia 2010; Iwu 2014). It is also known to enhance cerebral and peripheral blood circulation, thus improving memory (<http://www.infonet-biovision.org/default/ct/250/medicinal-plants>). Leaf extracts are used in traditional medicine to treat nervous disorders (Neergaard et al. 2010).

6) Pharmacological studies:

In a screening of plant extracts for their affinity to the serotonin reuptake transporter protein, making use of an in vitro serotonin reuptake transporter (SERT) protein binding assay, according to Plenge et al. (1990), aqueous extracts of *M. whitei* leaves and flowers showed a mild affinity to SERT in rat brain, while the ethanolic leaf extract showed moderate antidepressant activity in vitro in the same SERT assay (Nielsen et al. 2004). Ethanolic leaf extracts of *M. whitei* were screened for affinity to the SERT in the [³H]-citalopram-binding assay and for inhibitory effects on the SERT, the noradrenaline transporter (NAT), and the dopamine transporter (DAT) and showed antidepressant-like in vitro and in vivo effects (Pedersen et al. 2008). Further studies using a bioassay-guided fractionation lead to the isolation of the monoterpene-lactone loliolide (Neergaard et al. 2010), which showed affinity to SERT. Common antidepressant drugs showing SERT inhibitory activity contain an amine nitrogen atom and an aromatic ring. (-)-Loliolide, as a non-nitrogenous compound, seems to bind to SERT in a different way than standard nitrogen-containing serotonin reuptake inhibitors (Neergaard et al. 2010). According to these results, there seems to exist other success models of binding and blocking SERT, and further studies on functional SERT inhibition molecules are needed.

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9.17 *Palisota hirsuta* (Thunb.) K. Schum

9.17.1 (*Commelinaceae*)

1) Synonyms:

Dracaena hirsuta Thunb.; *Dianella triandra* Afzel.; *Palisota maclaudii* Cornu.

2) Common names:

GB: baru (fula); siquimbe (sosso); mabubé, m'bobé-n'kamasop (nalu).
Eng (not found).

3) Photograph of the species (Fig. 9.8)

4) Description of the species:

A) Habitat, world distribution, and PALOP distribution:

Widespread in tropical Africa; common from Senegal to Zaire. It occurs as a weed on farmlands and in forest zones. It is also grown as an ornamental and might be used as a component of hedges. Found in Guinea-Bissau and Angola.



Fig. 9.8 *Palisota hirsuta* (Thunb.) K. Schum., from Guinea-Bissau, detail of inflorescence and leaves (original photo taken by L. Catarino)

B) Morphology of the species:

Perennial herb 1–3 m high with several strong, simple, or little branched erect stems. Leaves opposite, sessile; sheath pubescent, the margin ciliate with about 5-mm-long reddish-brown hairs; lamina 15–25 × 4–9 cm, lanceolate to obovate, acute at the apex, attenuated to the base into a short pseudo-petiole, with long reddish-brown hairs at the margin, mainly to the base, parallel nerved. Flowers bisexual in a more or less cylindrical long panicle (sometimes 2–4 panicles) at the end of the stem, each branch or partial inflorescence with 1–3 cm long peduncle, perpendicular to the main axis, subtended by a small bract; pedicels 1–3 mm long; perianth of 6 subequal tepals, white sometimes tinged with purple; stamens 3 and 2–3 staminodes, hairy; ovary 3-celled, glabrous, each cell with 1–8 ovules. Fruit globular, indehiscent, fleshy, about 1 cm in diameter, red, turning black and shining at maturity; seeds 10–16, little compressed, almost smooth (vanden Berghen 1988).

C) Conservation status:

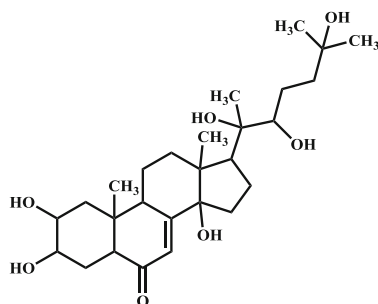
Not threatened.

D) Medicinal parts:

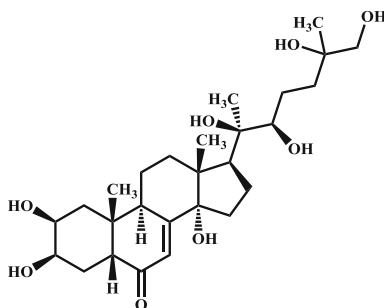
Roots and leaves.

E) Chemical composition:

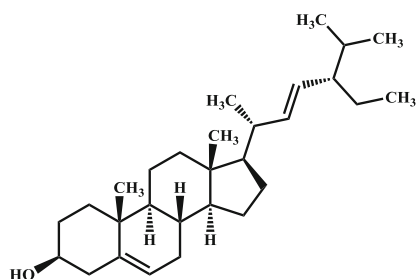
In the leaves, the presence of **terpenoids**, **alkaloids**, **tannins**, and **flavonoids** was tested by simple qualitative and quantitative methods being the last two groups and the most dominant constituents (Woode et al. 2010). In the roots, two rare **phytoecdysones** (ecdysteroids), ecdysterone, and 20, 26-dihydroxyecdysone along with **β -stigmasterol** and **eicosanoic acid** were isolated. In the fruits, **carotenoids** are the main pigments. These are esterified with **saturated fatty acids**, mainly with lauric acid (Neuwinger 1996).



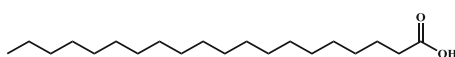
Ecdysterone



20,26-Dihydroxyecdysone



Beta-Stigmasterol



Eicosanoic acid

5) Major ethnomedicinal uses:

P. hirsuta is known for its analgesic and antiseptic effects. In many West African countries, a decoction of the twigs is used for gonorrhea; the roots for dysentery, anemia, and painful and inflammatory conditions (such as rheumatism); and the leaves as aphrodisiac (Benson et al. 2008) as well as in female infertility (Sarpong 2012). Whole plant is used as an analgesic and antiseptic (Mshana et al. 2000), antimicrobial (Anani et al. 2000; Iwu 2014), and antiviral (Anani et al. 2000). The root bark is employed as arrow poison and in the cicatrization of wounds (Neuwinger 1996). Dried leaves are smoked like tobacco for headaches and used in steam baths to treat malaria in southern Nigeria (Sarpong 2012).

6) Pharmacological studies:

The methanolic extract of the leaves of *P. hirsuta* showed antiviral activity against three test viruses, herpes simplex, Sindbis, and poliovirus (Anani et al. 2000), and the dominant activity in all cases was virucidal, that is, direct inactivation of virus particles (Hudson et al. 2000). The ethanolic root extract of *P. hirsuta* showed anti-inflammatory and antinociceptive/analgesic activities and a high antioxidant activity, which might explain in part the anti-inflammatory activity. These activities might be related with the compound 20-hydroxyecdysone, an ecdysteroid, isolated from the roots of *P. hirsuta*, which has proven to have a potent anti-inflammatory activity as well as antinociceptive action (Sarpong 2012). The ethanolic leaf extract of *P. hirsuta* also seems to have a hepatoprotective effect on carbon tetrachloride-induced hepatotoxicity on bioassays with rats (Imafidon et al. 2012). The hepatoprotective effects were dose dependent and more effective at higher doses. The presence of flavonoids, natural antioxidants, in the leaves plant might be responsible for that.

The ethanolic extract prepared from the roots of *P. hirsuta* exhibited an antipyretic effect in rats and an anti-inflammatory activity in the chick model of acute inflammation, comparable to the NSAID diclofenac, when administered preemptively and curatively (Boakye-Gyasi et al. 2008). According to these authors, the presence of flavonoids may contribute to the anti-inflammatory activity of the ethanolic root extract of *P. hirsuta*.

Woode et al. (2010) report on the effect of the ethanolic leaf extract of *P. hirsuta* in several common animal models used to study anxiety (light/dark box and elevated plus maze) and depression (forced swimming test and tail suspension test). The results suggest that the extract has anxiolytic and antidepressant-like effects in the models employed, possibly by GABAergic activation and/or effect on monoamine levels in the CNS. Those authors mentioned that it must be pointed out that the ethanolic leaf extract of *P. hirsuta* contains several secondary metabolites, and therefore apart from the speculated GABAergic and dopaminergic involvement in the anxiolytic and antidepressant effects, other mechanisms and neurotransmitters may be involved, such as serotonergic and glutamatergic neurotransmissions. Further experiments may be necessary therefore to confirm the exact mechanism/s involved in these CNS effects.

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9.19 *Securidaca longipedunculata* Fresen

9.19.1 (*Polygalaceae*)

1) Synonyms:

Securidaca longipedunculata var. *longipedunculata*; *Elsota longipedunculata* (Fresen.) Kuntze.

2) Common names:

Angola: Muipanhoca (muila); munduku (muquilengue); muripanhoca (dimba); m'tchacha, muxaxa (muila); omutate (handa); utata (Cangombe); vint'hata (Cuito-Cuanavale).



Fig. 9.9 *Securidaca longipedunculata* Fresen., from Guinea-Bissau, detail of fruits and inflorescences (original photos taken by L. Catarino)

GB: Mamampai (balanta); djutu (biafada); jurtú, jutù (creole); djúrô (fula); úli-élô (mandinga) (Catarino et al. 2006).

Moz: Boazi (Tete); colodi, colodji (Nampula); iosi (Namacurra); mupopo (Sofala); mupupo (Manica); naquehi, naquére (Cabo Delgado, Zambezia); tsatse (Maputo) (de Koning 1993)

Violet tree (Eng).

3) **Photograph of the species** (Fig. 9.9)

4) **Description of the species:**

A) **Habitat, world distribution, and PALOP distribution:**

Species widespread in tropical and subtropical parts of Africa, in different climates and altitudes, in woodland and arid savanna soils (Ndou 2006; <http://plants.jstor.org/compilation/Securidaca.longipedunculata>). It is found in PALOP countries: Guinea-Bissau, Angola, and Mozambique.

B) **Morphology of the species:**

Shrub or small tree up to 6 m high, sometimes spiny. Leaves alternate, simple; petiole up to 5 mm long; lamina 1–5×0.5–1.8 cm, very variable in shape and size, from very narrowly elliptic to broadly oblong-elliptic, pubescent when young soon glabrescent. Flowers pink or purple, in terminal and axillary 3–5 cm long racemes, zygomorphic, sweet-scented; pedicels up to 14 mm long, pubescent; sepals 5, unequal, two lateral ones petaloid, 5–11×4–9 mm, suborbicular, two anterior ones up to 5×4.5 mm, broadly ovate, the posterior one up to 5×4 mm, ovate-acuminate with ciliate margins; corolla with 3 petals, the upper 2 up to 7.5×3.5 mm narrowly elliptic, ciliate at the base, the lowest (carina) keel-shaped, up to 10 mm

long with a small lobed appendage 1 mm long near the apex. Stamens 8, the filaments united in staminal sheath ciliate on the upper margin. Fruit a samara, 3–5 × 0.8–2 cm, with an elliptic obliquely curved wing, sometimes with a second rudimentary wing and with a single rugulose or smooth seed 8–10 mm in diameter (Exell 1960).

C) **Conservation status:**

S. longipedunculata is a threatened and protected species; its roots are harvested and used as a medicine and that destroys the whole plant. Sustainable harvesting is difficult to implement in this model, but vegetative propagation of root cuttings is possible although difficult (Ndou 2006). Seeds germinate but seedlings are difficult to maintain (<http://tropical.ferninfo.org/viewtropical.php?id=Securidaca+longipedunculata>).

D) **Medicinal parts:**

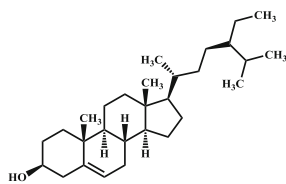
Roots, root bark, and leaves.

E) **Chemical composition**

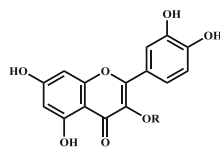
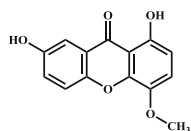
The distribution of the plant shows a variation in some features and chemical constituents, but the occurrence of **glycosides** (cardiac glycosides and glycosides of flavonoids and of saponins), **tannins**, **saponins**, and **alkaloids** was confirmed in different populations of Nigeria (Ajali and Chukwurah 2004; Junaid et al. 2008; Musa et al. 2013; Mongalo et al. 2015) and Cameroon (Moto et al. 2011).

The aqueous root extract of *S. longipedunculata* showed strong presence of saponins, alkaloids, and **volatile oil**, moderate presence of flavonoids and triterpenoids, and absence of steroids, tannins, and glycosides (Adebiyi et al. 2006). Another phytochemical analysis of *S. longipedunculata* root and root bark ethyl acetate, methanolic, and aqueous extracts confirms the existence of terpenes (methyl-2-hydroxybenzoate or methyl salicylate volatile oil), **steroids** (β -sitosterol), tannins, flavonoids (quercetin, rutin), **xanthone** (1,7-dihydroxy-4-methoxyxanthone), **phenolic acids** (*p*-coumaric acid, cinnamic acid, caffeic acid, and chlorogenic acid), and saponins (securidacaside A and securidacaside B, 3-*O*- β -D-glucopyranosylpresenegenin-28-*O*- β -D-apiofuranosyl-(1,3)- β -D-xylopyranosyl-(1,4)-[β -D-apiofuranosyl-(1,3)]- α -L-rhamnopyranosyl-(1,2)-{4-*O*-[(*E*)-3,4,5-trimethoxycinnamoyl]}- β -D-fucopyranosylester, and presenegenin) (Mongalo et al. 2015).

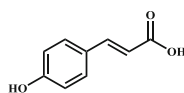
The essential oils of the root barks of *S. longipedunculata* were extracted by hydrodistillation with a Clevenger apparatus and analyzed by GC/MS and by ^1H and ^{13}C NMR spectra revealing methyl salicylate as the only compound (Nébié et al. 2004).



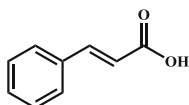
Beta-Sitosterol

R=H: Quercetin
R=rutinoside: rutin

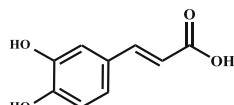
1,7-Dihydroxy-4-methoxyxanthone



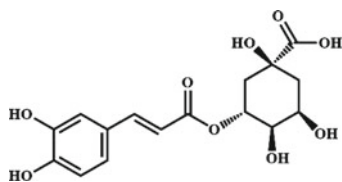
p-Coumaric acid



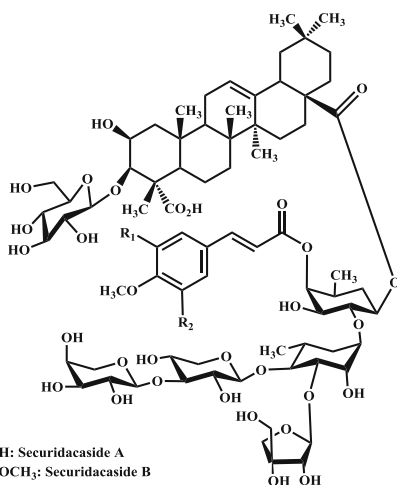
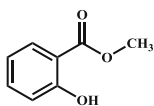
Cinnamic acid



Caffeic acid



Chlorogenic acid

R₁ = R₂ = H: Securidacside A
R₁ = R₂ = OCH₃: Securidacside B

Methyl salicylate

5) Major ethnomedicinal uses:

S. longipedunculata is a very popular plant in the African medicine with a wide diversity of uses for its roots, although these might be poisonous. The leaves but above all the roots and root barks are taken orally either powdered or as infusions for treating various purposes highlighting epilepsy, insomnia, headache, inflammation, tuberculosis, malaria, diarrhea, abortion, infertility problems, venereal diseases (Ndou 2006; Moto et al. 2011; Mustapha 2013), and male erectile dysfunction as well as snakebites and used as arrow poison, natural pesticide to stored grains, and natural repellent (Ndou 2006). In some regions, the roots are used to treat people who are believed to be possessed by evil spirits (<http://tropical.theferns.info/viewtropical.php?id=Securidaca+longipedunculata>).

6) Pharmacological studies:

The methanolic extract of the roots and root barks of *S. longipedunculata* showed significantly high antimicrobial activity against pathogenic Gram + and Gram – bacteria and against multidrug-resistant bacteria (Junaid et al. 2008; Musa et al. 2013; Mongalo et al. 2015). Further studies are required in order to isolate the active compounds responsible for this antimicrobial activity, but the phytochemical screening of the extracts revealed that flavonoids, tannins, and saponins are present in the entire fractions, alkaloids were present in methanol and ethyl acetate in fractions only, and tannins are present in all the fractions except hexane fraction (Mongalo et al. 2015).

The aqueous extract of *S. longipedunculata* roots exhibited anticonvulsant, anxiolytic, and sedative activities in mice in a dose-dependent manner (Adeyemi et al. 2010; Moto et al. 2011), suggesting that the plant extract may be used in the management of convulsion and psychosis. The sedative properties could be related to the presence of some components in the extracts activating the benzodiazepine and/or GABA (gamma-aminobutyric acid neurotransmitter) sites in the GABA_A receptor complex, and thus *S. longipedunculata* could be helpful in the treatment of insomnia and epilepsy in traditional medicine.

The aqueous root extract of *S. longipedunculata* was investigated for possible antinociceptive and central nervous system effects in mice using different assays, and results suggest that the extract possess antinociceptive and antidepressant-like effects with possible involvement of opioidergic pathways (Adebiyi et al. 2006). The tail-flick test is considered selective for opioid-like analgesic compound and the weak result of this test suggests that the extract of *S. longipedunculata* did not behave effectively as an opioid receptor agonist. It is possible that the extract presents a different central mechanism of action in this model (Adebiyi et al. 2006; Ojewole 2008). Concerning the exact mechanisms of anti-inflammatory effect of the aqueous root bark extract of *S. longipedunculata*, Ojewole (2008) suggests that, at least in part, it works by inhibiting the release, synthesis, and/or production of inflammatory mediators, including polypeptide kinins and prostaglandins, acting as the diclofenac.

On the other hand, the result of the forced swimming test (FST) clearly showed that the extract produced significant and dose-dependent antidepressant-like effect on the mice (Adebiyi et al. 2006). This effect was reversed by naloxone, an

opioid antagonist, which might suggest the involvement of opioidergic pathway in the antidepressant action. Previous studies have shown that analgesia by antidepressant drugs can be inhibited by naloxone and enhanced by enkephalinase inhibitors, which are inhibitors of the enzymes that degrade endogenous enkephalin opioid peptides (Gray et al. 1998). Adebisi et al. (2006) suggest that the extract might contain an antidepressant compound or the constituent of the extract may be simply behaving like an enkephalinase enzyme inhibitor. Once again further studies are needed to elucidate the chemical constituents responsible for the antidepressant effect of *S. longepedunculata* root extracts.

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9.21 *Xysmalobium undulatum* (L.) W.T. Aiton

9.21.1 (*Apocynaceae*)

1) **Synonyms:**

Asclepias undulata L.

2) **Common names:**

Angola: otyivatu (lunyaneka).

Milk bush, uzara, wild cotton, wave-leaved xysmalobium (Eng.).

3) **Photograph of the species (Fig. 9.10)**

4) **Description of the species:**

A) **Habitat, world distribution, and PALOP distribution:**

Xysmalobium comprises 40–45 species known from tropical Africa and South Africa. *X. undulatum* is common in grassland areas and seasonally wet localities, from sea level up to 2000 m of altitude (Schmelzer 2011). It is found in Angola and Mozambique.

B) **Morphology of the species:**

Robust perennial herb with white latex and a thick tuberous rootstock from which grow one to several annual stout unbranched stems with spreading white hairs. Leaves opposite, hispid, with a very short petiole; lamina very variable in shape, linear to ovate, 8–20×0.5–8.5 cm, acute or acuminate at apex, rounded, truncate or cordate at base, undulate or crispate and often revolute at the scabrid margins; stipules absent. Flowers 12–26 in pubescent umbelliform inflorescences arising laterally from the axils of the upper leaves; peduncles robust 1.2–4.5 cm long; bracts linear 3–4 mm long; pedicels slender, 14–18 mm long; sepals 5, ovate or lanceolate, 4–8 mm long, pubescent; corolla greenish or yellowish, often tinged with brown or



Fig. 9.10 *Xysmalobium undulatum* (L.) W.T. Aiton, from Angola (LISC Herbarium specimen, Mendes 2382)

pink outside divided almost to the base into 5 ovate lobes 5–10×2.5–6 mm, concave, acute and recurved at the apex, glabrous save in the upper 1/3 usually lanate or rarely glabrous or subglabrous. Corona very fleshy, without central cavity. Fruit a single follicle, 5–8 cm long and 1.5–2.5 cm wide, ovoid, often inflated, densely covered with soft hairy prickles; seeds flattened, ovate in outline with a tuft of long silky hairs (Goyder 2012).

C) Conservation status:

Not listed (African Herbal Pharmacopoeia 2010), but in some African regions, *X. undulatum* is officially protected because of overharvesting and habitat destruction. Tubers have been collected from the wild for local uses but export to the European market also happened. The tubers must be

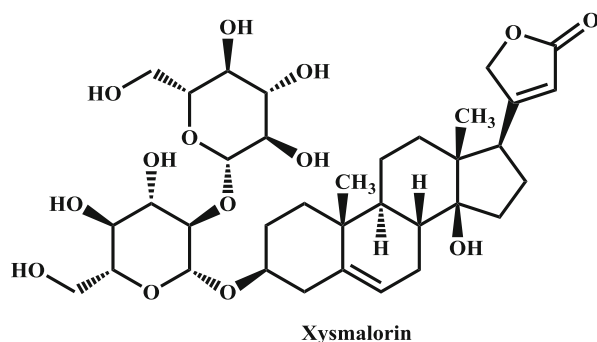
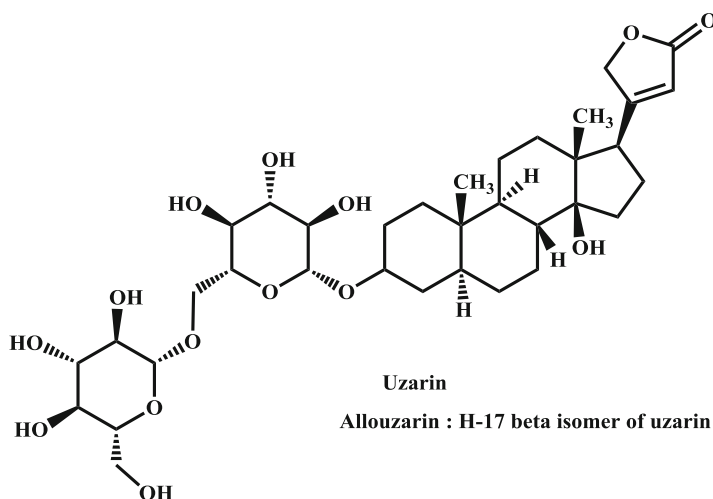
harvested at an early stage, as the older are thickened and deep-rooting. Seedlings should be transplanted by that time. Commercial plantations are currently made in small scale in South Africa (African Herbal Pharmacopoeia 2010; Schmelzer 2011).

D) Medicinal parts:

Tuberous roots.

E) Chemical composition:

The roots contain a mixture of **cardiac glycosides** (cardenolides) called uzarone or xysmalobin. The main compounds are uzarin (5.6 %), xysmalorin (1.5 %), and their isomers allo-uzarin (0.4 %) and allo-xysmalorin (0.1 %). Minor compounds include uzarigenin, ascleposide, coroglaucigenin, coroglaucigenin-3-*O*- β -glucoside, xysmalogenin, and pachygenol. From the seeds, the glycoside frugoside (0.5 %) was isolated (African Herbal Pharmacopoeia 2010; Schmelzer 2011).



5) *Major ethnomedicinal uses:*

The tubers of *X. undulatum* have traditional uses against acute diarrhea. A decoction or maceration of the pulverized tubercle is used against venereal diseases (African Herbal Pharmacopoeia 2010; Schmelzer 2011). The tubercle is also used as aphrodisiac and against stomach pain. The latexes are furthermore applied against snakebites (Schmelzer 2011).

6) *Pharmacological studies:*

The cardiac glycosides showed antidiarrheal and antispasmodic activity (African Herbal Pharmacopoeia 2010).

Several neurotransmitters are believed to be involved in the depression physiology, including serotonin, noradrenalin, and dopamine (Bang-Andersen 2006). It is assumed that depression is due to deficiency of one or another of these neurotransmitters (Walsh and Schwartz-Bloom 2005), although many other factors are believed to be involved. *X. undulatum* was screened, with other plant species as well, as a potential plant used for the treatment of depression, and ethanolic extracts from tubers and leaves showed high affinity to the serotonin reuptake transporter (SERT) (Nielsen et al. 2004). Other in vitro investigations (Pedersen et al. 2008), for affinity to the SERT in the [³H]-citalopram-binding assay and for inhibitory effects on the SERT, the noradrenalin transporter (NAT), and the dopamine transporter (DAT) using ethanol extracts of both aerial parts and roots of *X. undulatum*, showed significant antidepressant activity by exhibiting high affinity to the serotonin transporter (SERT) protein but was unable to inhibit the uptake of serotonin, noradrenaline, and dopamine. In a further assay, the same ethanolic extracts showed antidepressant-like effects in one animal model (FST). This action might be attributed to xysmalorin and uzarin but further studies are needed (Pedersen et al. 2008).

7) *Precautions and side effects:*

Safe when used appropriately (African Herbal Pharmacopoeia 2010).

8) *Dosage:*

1g of herb contains 75 mg of total glycosides. Adults, 45–90 mg of total glycosides; children, 15–30 mg of total glycosides (African Herbal Pharmacopoeia 2010).

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