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Review 1

The potential of South African plants in the development of new medicinal products 2

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Abstract 6

Southern Africa is an important focal point of botanical and cultural diversity but only a few plant species have hitherto become fully commercialised as medicinal products. In recent years there has been an upsurge in research and development activity, resulting in several new products and new crops. In this review, more than 90 of the best-known and most promising indigenous South African plants are listed and subjectively evaluated in the context of their potential for commercialisation as medicinal products for a variety of applications. The history of product development relating to the following species is briefly discussed and the plants and some of their products are illustrated: *Agathosma betulina* (buchu), *Aloe ferox* (bitter aloe), *Artemisia afra* (African wormwood), *Aspalathus linearis* (rooibos tea), *Bulbine frutescens* (burn jelly plant); *Cyclopia genistoides* (honeybush tea), *Harpagophytum procumbens* (devil's claw), *Hoodia gordonii* (hoodia, *ghaap)*, *Hypoxis hemerocallidea* ("African potato"), *Lippia javanica* (fever tea), *Mesembryanthemum tortuosum* (=*Sceletium tortuosum*) (*kanna*, *kougoed*), *Pelargonium sidoides* ("Umckaloabo"), *Siphonochilus aethiopicus* (African ginger), *Sutherlandia frutescens* (=*Lessertia frutescens*) (cancer bush), *Warburgia salutaris* (pepperbark tree) and *Xysmalobium undulatum* ("Uzara"). The main factors that are apparently responsible for failure or success will be highlighted, especially the importance of marketing strategy, proof of concept and barriers to market entry. 7

Keywords: Botanical diversity; Commercial potential; Commercial products; Herbal medicine; History; New products; Research and development 9

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1. Introduction

The first systematic account of the medicinal plants of South Africa were published by Pappe (1847, 1850, 1854, 1857, 1862, 1868), who described all the most important traditional herbal medicines known at the time. The *Flora Capensis* (a colonial flora) started by Harvey and Sonder (1860, 1862, 1864) included anecdotal information about the medicinal uses of several species and was probably intended as a plant use catalogue to facilitate the British imperial trade in plant products. A historically important book on medicinal plants is that of Smith (1888, revised in 1895) which provides insight into the most popular traditional medicine of the Eastern Cape region at that time. The *Flora of South Africa* published in six volumes by Marloth (1913–1932) also included information about commercially relevant plants. Marloth was a trained pharmacist with a special interest in medicinal plants. An important milestone in the documentation of medicinal plants was the detailed and comprehensive work of Watt and Breyer-Brandwijk (1962), "The Medicinal and Poisonous Plants of Southern and Eastern Africa", which is still regularly cited in scientific publications. Van Wyk et al. (1997) further conceptualised and popularised the field of medicinal plants in South Africa with the book entitled "Medicinal Plants of South Africa", which included short scientific monographs of 132 of the most popular and widely used medicinal plants. An updated and expanded edition, now including 150 monographs, is available (Van Wyk et al., 2009). Van Wyk and Gericke (2000) presented detailed information on a large number of medicinal plants in Part 2 of the book "People's Plants", which includes chapters on general medicines, tonic plants, mind and mood plants, women's health, wounds, burns and skin conditions, dental care, perfumes and repellents, and soaps and cosmetics. A comprehensive list of southern African medicinal plants (with literature references) is that of Arnold et al. (2002). Several other books provided valuable information on a regional level, especially those on Zulu medicinal plants by Hutchings et al. (1996), useful Namibian plants by Von Koenen (2001) and Sotho medicinal plants by Moffett (2010). Especially relevant in the context of new product development is the book edited by Diederichs (2006), entitled "Commercialising medicinal plants. A South African guide". The various chapters cover many aspects of research and development, including sustainable harvesting, conservation, trade regulations, economics, propagation, cultivation, chemistry and pharmacology, processing and packaging, marketing, business development and benefit-sharing.

The aim of this paper is to give a historical perspective on the commercialisation of medicinal plants in South Africa, to evaluate the progress that has been made and to highlight the potential of the South African medicinal flora for future research and development. A subjective evaluation of the commercial potential of more than 90 indigenous species is presented, together with brief reviews of a selection of 16 medicinal plants that are of particular interest in new product development.

2. The diversity of potentially useful medicinal plants in South Africa

The indigenous biological resources of Africa and the commercialisation of plants in Africa were reviewed by Geldenhuys and Van Wyk (2002) and Okole and Odhav (2002). According to the "African Plant Checklist and Database Project" (Klopper et al., 2006), 50 136 angiosperm taxa occur in Africa south of the Sahara (32 424 taxa in tropical Africa and 22 755 taxa in southern Africa). The last two numbers add up to 55 179 but the discrepancy is due to different taxonomic treatments in the two regions. This diversity represents perhaps 20 to 25% of the global total. The potential commercial importance of this resource can be judged by the comprehensive list of African medicinal plants (Neuwinger, 2000), where more than 5 400 medicinal plant taxa and over 16 300 medicinal uses are listed. This means that 10.8% of the African flora is known to be used in traditional medicine. The corresponding statistic for southern Africa is an estimated 3 000 species or 13.8% of the flora (Van Wyk and Gericke, 2000) or the more exact count of 2 942 species (administered to humans), representing 13.5% of the flora, presented by Arnold et al. (2002). These figures are based on an angiosperm species count of 21 817 for

southern Africa (Germishuizen and Meyer, 2003). The global review of commercialised medicinal plants by Van Wyk and Wink (2004) indicated that 83 African medicinal plants have been commercialised (as branded products) and that at best only 14 southern African species can be considered to be partially or fully commercialised compared to 336 species in Europe, for example. The most valuable of all medicinal plants may well be *Aloe vera* L. (of North African or perhaps Arabian origin) — fresh *Aloe vera* gel products had an annual retail value of approximately US$ 125 million in 2004 (Afolayan and Adebola, 2006).

From the data given above it is clear that there is a huge potential source of species, crops and products that are available for basic and applied research, as well as new product development. A list of the most promising indigenous South African species is presented in Table 1, showing that at least 90 medicinal plants can be considered for further development and commercialisation. Author citations for botanical species names are given in Table 1 and are not repeated in the text.

3. Historical perspectives on new herbal product development in South Africa

A large number of medicinal plants are regularly sold as crude, unprocessed drugs on traditional markets in various parts of South Africa (Cunningham, 1988; Williams et al., 1997; Mander, 1998; Von Ahlefeldt et al., 2003; Street et al., 2008; see also Ndhlala et al. (in press). The volumes and market value of these products are considerable. It has been estimated by Mander (1998) that the total volume of medicinal products traded annually in South Africa may exceed 20 000 tonnes, with a turnover of approximately US$ 60 million per year. There is a general trend to develop and brand these traditional products so that they resemble more closely those consumer products that are sold as over-the-counter medicines and herbal supplements. Some of the first products in these informal markets were produced by the company Impilo Drugs north of Durban. Examples are shown by Diederichs (2006) and Ndhlala et al. (in press).

In contrast to the large diversity of products in informal markets, only a few indigenous plants have thus far been developed for the formal market (health shops and pharmacies). These products are available as processed and standardised materials in modern packaging and in various branded dosage forms such as teas, tinctures, tablets, capsules or ointments. The 16 South African traditional medicines that have been partly or fully developed as commercial crops and products are shown in alphabetical order in Fig. 1. These are *Agathosma betulina*, *Aloe ferox*, *Artemisia afra*, *Aspalathus linearis*, *Bulbine frutescens*, *Cyclopia genistoides*, *Harpagophytum procumbens*, *Hoodia gordonii*, *Hypoxis hemerocallidea*, *Lippia javanica*, *Mesembryanthemum tortuosum* (=*Sceletium tortuosum*), *Pelargonium sidoides*, *S. aethiopicus*, *S. frutescens* (=*Lessertia frutescens*), *Warburgia salutaris* and *Xysmalobium undulatum*. These species are briefly discussed below, with emphasis on their commercial history.

The process of commercialisation in South Africa can be divided into four phases:

(1) Historical phase. Old South African products, first commercialised more than 100 years ago, which include *Agathosma* spp., *A. ferox*, *A. linearis*, *Cyclopia* spp., *H. procumbens*, *P. sidoides* and *X. undulatum*. These products are well known in the international trade and most of them have a long track record of exports to European countries.

(2) Bioprospecting phase. This phase involves the large-scale, ethnobotanically-guided screening of species to identify plants with commercial potential. This phase started in the early 1960s, with the companies Noristan and Smith-Kline Beecham, in collaboration with organic chemists from the Council for Scientific and Industrial Research (CSIR) and botanists from the National Botanical Institute (National Herbarium) in Pretoria, as the main role players. During this time a project on edible plants was started at the National Food Research Institute of the CSIR, which included the first work on *Hoodia* species (Maharaj, 2009). When the Noristan project was terminated, a large data base with confidential research results was transferred to the University of Cape Town. A bioprospecting project was started at the CSIR in 1993 and is still ongoing. More recently, there has been several multi-institutional projects (involving the South African National Biodiversity Institute and South African Universities) to explore the commercial potential of medicinal plants. Numerous scientific discoveries were made during this phase, including the isolation of monatin (a sweetener) from *Sclerochiton ilicifolius* (Vleggaar et al., 1992) and the discovery of P57 (an appetite suppressant) in *H. gordonii* (Van Heerden et al., 1998). Pioneering work on *H. hemerocallidea* also dates from this period, including the very first clinical study on an indigenous medicinal plant. The commercial history of *Hypoxis* (and subsequent "immune system boosters" derived from it) was reviewed by Drewes et al. (2008).

(3) Commercialisation phase. This phase started in the mid 1990s with research and development aimed at producing branded health care products from well-known and widely used indigenous medicinal plants. A feature of this phase was the development of several new crops, based on the consideration that large-scale commercial development may not be sustainable if the raw materials are taken from nature. The projects and products were not based on the results of bioprospecting, but focused on the most popular South African traditional medicines that were already widely traded in informal markets or extensively used as traditional household remedies. The health benefits of the plant species were already in the public domain for a long time (in most cases for at least a century). The logic of this approach is clear — why look for "new" products when the best ones have already been identified through centuries of trial and error? Plants developed into branded products during this phase include *A. afra*,

Table 1
Indigenous South African plant species of historic, current or potential importance in the formulation of commercial herbal medicines. Species which are partly or fully commercialised are shown in bold. (Subjective importance rating: +++ = high, ++ = average, + = low or none).

Species; family; common name(s) (partially or fully commercialised species are indicated in **bold**)	Plant parts used and medicinal use(s): (ro)ot (incl. rhizome, tuber or bulb); (st)em; (le)af; (fl)ower; (fr)uit; (se)ed; (ex)udate; (es)sential oil; (oil); (ed)ible oil/seed oil/fixed oil; leaf parenchyma (gel)
Acacia karroo Hayne; Fabaceae; sweet thorn	ba and le+ (diarrhoea), ex++ (emollient for conjunctivitis and haemorrhage, as pharmaceutical aid in solid formulations)
Adansonia digitata L.; Bombacaceae; baobab	fr++ (fever, diarrhoea), ba++ (urinary disorders, mild diarrhoea), le++ (fever)
Agathosma betulina (P.J.Bergius) Pillans; Rutaceae; round leaf buchu	le+++, es+++ (bitter tonic, digestive, diuretic, flavourant, externally for wounds)
Agathosma crenulata (L.) Pillans; Rutaceae; oval leaf buchu	le++, es++ (bitter tonic, digestive, diuretic, externally for wounds)
Alepidea amatymbica Eckl. & Zeyh.; Apiaceae; *lesoko*, *ikhathazo*	ro+++ (chest ailments, colds, influenza)
Alepidea cordifolia B.-E. Van Wyk; Apiaceae; *lesoko*, *ikhathazo*	ro+++ (chest ailments, colds, influenza)
Aloe arborescens Mill.; Xanthorrhoeaceae; kranz aloe, Japan aloe	gel+++ (topical uses, health drinks)
Aloe ferox Mill.; Xanthorrhoeaceae; bitter aloe, Cape aloe	ex+++ (laxative medicines, bitter tonics), gel+++ (topical uses, health drinks)
Aloe marlothii A.Berger; Xanthorrhoeaceae; mountain aloe (Natal aloes)	ex++ (laxative medicines, ethnoveterinary uses)
Artemisia afra Jacq. ex Willd.; Asteraceae; African wormwood, *wilde-als*	le+++ (bitter tonic, digestive, stomach pain, fever), es+++ (inhalant, aromatherapy)
Aspalathus linearis (Burm.f.) R.Dahlgren; Fabaceae; rooibos tea	st and le+++ (health drinks, anti-ageing?, anti-carcinogenic?)
Aspalathus pendula R.Dahlgren; Fabaceae; golden tea	st and le+++ (health drinks, source of rutin)
Asparagus laricinus Burch. (and other spp.); Asparagaceae; wild asparagus, *katdoring*	ro++ (diuretic, tonic, various uses)
Athrixia phylicoides DC.; Asteraceae; bush tea, Zulu tea	st, le and ro+++ (various uses, health drinks?)
Ballota africana (L.) Benth.; Lamiaceae; *kattekruid*	le+++ (infusions, tinctures: various uses, antispasmodic? sedative?)
Bulbine frutescens (L.) Willd.; Xanthorrhoeaceae; *ibhucu*	leaf gel+++ (topical uses, digestive tonic drinks)
Carpobrotus edulis (L.) L.Bolus; Mesembryanthemaceae; common sour fig	le++ (astringent, gargle for sore throat), fr++ (appetite suppressant)
Centella asiatica (L.) Urb.; Apiaceae; pennywort	le+++ (mainly topical uses, wound healing)
Chironia baccifera L.; Gentianaceae; Christmas berry, *aambeibos*	st and le+++ (bitter tonic, appetite stimulant)
Citrillus lanatus (Thunb.) Matsum. & Nakai; Cucurbitaceae; tsamma melon	se++ (oil for cosmetic use)
Conyza scabrida DC.; Asteraceae; *oondbos*	le+++ (inflammation, colds, fever)
Colenema album (Thunb.) Bartl. & H.L.Wendl.; C. *juniperinum* Sond. (and other spp.); confetti bush, fever bush	le+++ (colds and fever), es++ (topical uses, aromatherapy)
Cyclopia genistoides (L.) R.Br. (and other spp.); Fabaceae; honeybush tea	st and le+++ (health drinks)
Dicoma anomala Sond.; Asteraceae; *hloenya*, *umuna*, *maagbossie*	ro+or le+++ (colds and fever, stomach ailments, general medicine)
Dicoma capensis Less.; Asteraceae; *koorsbossie*, *wilde karmedik*	ro and le+++ (colds and fever, general medicine)
Dodonaea viscosa Jacq. var. *angustifolia* (L.f.) Benth.; Sapindaceae; *ysterhout*, *sandolien*	le+++ (colds and fever, venotonic, general medicine)
Elephantorrhiza elephantina (Burch.) Skeels; Fabaceae; *intolwane*, *elandboontjie*	ro+++ (antioxidant, skin ailments, diarrhoea, perforated ulcers, prostate hypertrophy, male pattern baldness)
Elytropappus rhinocerotis (L.f.) Less.; Asteraceae; renosterbos	st and le+(indigestion, dyspepsia, ulcers, stomach cancer, fumigant against influenza, appetite stimulant, bitter tonic)
Eriocephalus africanus L. (and other spp.); Asteraceae; Cape snowbush, *kapokbos*	le+++ (bitter tonic, digestive, stomach pain, fever), es+++ (inhalant, aromatherapy)
Eriocephalus punctulatus DC.; Asteraceae; Cape chamomile	le+++ (bitter tonic, digestive, stomach pain, fever), es+++ (inhalant, aromatherapy)
Euclea natalensis A.DC. (and other spp.); Ebenaceae; Natal guarri	ro++ (bronchitis, chest ailments, pleurisy, asthma, urinary tract infections, toothache, headache, toothbrush sticks/mouth rinses)
Eucomis autumnalis (Mill.) Chitt.; Asparagaceae (Hyacinthaceae); pineapple flower	ro++ (anti-inflammatory, urinary diseases, stomach ache, diarrhoea, enema for low back pain and healing of fractures)
Garuleum bipinnatum (Thunb.)Less.; Asteraceae; *slanghoutjie*	ro++ (expectorant, diaphoretic, diuretic)
Galenia africana L.; Aizoaceae; *kraalbos*, *geelbos*	le++ (topical products to treat skin ailments and infections)
Geranium incanum Burm.f. (and other spp.); Geraniaceae; *vrouebossie*, *bergtee*	le+ (health tea, bitter tonic, anti-diarrhoeal)

(continued on next page)

Table 1 (*continued*)

Species; family; common name(s) (partially or fully commercialised species are indicated in **bold**)	Plant parts used and medicinal use(s): (ro)ot (incl. rhizome, tuber or bulb); (st)em; (le)af; (fl)ower; (fr)uit; (se)ed; (ex)udate; (es)sential oil; (oil); (ed)ible oil/seed oil/fixed oil; leaf parenchyma (gel)
Gethyllis spp.; Amaryllidaceae; *kukumakranka*	fr+++ (digestives, tonics)
Gunnera perpensa L.; Gunneraceae; river pumpkin, *gobo*, *ughobo*	ro++ (uterotonic, stomach ailments, menstrual pain, rheumatic fever, topical application for wounds and psoriasis)
Harpagophytum procumbens (Burch.) DC. ex Meisn.; Pedaliaceae; devil's claw	ro+++ (arthritis, painful joints, dyspepsia and loss of appetite, topical application for wounds)
Helichrysum nudifolium (L.) Less.; Asteraceae; *hottentotsteebossie*	le+ (colds, chest ailments)
Helichrysum odoratissimum (L.) Sweet; Asteraceae; *imphepho*, Nguni incense, everlastings	le+++ (ritual incense, sedative), es+++ (inhalant, aromatherapy)
Heteromorpha arborescens (Spreng.) Cham. & Schltdl.; Apiaceae; parsley tree	es++ (headache, inhalant, aromatherapy?)
Heteropyxis natalensis Harv.; Myrtaceae; lavender tree	le++ (colds, weaning, roots for nose bleeds and bleeding gums, menorrhagia) , es++ (aromatherapy, topical products)
Hoodia gordonii (Masson) Sweet ex Decne. (and other spp.); Apocynaceae; *ghaap*, *ghôba*, hoodia	st++ (appetite suppressant)
Hypoxis hemerocallidea Fisch. & Avé-Lall.; Hypoxidaceae; *inkomfe*, "African potato"	ro++ (traditional tonic, benign prostate hyperplasia)
Kigelia africana (Lam.) Benth.; Bignoniaceae; sausage tree	fr++ (skin care, cosmetics)
Leonotis leonurus (L.) R.Br. (and other spp.); Lamiaceae; wild dagga	le+++ (coughs, colds, influenza, asthma, bronchitis, ethnoveterinary uses)
Lessertia frutescens: see *Sutherlandia frutescens*	
Leysera gnaphalodes (L.) L.; Asteraceae; *duinetee*, *hongertee*	st and le+++ (health tea, coughs, appetite stimulant)
Lippia javanica (Burm.f.) Spreng.; Verbenaceae; fever tea	le+++ (health tea, fever, cough, colds, bronchitis, influenza)
Lippia scaberrima Sond.; Verbenaceae; *mosukujane*	le+++ (health tea, fever, cough, colds, bronchitis, influenza)
Mentha longifolia (L.) Huds.; Lamiaceae; wild mint, *ballerja*	le+++ (headache, indigestion, fever, cough, colds, bronchitis, influenza, insomnia), es++ (aromatherapy)
Mesembryanthemum tortuosum L. [=*Sceletium tortuosum* (L.) N.E.Br.]; Mesembryanthemaceae; sceletium, k*anna*, *channa*, *kougoed*	le+++ (sedative, hypnotic)
Monsonia angustifolia E.Mey. ex A.Rich; Geraniaceae; *mokorotswana*	st and le++ (diarrhoea, low libido)
*Muraltia spinos*a (L.) F.Forest. & J.C.Manning [=*Nylandtia spinosa* (L.) Dumort.]; Polygalaceae; *cargoe*, *skilpadbessie*	st and le++ (digestive drinks, appetite stimulant, bitter tonic)
Myrothamnus flabellifolius Welw.; Myrothamnaceae; resurrection plant, *bergboegoe*	le+++ (health drinks, oral hygiene, gingivitis, topical products), es+++ (topical antiseptic, aromatherapy)
Ocotea bullata (Burch.) Baill.; Lauraceae; stinkwood	ba++ (headache, stomach ailments), es++ (aromatherapy)
Olea europaea L. subsp. ***africana*** (Mill.) P.S.Green; Oleaceae; wild olive	le+++ (bitter tonic, cardiotonic, hypotensive, diuretic)
Oncosiphon suffruticosum (L.) Källersjö (and other spp.); Asteraceae; *stinkkruid*	st and le++ (digestive tonic, stomachic, colds, fever, respiratory ailments, topically for skin ailments and inflammation)

Osmitopsis asteriscoides (P.J.Bergius) Less.; Asteraceae; *bels*, *belskruie*	le+++ (respiratory ailments, colds, fever, topically for inflammation and wounds), es+++ (ointments, aromatherapy)
Pelargonium graveolens L'Hér. (and other spp.); Geraniaceae; rose geranium	le+++ (colds, respiratory ailments, topically as emollient for wound healing), es+++ (aromatherapy)
Pelargonium sidoides DC.; Geraniaceae; rabas, "Umckaloabo"	ro+++ (colic, dysentery, colds and influenza, bronchitis)
Pelargonium reniforme Curtis.; Geraniaceae; rabas	ro++ (colic, dysentery, colds and influenza, bronchitis)
Pittosporum viridiflorum Sims; Pittosporaceae; cheesewood	ba+ (stomach ailments, fever)
Plumbago auriculata Lam.; Plumbaginaceae; plumbago	ro, ste and le+ (antispasmodic, coughs, headache)
Prunus africana (Hook.f.) Kalkman; Rosaceae; red stinkwood	ba+ (benign prostate hyperplasia)
Salvia africana-caerulea L. (and other spp.); Lamiaceae; *bloublomsalie*, wild sage	le+++ (respiratory and digestive ailments)
Sansevieria hyacinthoides (L.) Druce (and other spp.); Asparagaceae; piles root	ro and le++ (topical uses, ear infection, haemorrhoids, skin ulcers)
Scabiosa columbaria L.; Caprifoliaceae; wild scabious	le and ro++ (colic, heartburn)
Sceletium tortuosum: see *Mesembryanthemum tortuosum*	
Sclerocarya birrea (A.Rich.) Hochst.; Anacardiaceae; marula	se(oil)+++ (skin care), ba++ (stomach ailments, fever, diabetes)
Securidaca longepedunculata Fresen.; Polygalaceae; violet tree	ro+ (chest complains, rheumatism, various other uses)
Senecio serratuloides DC.; Asteraceae; two days, *insukumbili*	le++ (wound-healing ointments)
Siphonochilus aethiopicus (Schweinf.) B.L.Burtt; Zingiberaceae; African ginger	ro+++ (colds, cough, influenza, hysteria, pain, asthma, dysmenorrhoea, anti-inflammatory, bronchodilatory)
Sutherlandia frutescens (L.) R.Br.; Fabaceae; cancer bush	le+++ (adaptogen, tonic, anti-diabetic, cancer prophylaxis?)
Syzygium cordatum Hochst. ex C.Krauss.; Myrtaceae; water berry, *umdoni*	ba+ (respiratory ailments, stomach complaints)
Tarchonanthus camphoratus L. (*sensu lato*); Asteraceae; wild camphor bush	le+ (respiratory and stomach ailments), es+++ (inhalant, aromatherapy)
Tetradenia riparia (Hochst.) Codd; Lamiaceae; *iboza*, ginger bush	le++ (respiratory ailments), es+++ (inhalant, aromatherapy)
Teucrium africanum Thunb., *T. trifidum* Retz.; Lamiaceae; *katjiedrieblaar*	le++ (indigestion, colds, fever, general tonic)
Trichilia dregeana Sond., ***T. emetica*** Vahl; Meliaceae; *umkhuhlu*, Natal mahogany	se(oil)+++ (skin care, rheumatism)
Tulbaghia alliacea L.f.; Alliaceae; wild garlic	le++ (fever, colds)
Tulbaghia capensis L.; Alliaceae; Cape wild garlic	le++ (fever, colds)
Tulbaghia violacea Harv.; Alliaceae; wild garlic	le+++ (fever, colds)
Typha capensis (Rohrb.) N.E.Br.; Typhaceae; bulrush	ro+ (venotonic, male tonic)
Valeriana capensis Thunb.; Caprifoliaceae; Cape valerian	ro++ (asthma, insomnia, hysteria, nervous disorders)
Vernonia oligocephala (DC.) Sch.Bip. ex Walp.; Asteraceae; *groenamara*	le+ (stomachic, bitter tonic)
Viscum capense L.f., Viscaceae; Cape mistletoe; *litjiestee*	st+++ (health tea, tonic drinks)
Warburgia salutaris (Bertol.f.) Chiov.; Canellaceae; pepperbark tree	ba+, le+++ (coughs, colds, chest complaints, oral and oesophageal thrush, cystitis, natural antibiotic)
Withania somnifera (L.) Dunal; Solanaceae; Indian ginseng, *geneesblaarbossie*	ro+++ (adaptogen, tonic, sedative), le+++ (wound-healing ointments)
Ximenia americana L., ***X. caffra*** Sond.; Olacaceae; sourplum	se (oil)+++ (skin care)
Xysmalobium undulatum (L.) Aiton f.; Apocynaceae; *ishongwe*, "uzara"	ro+++ (anti-diarrhoeal, spasmolytic, wound-healing)
Zanthoxylum capense (Thunb.) Harv.; Rutaceae; small knobwood	ro, le, fr++ (dental plaque, oral rinses)
Ziziphus mucronata Willd.; Rhamnaceae; buffalo-thorn, *mokgalo*	le, ro++ (general tonic)

B. frutescens, *L. javanica*, *M. tortuosum*, *S. aethiopicus*, *S. frutescens* and *W. salutaris*. Amongst the earliest products were *L. javanica* and *L. scaberrima* herbal teas produced by the Veld Foods initiative in Botswana (ca. 1995) and the Healer's Choice range of branded products developed by South African Druggists (now incorporated

Fig. 1. South African medicinal plants of current commercial interest and examples of products. 1, *Agathosma betulina* (1A, plantation, planted ca. 1993; 1B, flowers; 1C, leaves; 1D, traditional tincture; 1E, tincture developed by South African Druggist in 1996); 2, *Aloe ferox* (2A, plantation, planted 1976; 2B, flowering plant; 2C, aloe lump/aloe bitters; 2D, cut leaf showing gel and yellow juice; 2E, example of container with aloe bitters; 2F, an example of an aloe gel drink; 2G, example of a bitter tonic containing aloe lump); 3, *Artemisia afra* (3A, plantation, planted 1995; 3B, leaves and flower heads; 3C, tincture developed by SA Druggists in 1996; 3D, tablets, developed by Phyto Nova in 2002); 4, *Aspalathus linearis* (4A, plantation; 4B, plant of the commercial Red tea type; 4C, leaves and flowers; 4D, red and green rooibos tea; 4E, modern rooibos product). 5, *Bulbine frutescens* (5A, plantation; 5B, flowering plant; 5C, flowers; 5D, leaves showing gel; 5E, commercial product, ca. 2002); 6, *Cyclopia* species (6A, *C. genistoides*; 6B, *C. intermedia*; 6C, *C. subternata*; 6D, honeybush tea; 6E, example of modern packaging); 7, *Harpagophytum procumbens* (7A, experimental plantation, 1995; 7B, leaves and flowers; 7C, fruit and product — sliced and dried secondary tubers; 7D, tincture); 8, *Hoodia gordonii* (8A,B, flowering plants; 8C, stems of various *Hoodia* species; 8D, example of modern product). 9, *Hypoxis hemerocallidea* (9A, experimental plantation, ca. 2000; 9B, 9C, flowering plants; 9D, corms; 9E, tincture); 10, medicinal teas (10A, *Leonotis leonurus* flowers; 10B, *Leysera gnaphalodes* flowers; 10C, *Lippia javanica* plant; 10D, *Lippia javanica* leaves and flowers; 10E, *Mentha longifolia* leaves and flowers); 11, *M. tortuosum* (11A, experimental plantation, planted 1996; 11B, stems, showing scletonised leaves; 11C, flowering plant; 11D, traditional product; 11E, tablets developed by Phyto Nova in 2000); 12, *Pelargonium sidoides* (12A, first plantation, planted 1995; 12B, flowering plant; 12C, flowers; 12D, roots; 12E, tincture). 13, *Siphonochilus aethiopicus* (13A, plantation; 13B, flowering plant; 13C, rhizome and roots; 13D, tablets developed by Phyto Nova in 2000); 14, *Sutherlandia frutescens* (14A, plantation, planted 2002; 14B, flowering and fruiting plant; 14C, dried leaves; 14D, tablets – prototypes and products – developed by Phyto Nova in 2000); 15, *Warburgia salutaris* (15A, tree; 15B, fruit; 15C, leaves and flowers; 15D, bark; 15E, tablets made from leaves, developed by Phyto Nova in 2000); 16, *Xysmalobium undulatum* (16A, commercial plantation; 16B, flowering plant; 16C, leaves and flowers; 16D, roots). Photographs: all by B.-E. Van Wyk.

Fig. 1 (*continued*).

into Aspen Pharmacare) in 1995 and 1996, which included a tincture made from low-thujone clones of *Artemisa afra*. The first research and development of *M. tortuosum* (=*Sceletium tortuosum*) also occurred during this period (Gericke and Van Wyk, 1997). The branded tinctures produced in the SA Druggists era served as role models and numerous similar tinctures (small and large scale) are now available. Another noteworthy effort to produce new crops and new herbal health care products is that of the company Phyto Nova (Pty) Ltd, responsible for the first branded products developed from *M. tortuosum*, *S. aethiopicus*, *S. frutescens* and *W. salutaris*. The last-mentioned was the origin of the concept of plant part replacement, i.e. the replacement of bark with chemically similar leaves, as a conservation measure. These products were developed as tablets and some are still available under the Phyto Nova Natural Medicines brand (a new name given to the company when it was taken over by Thebe Medicare in 2005). Some of the prototypes and first branded products developed by Phyto Nova are shown in Fig. 1. This phase has seen an unprecedented increase in the number of scientific publications and citations in patents (details are given in Van Wyk, 2008a and Makunga et al., 2008). A scopus search on 25 April 2008 showed that the number of citations in publications of the above-mentioned 16 commercial species increased from a total of 102 up to the year 1995, to 469 in the period 1996 to 2005, whilst the number of citations in patents rose from 72 to 438 in the corresponding periods (data from Table 1 in Van Wyk, 2008a).

(4) Regulated bioprospecting phase. This phase started in 2008 when the regulations of the National Environmental

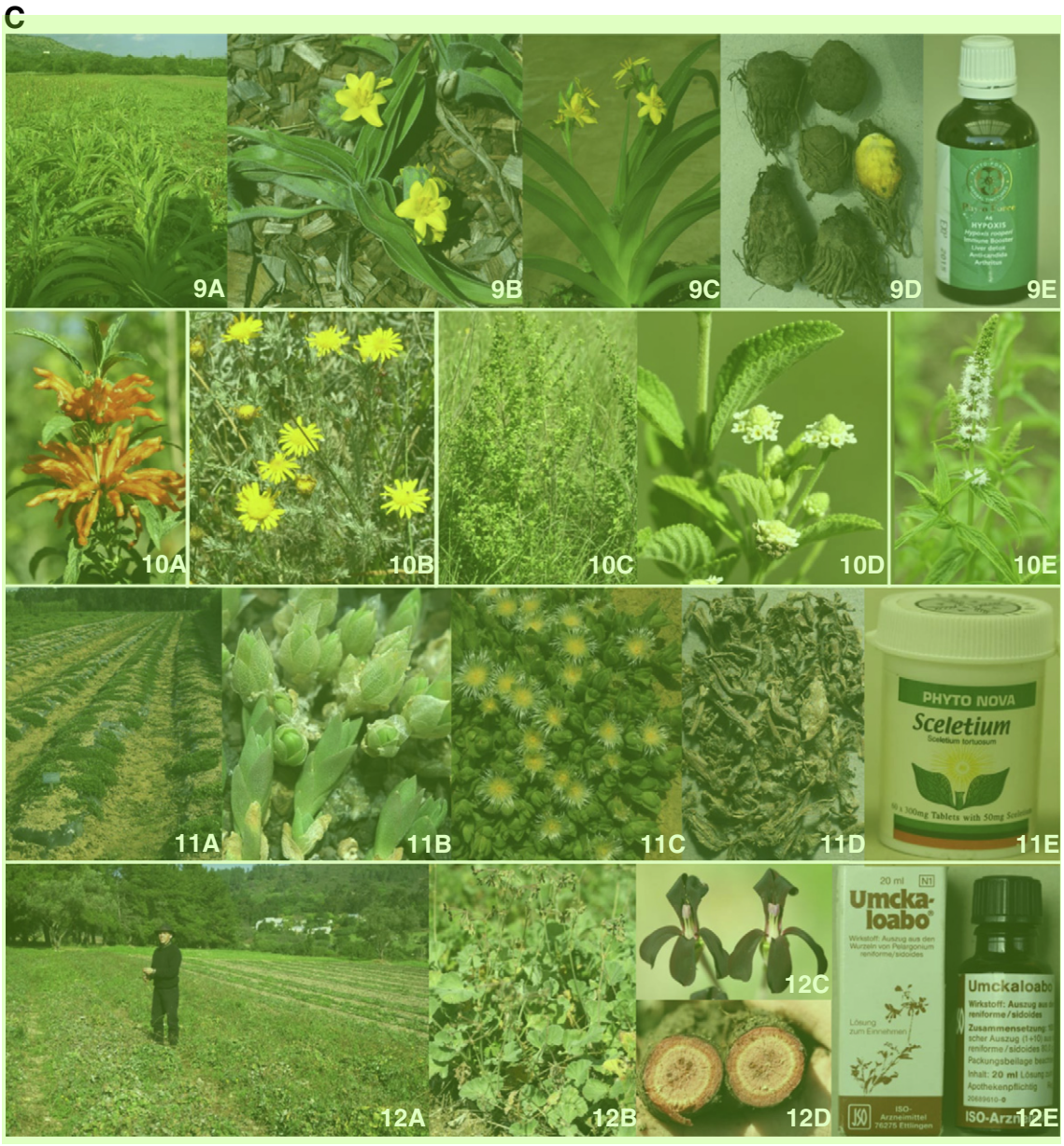

Fig. 1 (*continued*).

Management: Biodiversity Act of 2004 (NEMBA) came into effect on the 1st of April 2008. The Act attempts to ensure the equitable distribution of the benefits to be derived from the commercialisation of the South African flora. The implications of benefit sharing in practice have been discussed by several authors in the book edited by Denzil Phillips International (2009). Whilst the aims of the Act are laudable, the implementation of the regulations is impractical and may inadvertently discourage rather than encourage innovation in this potentially important sector of the economy. A review of relevant legislation and regulations can be found elsewhere in this issue (Myburgh, in press).

A very brief summary of the commercial history and published information for each of 16 commercially important medicinal plants of South Africa (see Fig. 1 and Table 1) is presented below. Monographs of these plants and general information about them can be found in Watt and Breyer-Brandwijk (1962), Hutchings et al. (1996), Van Wyk et al. (1997, 2009), Van Wyk and Gericke (2000), Von Ahlefeldt et al. (2003), Van Wyk and Wink (2004), Diederichs (2006), Van Wyk (2008a), Brendler et al. (2010) and Gurib-Fakim et al. (2010). A broad review of the ethnobotany, basic biology, taxonomy, biosystematics, genetics, chemistry and biological activity of most of the species was provided by Van Wyk (2008a), so that these aspects are not discussed in detail here. Also excluded are pan-African species which have been commercialised elsewhere (or with manufacturing based on raw material supplies from other African countries), such as *Adansonia digitata*, *Centella asiatica*, *Kigelia africana*, *Prunus africana*, *Trichilia emetica* and *Withania somnifera*.

Fig. 1 (*continued*).

3.1. *A. betulina* (Rutaceae) — round leaf buchu (Fig. 1, 1A to E)

Round leaf buchu is endemic to the Cederburg region of South Africa and is an important plant in the Khoi-San tradition. It has been wild-harvested at least since 1820 and cultivated since the 1970s or perhaps even earlier (Fig. 1, 1A). Recent efforts in crop development have resulted in buchu now being a viable option for small-scale farming (although producer prices have fluctuated wildly in recent years). Recently growers experienced severe losses, ascribed to a soilborne disease (Bezuidenhout et al., 2010). Tinctures of buchu ("buchu brandy", Fig. 1, 1D and medicinal products, Fig. 1, 1E) have a great reputation as general health tonics, stomachics, aromatic bitters, diuretics and mild urinary antiseptics (Van Wyk and Gericke, 2000). The major volatile compounds of round leaf buchu are isomenthone and diosphenol (Kaiser et al., 1975; Posthumus et al., 1996; Collins et al., 1996; Moolla and Viljoen, 2008), which are not only responsible for the distinctive flavour (not unlike *cassis*) but probably also for antispasmodic, antiseptic and diuretic activities (Wichtl and Bisset, 2000, Lis-Balchin et al., 2001; Moolla and Viljoen, 2008). The closely related oval leaf buchu (*A. crenulata*), as well as hybrids between the two species, are less desirable due to high levels of pulegone, a potentially harmful substance.

3.2. *A. ferox* (Xanthorrhoeaceae) — bitter aloe, Cape aloe (Fig. 1, 2A to G)

A. ferox has a very long history of use in southern Africa, as is evidenced by a San rock painting (Reynolds 1950) depicting

humans interacting with aloes. At current levels of demand, wild-crafting can be done without serious damage to natural populations (Newton and Vaughan, 1996). The first *A. ferox* plantation (6 ha) was established by Dr Tewis Muller on the farm Vinklaagte near Albertinia in 1976 (Fig. 1, 2A). Several other plantations have recently been established (e.g. 19 ha on the farm Tierfontein near Albertinia, in February 2008). By growing the plants in rows on open flat terrain, the harvesting operation becomes more efficient (because of easy access to the plants by both people and vehicles) thus reducing overall production costs and allowing for irrigation (by tractor-drawn water carts) during droughts so as to ensure a steady supply of raw materials. The bitter yellow leaf exudate (Fig. 1, 2D) is tapped by stacking the cut leaves around a hollow in the ground (lined with an animal skin or nowadays plastic sheeting), allowing the liquid to collect in the hollow. The exudate is boiled on open fires to reduce the water content, so that it solidifies to form a dark brown or black, glass-like substance known as aloe lump or Cape aloes (Fig. 1, 2C). This laxative medicine has been exported to Europe since 1761 (Marloth, 1913–1932; Kruger and Beyers, 1977; Robertson, 1979). Aloin (syn. barbaloin), an anthrone-*C*-glycoside, is the main laxative compound in aloe lump (Van Wyk et al., 1995). Annual exports in recent years amounted to ca. 350 tonnes (Knapp, 2006). The aloe lump is sold as is (Fig. 1, 2E) or tinctures containing aloe lump are used as traditional bitter tonics and stomachics (Fig. 1, 2F, 2G), reputed to also have anti-arthritic and anti-inflammatory properties (Newall et al., 1996; Blumenthal et al., 1998; Wichtl and Bisset, 2000; ESCOP, 2003). Nowadays the non-bitter, leaf parenchyma gel, obtained as "jelly" through a patented process (O'Brien et al., in press) and used to produce gel drinks, is the most popular product for the local industry (Fig. 1, 2F). A wide range of cosmetics and skin care products are also based on *A. ferox* gel. Another potential use of the gel is as a pharmaceutical excipient in novel drug delivery systems from renewable sources (Fischer et al., 2000). The work of the Aloe Council of South Africa (a non-profit company founded in 2003) has led to the development of a South African national standard for aloe raw materials, published in 2007 (Standards South Africa, 2007). There are important differences between the gels of *A. ferox* and *A. vera* — the South African gel product has polysaccharides of the arabinogalactan and rhamnogalacturonan types and it lacks acetylated sugars (Mabusela et al., 1990; O'Brien et al., in press). The quality control criteria for *A. vera* gel are therefore not applicable to *A. ferox*. There are opportunities to develop new products for human and animal health care, not only from *A. ferox* but also from other species such as *A. arborescens* and *A. marlothii*. Grace et al. (2008, in press) provided reviews of the traditional uses of *Aloe* species in southern Africa.

3.3. A. afra (Asteraceae) — African wormwood (Fig. 1, 3A to F)

African wormwood (*wildeals* in Afrikaans, *lengana* in Sotho and *umhlonyane* in Xhosa and Zulu) is one of the most popular and widely used traditional medicines in southern and eastern Africa (from Cape Town to Addis Abeba). The aromatic leaves are used for the treatment of a wide range of ailments (Dykman, 1908; Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Van Wyk et al., 1997; Neuwinger, 2000; Von Koenen, 2001; see also Bora and Sharma, 2011). It is the most important bitter tonic and appetite stimulant of Cape herbal medicine (Dykman, 1908; Thring and Weitz, 2006; Rood, 2008, Van Wyk 2008b) and is commonly taken for respiratory ailments and stomach pain. The essential oil of *A. afra* is exceptionally variable (Graven et al., 1990; Lawrence, 1996; Viljoen et al., 2006) but often contains 1,8-cineole (=eucalyptol), α-thujone, β-thujone, camphor and borneol as main monoterpenoids, together with chrysanthenyl acetate and other sesquiterpenoids. It is considered to be a useful substitute for armoise oil, which is produced from *A. vulgaris* L. and used in perfumes and as flavouring agent. Mukinda and Syce (2007) studied acute and chronic toxicity of *A. afra* essential oil (both quite low) but the level of thujone (which is a toxic compound) in the experimental material was not reported.

The plant is cultivated in home gardens as a medicinal herb and rooted cuttings are available from retail nurseries in South Africa. The first experimental plantings were made by Prof. Earle Graven at Fort Hare University (see Graven et al., 1990) in the late 1980s as part of a still ongoing research project on essential oils and the first commercial plantation at Gouda in the Western Cape Province of South Africa in 1995 (Fig. 1, 3A) as part of the South African Druggists project. The first commercial products based on low-thujone material were developed under the brand names of Healer's Choice in 1996 (as a tincture, Fig. 1, 3C) and Phyto Nova in 2002 (as tablets, Fig. 1, 3D).

3.4. A. linearis (Fabaceae) — rooibos tea (Fig. 1, 4A to E)

Rooibos tea has become a popular herbal tea with a growing reputation of having important health benefits, including antispasmodic, anti-oxidant, anti-ageing and anti-eczema activities (Watt and Breyer-Brandwijk, 1962; Van Wyk et al., 1997, 2009; Burger and Wachter, 1998; Van Wyk and Gericke, 2000; Van Wyk and Wink, 2004; Joubert et al., 2008; Joubert and De Beer, 2011). It has been used as a milk substitute for infants suffering from colic and has become popular as a health drink because of the absence of caffeine or other stimulants. It is one of the most successful and important of the indigenous industries. Annual production from plantations has reached 20 000 tonnes per annum and export volumes now exceed local consumption. The modest beginnings and early growth of the industry is described by Anonymous (1975), where mention is made of the first tea-makers of the Cederberg (of Khoi-San descent), the first commercialisation by Benjamin Ginsberg in 1904, the pioneering crop development efforts of Louis Leipoldt, P. le Fras Nortier and Oloff Bergh (and later also James Van Putten) and the background history of the establishment of the Rooibos Tea Control Board in 1954, as a single-channel marketing system to try and stabilise the wildly fluctuating supply and demand for rooibos tea. Amongst the early brands were Cederberg, Cedro, Clantee, Eleven O'Clock, Freshpak,

Grandiflora, Laager and Union. The chalcone aspalathin is the main phenolic compound (1 mg per g in fermented and up to 50 mg per g in unfermented tea) and is used for quality control (Joubert et al., 2008; Joubert and De Beer, 2011). Only the so-called Red type or Rocklands type is cultivated, but there is a renewed interest in harvesting some of the wild types for niche markets and Fair Trade networks (Van Wyk et al., 1997, 2009; Raynolds and Ngcwangu, 2010; Hawkins et al., 2011). Noteworthy recent innovations are the development of green and espresso rooibos tea (Fig. 1, 4D, E). Detailed reviews of rooibos tea are those of Joubert et al. (2008) and especially Joubert and De Beer (2011).

3.5. *B. frutescens* (Xanthorrhoeaceae) — burn jelly plant, ibhucu (Fig. 1, 5A to E)

The fresh leaf gel of *B. frutescens* and several other species are traditionally used topically to stop bleeding and to treat burns, cracked lips, cuts, grazes, itches, mosquito bites, rashes, ringworm, sores, wounds and herpes (Smith, 1895; Watt and Breyer-Brandwijk 1962; Roberts, 1990; Van Wyk et al. 1997, 2009; Van Wyk and Gericke 2000; Rood, 2008). A recent in vivo study has validated the traditional use of *B. frutescens* and *B. natalensis* leaf gel in the treatment of wounds (Pather et al., 2011). A tea made from the fresh whole plant (including roots) of *B. abyssinica* is taken by women to treat back pain, bladder and vaginal problems, cough, infertility and unspecified ailments (Van Wyk et al., 2008). Infusions of the roots of several *Bulbine* species are taken to treat blood disorders, convulsions, diabetes, diarrhoea, nausea (vomiting), rheumatism, urinary complaints and venereal diseases (Watt and Breyer-Brandwijk, 1962; Van Wyk et al., 1997, 2009; Felhaber and Mayeng, 1997; Van Wyk and Gericke, 2000; Rood, 2008). The main commercial interest is in the leaf gel, developed as branded products since 1995, for example as Montagu Museum Bulbine Crème (Fig. 1, 5E) and the BulbAloe range developed by J. Levine in 2004. A patented product (Widgerow and Chait, 1998) comprising microporous paper tape impregnated with a combination of bulbine gel (12.5 to 25% but preferable 20%) with pantheol and asiaticoside was shown (in a clinical study of nearly 300 patients) to enhance wound healing and hasten scar maturation. The healing effects are likely to be due to polysaccharides and/or glycoproteins in the leaf gel, as well as hydrating effects (Widgerow et al., 2000).

3.6. *C. genistoides* (Fabaceae) — honeybush tea (Fig. 1, 6A to E)

A comprehensive review of this important health drink is presented by Joubert et al. (in press). Honeybush tea lacks caffeine and has proven health benefits, including antioxidant, antimutagenic, anticarcinogenic and oestrogenic activity. The original product dates back to at least the middle of the eighteenth century (Pappe, 1847) and was made from *C. genistoides* (Marloth, 1913–1932) (Fig. 1, 6A). However, *C. intermedia* E. Mey. (Fig. 1, 6B) and *C. subternata* Vogel (Fig. 1, 6C) are also important sources of this tea, known respectively as mountain tea and *vlei* tea. The first branded products date back to the 1960s (e.g. Caspa Cyclopia Tea) (Joubert et al., in press). The industry is rapidly growing as a result of crop development by De Lange (1997), as well as improved processing and pharmacological studies, as summarised by Joubert et al. (in press). Important basic scientific information was contributed by De Nysschen et al. (1996), who first discovered and identified mangiferin as the major phenolic compound in honeybush tea, and Schutte (1997), who resolved the complicated infrageneric taxonomy of the genus *Cyclopia*. Honeybush tea has become very popular in recent years and the industry is poised for substantial growth (Joubert et al., in press).

3.7. *H. procumbens* (Pedaliaceae) — devil's claw (Fig. 1, 7A to D)

Devil's claw is widely distributed in the Kalahari region of southern Africa (Angola, Botswana, Namibia, South Africa and Zimbabwe) and has become a popular herbal medicine to treat arthritis, painful joints, dyspepsia and loss of appetite (Blumenthal et al., 1998; Newall et al., 1996; Wichtl and Bisset, 2000; Wegener, 2000; ESCOP, 2003; Van Wyk and Wink, 2004). Mild analgesic and anti-inflammatory properties have been reported in several clinical studies, reviewed by Wegener (2000), Chrubasik et al. (2003), Gagnier et al. (2004) and De Silva et al. (2011). The activity has been ascribed to iridoid glycosides — mainly harpagoside (0.5% to 3%), with smaller amounts of harpagide and procumbide, but total extracts are more active than the individual iridoids. The commercial history of devil's claw is poorly recorded but can be traced back to at least ca. 1907, when G.H. Mehnert started exporting dried tubers from Namibia to Germany (Cole, 2009). It is interesting that the plant is depicted in rock engravings in the Northern Cape Province of South Africa, indicating that the plant may have been important to Khoi-San people since ancient times. One of the first experimental plantations (1 ha) was established at Gouda in the Western Cape Province of South Africa in 1995 (Fig. 1, 7A). A review of the harvesting and export of this internationally well-known herbal product (mainly from Namibia) is presented by Stewart and Cole (2005) and Cole (2009), who highlighted the problems associated with benefit sharing when a plant is distributed across national boundaries.

3.8. *H. gordonii* (Apocynaceae) — hoodia, ghaap (Fig. 1, 8A to D)

Hoodia species and related plants of the family Apocynaceae are important traditional food sources of the Khoi-San people, first explicitly recorded by Marloth in 1932 as being useful in suppressing appetite (Marloth, 1913–1932). The history of research and development work on hoodia was reviewed by Maharaj (2009). The appetite-suppressant effect has been ascribed to a pregnane compound known as P57 (Van Heerden et al., 1998; Van Heerden, 2008) but there is as yet no published human clinical data to support the claim that

hoodia products can safely suppress appetite. Despite the lack of scientific information on efficacy and appropriate therapeutic doses, hoodia products have become popular all over the world (Jayawardane, 2011). The agreement reached between the CSIR and the San community (Maharaj, 2009) is one of the first examples of compensation of a local community for the benefits derived from the commercialisation of indigenous knowledge. A comprehensive review of *H. gordonii* was recently presented by Vermaak et al. (2011).

3.9. H. hemerocallidea (Hypoxidaceae) — star flower, inkomfe, "African potato" (Fig. 1, 9A–E)

This plant has become famous as a result of millions of rands spent on research and development since 1967, when *Hypoxis* phytosterols were first developed into a branded product (Harzol®) by an entrepreneur from Johannesburg (R. W. Liebenberg), who successfully marketed and sold it in Germany for the treatment of benign prostate hypertrophy (Drewes et al., 2008). A commercial preparation initially based on *Hypoxis* phytosterols (later on industrial sources) and claimed to have immune-stimulating effects was a huge market success in South Africa (Drewes and Horn, 1999; Drewes et al., 2008). The main active compounds of *Hypoxis* include rooperol (Drewes et al., 1984) which has patented anti-cancer activity (Drewes and Liebenberg, 1983) and phytosterols, which are still associated with over-the-counter immune-boosting products (Pegel 1973, 1997). Some in vitro evidence was published for the claimed immune-stimulant effects (Bouic et al., 1996). Extracts of the corms of *Hypoxis* (Fig. 1, 9D) are ingredients of an ever diversifying range of products used as anti-oxidants, anti-inflammatories, anti-diabetics and anti-convulsants (Drewes et al., 2008; see also the review by Owira and Ojewole, 2009).

3.10. L. javanica (Verbenaceae) — fever tea (Fig. 1, 10C to D)

Wild-harvested leaves of *L. javanica* and *L. scaberrima* have been used since the mid 1990s in branded infusions (herbal teas) to treat bronchitis, colds, coughs and fever. The plants are also traditionally used against numerous other ailments (Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Van Wyk et al., 1997, 2009; Van Wyk and Gericke, 2000). The traditional uses, chemistry and pharmacology were reviewed by Pascual et al. (2001). The essential oil of *L. javanica* is highly variable and five distinct chemotypes, each with its own main compound (myrcenone, carvone, piperitenone, ipsenone or linalool) were described by Viljoen et al. (2005). Leaves of *Lippia scaberrima* are also used as tea but the main components of the oil are carvone, 1,8-cineole and limonene (Combrinck et al., 2006). Standardised chemotypes may be suitable for use as flavour components in herbal teas, in addition to their reputed medicinal benefits. Other species that have potential as ingredients of herbal teas (individually or in combination with other species) include *Leonotis leonurus* (Fig. 1, 10A), *Leysera gnaphalodes* (Fig. 1, 10B) and *Mentha longifolia* (Fig. 1, 10E), all of which have a long history of traditional use as medicinal teas in southern Africa (Van Wyk and Gericke, 2000).

3.11. M. tortuosum [syn. Sceletium tortuosum] (Mesembryanthemaceae) — sceletium, kanna, kougoed (Fig. 1, 11A to E)

Kougoed, *kanna* or sceletium is a traditional masticatory and sedative of the Nama people of South Africa, first recorded in detail by Simon van der Stel (1685) under the name "Channa". In a molecular systematic study (Klak et al., 2007), *Sceletium* and other genera were formally subsumed under the genus *Mesembryanthemum*. The uses and properties have been described by Watt and Breyer-Brandwijk (1962), Watt (1967), Smith et al. (1996), Van Wyk and Gericke (2000), Van Wyk and Wink (2004), Gericke and Viljoen (2008) and Van Wyk et al. (2009). It is interesting to note that the first experimental plantings (Fig. 1, 11A) were made in 1996, more than 300 years after Van der Stel (1685) first suggested that profit could be made from growing and trading with *channa*. The activity of the plant and the traditional product (Fig. 1, 11B–D) is ascribed to serotonin reuptake-inhibiting alkaloids, of which mesembrine is the main compound (Gericke and Van Wyk, 1997). The first tablets containing powdered whole plants were produced by Phyto Nova in 2000 (Fig. 1, 11E). A benefit-sharing agreement was recently signed between HGH Pharmaceuticals and the South African San Council, who in turn entered into an agreement with the Nama communities of Kamiesberg in Namaqualand to share financial benefits that may result from commercialisation. Research and development work is currently underway to create what may become an important and commercially successful herbal sedative for international markets.

3.12. P. sidoides (Geraniaceae) — rooirabas, "Umckaloabo" (Fig. 1, 12A to D)

The interesting commercial history of this important plant, first developed and marketed in England in 1898 (for the treatment of tuberculosis), was described by Brendler and Van Wyk (2008). It is now mainly used for the treatment of bronchitis. Crop development started near Wellington in the Western Cape Province of South Africa in 1995 (Feiter, 2009), when the first plantations (Fig. 1, 12A) were established. Since the early 1990s, a tincture made from the tuberous roots (Fig. 1, 12C,D) has become one of the most successful phytomedicines in the world, with annual sales in Germany alone exceeding € 80 million. The medicinal properties are associated with coumarins, including umckalin and 5,6,7-methoxycoumarin (Kolodziej and Kayser, 1998; Kayser et al., 2001). Details of the commercial history, botany, chemistry, pharmacology and clinical studies can be found in the review of Brendler and Van Wyk (2008), whilst recent developments related to intellectual property rights are presented by Feiter (2009) and Myburgh (in press).

3.13. S. aethiopicus (Zingiberaceae) — African ginger (Fig. 1, 13A to D)

This plant is widely distributed in tropical Africa and the rhizomes and roots are very important and popular traditional

medicines, mainly used to treat asthma, candida, colds, coughs, headache and malaria (Watt and Breyer-Brandwijk, 1962; Van Wyk et al., 1997, 2009; Van Wyk and Gericke, 2000; Crouch et al., 2000; Van Wyk and Wink, 2004; Van Wyk, 2008a). Pioneering research on the cultivation and tissue culture propagation of *S. aethiopicus* were done during the early 1990s by G. Nichols (at the Silverglen Municipal Nursery near Durban — Fig. 1, 13A) and J.N. Eloff (at the Kirstenbosch Research Centre in Cape Town). It is now commercially cultivated on a small scale at several locations in South Africa. The first branded products (tablets made from freeze-dried rhizomes and roots) were marketed by Phyto Nova in 2000 (Fig. 1, 13C,D). The major chemical constituents are sesquiterpenoids of the furanoid type (Van Wyk et al., 1997; Holzapfel et al., 2002; Viljoen et al., 2002) and diarylheptanoids (Van Wyk et al., 2009). Research and development at the CSIR is ongoing (see brief review by Van Wyk, 2008a).

3.14. S. frutescens [syn. Lessertia frutescens] (Fabaceae) — cancer bush, sutherlandia (Fig. 1, 14A to D)

Cancer bush is traditionally used in southern Africa as a tonic and adaptogen (known in Sesotho as *Musapelo*) to alleviate stress and anxiety (Moteetee and Van Wyk, 2007). Published and unpublished traditional uses and anecdotes are summarised in a review by Van Wyk and Albrecht (2008). These include asthma, cancer (prevention and treatment), chronic bronchitis, colds, cough, diabetes, dysentery, fever, gastritis, heartburn, heart failure, indigestion, influenza, kidney and liver ailments, oesophagitis, peptic ulcers, poor appetite, rheumatism, unspecified wasting diseases and urinary tract infections. It has received special attention because of anecdotes suggesting dramatic improvements in the quality of life in HIV/AIDS patients and a reduction in the muscle-wasting (cachexia) effect of AIDS. A safety study done by the Medical Research Council of South Africa (Seier et al., 2002) and a clinical (phase I) study (Johnson et al., 2007) showed no signs of toxicity or side effects. The leaves contain a diversity of chemical compounds (reviewed by Van Wyk and Albrecht, 2008), including pinitol, triterpenoid saponins, flavonoids and amino acids (such as *L*-canavanine and GABA), to which various biological activities have been ascribed. Commercial plantations were established in the late 1990s (e.g. at Sannieshof in the North-West Province, Fig. 1, 14A). The first branded products were tablets made from powdered leaves of a selected chemotype that became known as the SU1 type — the protypes and products dating from 2000 and marketed by Phyto Nova are shown in Fig. 1, 14D.

3.15. W. salutaris (Canellaceae) — pepperbark tree (Fig. 1, 15A to E)

The pepperbark tree is one of the most important and popular traditional medicines of tropical Africa. The bark (Fig. 1, 15D) is widely used to treat abdominal pain, cancer, constipation, colds, coughs, fever, headache, influenza, malaria, rheumatism and venereal diseases (Van Wyk and Gericke, 2000; Van Wyk et al., 2009). The tree has become rare and endangered in South Africa as a result of excessive harvesting of bark, so that chemically similar leaves (with the same pungent taste as the bark) were used to produce the first branded product (tablets), marketed by Phyto Nova in 2000 as a natural antibiotic to treat oral and oesophageal thrush (Fig. 1, 15E). The conservation and cultivation of *W. salutaris* were initiated by the company HL& H (now Mondi Forests), who started a living gene bank of about 3000 trees at their White River Nursery. Using expertise in the rooting of *Eucalyptus* cuttings, a large number of trees were propagated for distribution in 1996, when *W. salutaris* was chosen as South Africa's "Tree of the Year". By the year 2000, Mr Rodger Stewart has established a small plantation on a farm north of Durban, KwaZulu-Natal, using horticultural experience gained in commercial tea plantations. As a result, freeze-dried leaves and bark are now available in small commercial quantities. Recently, a new product was developed by Phyto Nova Natural Medicines (from freeze-dried *Warburgia* leaf) to treat cystitis. The bark and leaves contain drimane sesquiterpenoids (Mashimbye et al., 1999), including warburganal, mukaadial, salutarisolide, polygodial and isopolygodial, as well as muzigadial (Rabe and Van Staden, 2000).

3.16. X. undulatum (Apocynaceae) — Uzara, ishongwe (Fig. 1, 16A to D)

The roots of *X. undulatum* are important in traditional medicine in South Africa. It is used to treat abscesses, afterbirth cramps, colic, diarrhoea, headache, hysteria, stomach cramps and wounds, as recorded by Watt (1935), Watt and Breyer-Brandwijk (1962), Pujol (1990), Hutchings and Van Staden (1994), Hutchings et al. (1996), Van Wyk et al. (1997, 2009) and Von Koenen (2001). It also has a long history of commercial use and has been cultivated in South Africa (near Pretoria) since 1904 (Fig. 1, 16A). Extracts were introduced into the German pharmaceutical market in 1909 (or 1911, according to Ghorbani et al., 1997) and marketed (under the name "Uzara") for the treatment of non-specific, acute diarrhoea. The roots contain uzarin and xysmalorin as major cardenolide glycosides (Ghorbani et al., 1997), to which the inhibition of intestinal motility is ascribed.

4. Species with commercial potential as herbal products

As shown in Table 1, there are numerous species that stand out as having exceptional potential for the development of new phytomedicines, dietary supplements or general tonics. Some are also suitable for new ethnoveterinary products, although this application is not specifically dealt with here (see McGaw and Eloff, 2008). The evaluation of species in Table 1 is somewhat subjective, but the following aspects are important: (1) The species must be suitable for cultivation (or be abundant in nature to allow wild-crafting — i.e. sustainable harvesting from the wild); (2) it must have a well-recorded history of traditional use (preferably in more than one traditional healing culture); (3) it must be regularly used, with no evidence of side

effects; (4) it must be amongst the most popular indigenous remedies for the particular indication it is being developed/marketed for and (5) there must be a potential demand for the product. There may be a demand for more sophisticated dosage forms and standardised products within the culture where it is well known, or a new demand may be created around compelling evidence of safety and efficacy in the historical track record of the species, preferably with interesting ethnobotanical information to support the marketing efforts.

The list in Table 1 includes several well-known and commercially important species that have for unknown reason never received much attention in South Africa, such as *Aloe arborescens*, *Centella asiatica*, *Kigelia africana*, *Pelargonium graveolens* and *Withania somnifera*. Also listed are several plants that appear to have considerable potential, including *Alepidea amatymbica*, *Aloe marlothii*, *Aspalathus pendula*, *Ballota africana*, *Chironia baccifera*, *Colenema album*, *Dicoma anomala*, *D. capensis*, *Dodonaea viscosa*, *Eriocephalus africanus*, *E. punctulatus*, *Gethyllis* species, *Gunnera perpensa*, *Helichrysum odoratissimum*, *Heteropyxis natalensis*, *Leonotis leonurus*, *Leysera gnaphalodes*, *Mentha longifolia*, *Myrothamnus flabellifolius*, *Olea europaea* subsp. *africana*, *Osmitopsis asteriscoides*, *Salvia africana-caerulea*, *Sclerocarya birrea*, *Tarchonanthus camphoratus*, *Tetradenia riparia*, *Teucrium trifidum*, *Trichilia dregeana*, *T. emetica*, *Tulbaghia violacea*, *Viscum capense*, *Ximenia americana* and *X. caffra*.

5. Discussion

5.1. Proof of concept and scientific data

Scientific evidence to substantiate medicinal claims appears to be the most important limiting factor in the development of indigenous herbal products. Traditional uses may be a good starting point in product development but is unlikely to lead to sustainable commercial success in the long run. Examples that come to mind are *H. hemerocallidea*, *Aloe vera* and *H. gordonii*. *Hypoxis* was the subject of numerous studies in the 1970s and formed the basis of a lucrative trade in so-called "immune-stimulants" but as yet there is no convincing in vivo evidence published in peer-reviewed journals. Aloe gel health drinks are perhaps the best example of a major international herbal product that still lacks convincing clinical evidence of therapeutic benefits. The almost complete absence of published clinical studies is especially noteworthy when the enormous annual turnover of this industry is considered. (Perhaps no-one wants to spoil a good marketing story with inconvenient facts?). Weight loss products are often purely market-driven and *Hoodia* appears to be no exception. The lack of reliable published clinical evidence on the therapeutic dose and its efficacy as appetite suppressant does not seem to be regarded as a serious concern and there are still numerous *Hoodia*-containing products available on the international market.

The main stimulus for marketing success of herbal products appears to be proof of concept in the form of human trials. The commercial success of two of the most famous and valuable indigenous species can be related to clinical evidence of efficacy in the form of double-blind, placebo-controlled studies: *H. procumbens* became internationally known after the first clinical studies were conducted in France and Germany in the 1960s; *P. sidoides* became the basis of a very lucrative over-the-counter medicine only after several clinical studies (summarised in Brendler and Van Wyk, 2008). The recent boom in the rooibos tea industry may at least partly be ascribed to a growing body of scientific evidence indicating important health benefits. Clinical evidence in the form of post-marketing surveillance or double-blind, placebo-controlled studies may pay healthy dividends in the long run, despite the large financial inputs required for this type of research. A good example is the marketing success achieved with *P. sidoides*. However, this depends on the product being developed. No company will spend a lot of money on clinical research to develop an anti-diarrhoeal as there are already many such products available.

5.2. Intellectual property rights

Legislation aimed at protecting the intellectual property rights of indigenous communities, despite good intentions, is likely to become an important new barrier to entry in commercialisation and product development. Recent experiences (Denzil Phillips International, 2009), have shown that some of the regulations are impractical and that prospective developers are subjected to excessive bureaucracy. See also the review by Myburgh (in press) in this issue.

5.3. The importance of marketing

Sustainable commercial success appears to be achieved only after many years of investment and marketing. The few indigenous plants that have become important commercial crops and products all have a very long history of crop and product development, with large amounts of money spent on marketing over many years. These include *A. betulina* (since 1820), *A. ferox* (since 1761), *A. linearis* (since 1904), *C. genistoides* (since 1847; branded since the 1960s), *H. procumbens* (since ca. 1907), *P. sidoides* (since 1898) and *X. undulatum* (since 1909). In 2002, it was estimated that the establishment of a new brand of herbal medicine in South Africa would cost at least R 12 million rands or ca. € 1.2 million (Louis Schutte, S.A. Natural Products, personal communication, 2002). Multi-level marketing, the backbone of the enormous *Aloe vera* industry in the USA, has in recent years proven to be a highly successful strategy in South Africa and may become increasingly important in response to a very competitive retail market. There is no doubt that opportunities still exist for market-driven development projects based on those indigenous medicinal plant species listed in Table 1.

6. Conclusions

The exceptionally diverse South African flora comprises numerous species that can be developed as exciting new products (including herbal medicines and other health care products, herbal teas and functional foods). There is an urgent need to

encourage bioprospecting and new product development, to build local capacity in this field and to implement measures to counteract the negative perceptions and practical difficulties associated with restrictive new regulations. The development of a successful new product is a complicated process that requires hard work, technical skills, substantial investment and innovative marketing, sustained over long periods. The pioneers involved in this process often gain nothing except the satisfaction that they have created opportunities for the next generation of skillfull entrepreneurs to achieve market success. It is hoped that inspired and talented individuals will be allowed the freedom to maximise the opportunities presented by the rich diversity of the South African flora by developing innovative products in order to create new marketing opportunities in local and international markets, and to find new ways of generating wealth for the benefit of all.

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References

Afolayan, A.J., Adebola, P.O., 2006. *Aloe vera* (L.) Burm.f. [Internet] record from protabase. In: Schmelzer, G.H., Gurib-Fakim, A. (Eds.), PROTA (Plant Resources of Tropical Africa / Ressources végétales de l'Afrique tropicale), Wageningen, Netherlandshttp://database.prota.org/search.htm. Accessed 14 July 2011.

Anonymous, 1975. Rooibosteebeheerraad 1954–1975. The Rooibos Tea Control Board, Clanwilliam.

Arnold, T.H., Prentice, C.A., Hawker, L.C., Snyman, E.E., Tomalin, M., Crouch, N.R., Pottas-Bircher, C., 2002. Medicinal and magical plants of southern Africa: an annotated checklist. Strelitzia 13. National Botanical Institute, Pretoria.

Bezuidenhout, C.M., Denman, S., Kirk, S.A., Botha, W.J., Mostert, L., McLeod, A., 2010. *Phytophthora* taxa associated with cultivated *Agathosma*, with emphasis on the *P. citricola* complex and *P. capensis* sp. nov. Persoonia 25, 32–49.

Blumenthal, M., Busse, W.R., Goldberg, A., Gruenewald, J., Hall, T., Riggins, C.W., Rister, R.S. (Eds.), 1998. The Complete German Commission E Monographs. American Botanical Council, Austin, Texas.

Bora, K.S., Sharma, A., 2011. The genus *Artemisia*: a comprehensive review. Pharmaceutical Biology 49, 101–109.

Bouic, P.J.D., Etsebeth, S., Liebenberg, R.W., Albrecht, C.F., Pegel, K., Van Jaarsveld, P.P., 1996. β-Sitosterols and β-sitosterol glucoside stimulate human peripheral blood lymphocyte proliferation: implications for their use as an immunomodulatory vitamin combination. International Journal of Immunopharmacology 18, 693–700.

Brendler, T., Van Wyk, B.-E., 2008. A historical, scientific and commercial perspective on the medicinal use of *Pelargonium sidoides* (Geraniaceae). Journal of Ethnopharmacology 119, 420–433.

Brendler, T., Eloff, J.N., Gurib-Fakim, A., Phillips, L.D. (Eds.), 2010. African Herbal Pharmacopoeia. AAMPS Publishing, Port Louis, Mauritius.

Burger, A., Wachter, H. (Eds.), 1998. Hunnius Pharmazeutisches Wörterbuch, 8th ed. Walter de Gruyter, Berlin.

Chrubasik, S., Conradt, C., Black, A., 2003. The quality of clinical trials with *Harpagophytum procumbens*. Phytomedicine 10, 613–623.

Cole, D., 2009. Sustainable harvesting of devil's claw in Namibia. Case study 7a. In: Denzil Phillips International (Ed.), Plants, People and Nature. Benefit sharing in practice. AAMPS Publishing, Port Louis, Mauritius.

Collins, N.F., Graven, E.H., Van Beek, T.A., Lelyveld, G.P., 1996. Chemotaxonomy of commercial buchu species (*Agathosma betulina* and *A. crenulata*). Journal of Essential Oil Research 8, 223–228.

Combrinck, S., Bosman, A.A., Botha, B.M., Du Plooy, W., McCrindle, R.J., Retief, E., 2006. Effects of post-harvest drying on the essential oil and glandular trichomes of *Lippia scaberrima* Sond. Journal of Essential Oil Research 18, 80–84.

Crouch, N.R., Lötter, M.C., Krynauw, S., Pottas-Bircher, C., 2000. *Siphonochilus aethiopicus* (Zingiberaceae), the prized Indungulu of the Zulu — an overview. Herbertia 55, 115–129.

Cunningham, A.B., 1988. An investigation of the herbal medicine trade in Natal/KwaZulu. Institute of Natural Resources Investigative Report No. 29. Institute of Natural Resources, Pietermaritzburg.

De Lange, H., 1997. Honeybush Tea – Information – 19 May 1997. National Botanical Institute, Claremont. [in Afrikaans].

De Nysschen, A.M., Van Wyk, B.-E., Van Heerden, F.R., Schutte, A.L., 1996. The major phenolic compounds in the leaves of *Cyclopia* species (honeybush tea). Biochemical Systematic and Ecology 24, 243–246.

De Silva, V., El-Metwally, A., Ernst, E., Lewith, G., Macfarlane, G.J., 2011. Evidence for the efficacy of complementary and alternative medicines in the management of osteoarthritis: a systematic review. Rheumatology (Oxford, England) 50, 1672–1683.

Denzil Phillips International, 2009. Plants, people and nature. Benefit Sharing in Practice. AAMPS Publishing, Port Louis, Mauritius.

Commercialising medicinal plants. In: Diederichs, N. (Ed.), A South African guide. Sun Press, Stellenbosch.

Drewes, S.E., Horn, M.M., 1999. The 'African Potato', *Hypoxis hemerocallidea* — myth or miracle muthi? PlantLife 20, 29.

Drewes, S.E., Liebenberg, R.W., 1983. Extracts of plants from the Hypoxidaceae family for treatment of cancer. European Patent No. EP 92226, filed 26 October 1983.

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

Drewes, S.E., Elliot, E., Khan, F., Dhlamini, J.T.B., Gcumisa, M.S.S., 2008. *Hypoxis hemerocallidea* — not merely a cure for benign prostate hyperplasia. Journal of Ethnopharmacology 119, 593–598.

Dykman, E.J., 1908. De Suid Afrikaanse Kook-, Koek- en Resepte Boek (14th improved impression). Paarl Printers Ltd, Paarl (Cape Colony), South Africa.

Monographs on the Medicinal Uses of Plant Drugs, In: ESCOP (Ed.), 2nd ed. European Scientific Cooperative on Phytotherapy, Exeter.

Feiter, U., 2009. The impact of new legislation on the development of *Pelargonium sidoides* in southern Africa. Case study 7a. In: Denzil Phillips International (Ed.), Plants, People and Nature. Benefit sharing in practice. AAMPS Publishing, Port Louis, Mauritius.

Felhaber, T., Mayeng, I. (Eds.), 1997. South African Traditional Healers' Primary Health Care Handbook. Kagiso Publishers, Cape Town.

Fischer, W., Stoeger, K., Huber, P., 2000. Intradermal-penetration agents for topical local anaesthetic administration. United States Patent No. 6455066, filed 10 March 2000.

Gagnier, J.J.S., Chrubasik, S., Manheimer, E., 2004. *Harpagophytum procumbens* for osteoarthritis and low back pain: a systematic review. BMC Complementary and Alternative Medicine 4, 13–22.

Geldenhuys, C.J., Van Wyk, B.-E., 2002. Indigenous biological resources of Africa. In: Baijnath, H., Singh, Y. (Eds.), Rebirth of science in Africa. A shared vision for life and environmental sciences. Umdaus Press, Hatfield, South Africa, pp. 116–132.

Gericke, N., Van Wyk, B.-E., 1997. Pharmaceutical compositions containing mesembrine and related compounds. (filed 3 June) . PCT/GB97/01493.

Gericke, N., Viljoen, A.M., 2008. *Sceletium* — a review update. Journal of Ethnopharmacology 119, 653–663.

Plants of southern Africa: an annotated checklist. In: Germishuizen, G., Meyer, N.L. (Eds.), Strelitzia 14. National Botanical Institute, Pretoria.

Ghorbani, M., Kaloga, M., Frey, H.-H., Mayer, G., Eich, E., 1997. Phytochemical reinvestigation of *Xysmalobium undulatum* roots (Uzara). Planta Medica 63, 343–346.

Grace, O.M., Simmonds, M.S.J., Smith, G.F., Van Wyk, A.E., 2008. Therapeutic uses of *Aloe* L. (Asphodelaceae) in southern Africa. Journal of Ethnopharmacology 119, 604–614.

Grace, O., et al., 2011. Aloes: the people–plant relationship. South African Journal of Botany 77.

Graven, E.H., Webber, L., Venter, M., Gardner, J.B., 1990. The development of *Artemisia afra* (Jacq.) as a new essential oil crop. Journal of Essential Oil Research 2, 215–220.

Gurib-Fakim, A., Brendler, T., Phillips, L.D., Eloff, J.N. (Eds.), 2010. Green gold: success stories using southern African plant species. AAMPS Publishing, Port Louis, Mauritius.

Harvey, W.H., Sonder, O.W. (Eds.), 1860, 1862, 1864. Flora Capensis, Vol. 1, 2 and 3. Hodges, Smith, Dublin.

Hawkins, H.-J., Malgas, R., Biénabe, E., 2011. Ecotypes of wild rooibos (*Aspalathus linearis* (Burm. f.) Dahlg., Fabaceae) are ecologically distinct. South African Journal of Botany 77, 360–370.

Holzapfel, C.W., Marais, W., Wessels, P.L., Van Wyk, B.-E., 2002. Furanoterpenoids from *Siphonochilus aethiopicus*. Phytochemistry 59, 405–407.

Hutchings, A., Van Staden, J., 1994. Plants used for stress-related ailments in traditional Zulu, Xhosa and Sotho medicine. Part 1: plants used for headaches. Journal of Ethnopharmacology 43, 89–124.

Hutchings, A., Scott, A.H., Lewis, G., Cunningham, A., 1996. Zulu Medicinal Plants. Natal University Press, Pietermaritzburg.

Jayawardane, N.M., 2011. Impenetrable bodies/disappearing bodies: Fat American celebrities, lean indigenous people, and multinational pharmaceuticals in the battle to claim *Hoodia gordonii*. Popular Communication 9, 79–98.

Johnson, Q., Syce, J., Nell, H., Rudeen, K., Folk, W.R., 2007. A randomized, double-blind, placebo-controlled trial of *Lessertia frutescens* in healthy adults. PLoS Clinical Trials 2. article number e16.

Joubert, E., De Beer, D., 2011. Rooibos (*Aspalathus linearis*) beyond the farm gate: from herbal tea to potential phytopharmaceutical. South African Journal of Botany 77 000–000.

Joubert, E., Gelderblom, W.C.A., Louw, A., De Beer, D., 2008. South African herbal teas: *Aspalathus linearis*, Cyclopia spp. and Athrixia phylicoides — a review. Journal of Ethnopharmacology 119, 376–412.

Joubert, E., Joubert, M.E., Bester, C., De Beer, D., De Lange, J.H., in press. Honeybush (Cyclopia spp.): from local cottage industry to global markets—the catalytic and supporting role of research. South African Journal of Botany 77.

Kaiser, R., Lamparsky, D., Schudel, P., 1975. Analysis of buchu leaf oil. Journal of Agricultural and Food Chemistry 23, 943–950.

Kayser, O., Kolodziej, H., Kideren, A.F., 2001. Immunomodulatory principles of *Pelargonium sidoides*. Phytotherapy Research 15, 122–126.

Klak, C., Bruyns, P.V., Hedderson, T.A.J., 2007. A phylogeny and new classification for Mesembryanthemoideae (Aizoaceae). Taxon 56, 737–756.

Klopper, R.R., Chatelain, C., Bänninger, V., Habashi, C., Steyn, H.M., De Wet, B.C., Arnold, T.H., Gautier, L., Smith, G.F., Spichiger, R., 2006. Checklist of the flowering plants of Sub-Saharan Africa. An index of accepted names and synonyms. South African Botanical Diversity Network Report No. 42. SABONET, Pretoria.

Knapp, A., 2006. A review of the trade in *Aloe ferox*, with a focus on the role of the European Union. A TRAFFIC Europe Report for the European Commission, Brussels, Belgium.

Kolodziej, H., Kayser, O., 1998. *Pelargonium sidoides* DC. Zeitschrift für Phytotherapie 19, 141–151.

Kruger, D.W., Beyers, G.J., 1977. Dictionary of South African Biography, Vol. 3. Tafelberg Publishers, Cape Town, pp. 231–232.

Lawrence, B.M., 1996. *Artemisia afra* oil. Perfumer and Flavorist 21, 37.

Lis-Balchin, M., Hart, S., Simpson, E., 2001. Buchu (*Agathosma betulina* and *A. crenulata*, Rutaceae) essential oils: their pharmacological action on guinea-pig ileum and antimicrobial activity on microorganisms. Journal of Pharmacy and Pharmacology 53, 579–582.

Mabusela, W.T., Stephen, A.M., Botha, M.C., 1990. Carbohydrate polymers from *Aloe ferox* leaves. Phytochemistry 29, 3555–3558.

Maharaj, V.J., 2009. Hoodia. A benefit sharing case study at CSIR. Case study 2. In: Denzil Phillips International (Ed.), Plants, People and Nature. Benefit sharing in practice. AAMPS Publishing, Port Louis, Mauritius.

Makunga, N.P., Philander, L.E., Smith, M., 2008. Current perspectives on an emerging formal natural products sector in South Africa. Journal of Ethnopharmacology 119, 365–375.

Mander, M., 1998. Marketing of indigenous medicinal plants in South Africa. A Case Study in KwaZulu-Natal. Food and Agricultural Organization of the United Nations, Rome.

Marloth, R., 1913–1932. The Flora of South Africa. 4 vols. Darter, Cape Town and William Wesley, London.

Mashimbye, M.J., Munaka, C., Maumela, M.C., Drewes, S.E., 1999. A drimane sesquiterpenoid lactone from *Warburgia salutaris*. Phytochemistry 51, 435–438.

McGaw, L.J., Eloff, J.N., 2008. Ethnoveterinary use of southern African plants and scientific evaluation of their medicinal properties. Journal of Ethnopharmacology 119, 559–574.

Moffett, R., 2010. Sesotho Plant and Animal Names and Plants Used by the Basotho. Sun Press, Bloemfontein.

Moolla, A., Viljoen, A.M., 2008. 'Buchu' — *Agathosma betulina* and *Agathosma crenulata* (Rutaceae): a review. Journal of Ethnopharmacology 119, 413–419.

Moteetee, A.N., Van Wyk, B.-E., 2007. The concept of Musa-pelo and the medicinal use of shrubby legumes (Fabaceae) in Lesotho. Bothalia 37, 75–77.

Mukinda, J.T., Syce, J.A., 2007. Acute and chronic toxicity of the aqueous extract of *Artemisia afra* in rodents. Journal of Ethnopharmacology 112, 138–144.

Myburgh, A., in press. Legal developments in the protection of plant-related traditional knowledge: a review of the international and South African legal framework with case studies of South African plant extracts used in herbal products. South African Journal of Botany 77.

Ndhlala, A.R., Stafford, G.I., Finnie, J.F., Van Staden, J., in press. Unregistered commercial herbal preparations in KwaZulu-Natal: the urban face of traditional medicine. South African Journal of Botany 77.

Neuwinger, H.D., 2000. African traditional medicine. A Dictionary of Plant Use and Applications. Medpharm Scientific Publishers, Stuttgart.

Newall, C.A., Anderson, L.A., Phillipson, J.D., 1996. Herbal Medicine — a guide for health care professionals. The Pharmaceutical Press, London.

Newton, D.J., Vaughan, H., 1996. South Africa's *Aloe ferox* plant, parts and derivatives industry. A trade review. TRAFFIC East/Southern Africa, Johannesburg.

O'Brien, C., Van Wyk, B.-E., Van Heerden, F.R., in press. Physical and chemical characteristics of Aloe ferox leaf gel. South African Journal of Botany 77.

Okole, B., Odhav, B., 2002. Commercialisation of plants in Africa. In: Baijnath, H., Singh, Y. (Eds.), Rebirth of Science in Africa. A Shared Vision for Life and Environmental Sciences. Umdaus Press, Hatfield, South Africa, pp. 106–115.

Owira, P.M.O., Ojewole, J.A.O., 2009. African potato (*Hypoxis hemerocallidea* corm): a plant-medicine for modern and 21st century diseases of mankind? — a review. Phytotherapy Research 23, 147–152.

Pappe, C.W.L., 1847. A List of South African Indigenous Plants, Used as Remedies by the Colonists of the Cape of Good Hope. G.J. Pike, Cape Town.

Pappe, C.W.L., 1850. Florae Capensis Medicae Prodromus, or, an Enumeration of South African Indigenous Plants, Used as Remedies by the Colonists of the Cape of Good Hope. A.S. Robertson, Cape Town.

Pappe, C.W.L., 1854. Silva Capensis, or a Description of South African Forest-Trees and Arborescent Shrubs Used for Technical and Economical Purposes by The Colonists of the Cape of Good Hope. Van de Sandt de Villiers, Cape Town.

Pappe, C.W.L., 1857. Florae Capensis Medicae Prodromus, or, an Enumeration of South African Indigenous Plants, Used as Remedies by the Colonists of the Cape of Good Hope. Second Edition: with Corrections and Numerous Additions. W. Britain, Cape Town.

Pappe, C.W.L., 1862. Silva Capensis, or a Description of South African Forest-Trees and Arborescent Shrubs Used For Technical and Economical Purposes by the Colonists of the Cape of Good Hope. Second Revised and Enlarged Edition. Van de Sandt de Villiers, Cape Town.

Pappe, C.W.L., 1868. Florae Capensis Medicae Prodromus, or, an Enumeration of South African Indigenous Plants, Used as Remedies by the Colonists of the Cape of Good Hope. Third Edition: with Corrections and Numerous Additions. W. Britain, Cape Town.

Pascual, M.E., Slowing, K., Carretero, E., Sanchez Mata, D., Villar, A., 2001. *Lippia*: traditional uses, chemistry and pharmacology: a review. Journal of Ethnopharmacology 76, 201–214.
Pather, N., Viljoen, A.M., Kramer, B., 2011. A biochemical comparison of the *in vivo* effects of *Bulbine frutescens* and *Bulbine natalensis* on cutaneous wound healing. Journal of Ethnopharmacology 133, 364–370.
Pegel, K.H., 1973. Extraction of phytosterol glycosides from *Hypoxis* tubers. South African Patent No. ZA 7201855.
Pegel, K.H., 1997. The importance of sitosterol and sitosterolin in human and animal nutrition. South African Journal of Science 93, 263–268.
Posthumus, M.A., Van Beek, T.A., Collins, N.F., Graven, E.H., 1996. Chemical composition of the essential oils of *Agathosma betulina*, *A. crenulata* and an *A. betulina* x *crenulata* hybrid (buchu). Journal of Essential Oil Research 8, 223–228.
Pujol, J., 1990. Naturafrica — The Herbalist Handbook. Jean Pujol Natural Healers' Foundation, Durban.
Rabe, T., Van Staden, J., 2000. Isolation of an antibacterial sesquiterpenoid from *Warburgia salutaris*. Journal of Ethnopharmacology 73, 171–174.
Raynolds, L.T., Ngcwangu, S.U., 2010. Fair Trade Rooibos tea: connecting South African producers and American consumer markets. Geoforum 41, 74–83.
Reynolds, G.W., 1950. The Aloes of South Africa. The Trustees of the Aloes of South Africa Book Fund, Johannesburg.
Roberts, M., 1990. Indigenous Healing Plants. Southern Book Publishers, Halfway House.
Robertson, H.M., 1979. The aloe boers of the Gouritz River district. Quarterly Bulletin of the South African Library 34, 59–69.
Rood, B., 2008. Uit die veldapteek. Protea Boekhuis, Pretoria.
Schutte, A.L., 1997. Systematics of the genus *Cyclopia* Vent. (Fabaceae, Podalyrieae). Edinburgh Journal of Botany 54, 125–170.
Seier, J.V., Mdhluli, M., Dhansay, M.A., Loza, J., Laubscher, R., 2002. A toxicity study of Sutherlandia leaf powder (*Sutherlandia microphylla*) consumption. Final report April 2002. Study by the South African Medical Research Council www.sa-healthinfo.org/traditionalmeds/firststudy.htm.
Smith, A., 1888. A Contribution to the South African Materia Medica, 1st ed. Lovedale, South Africa.
Smith, A., 1895. A Contribution to the South African Materia Medica, 3rd ed. Lovedale, South Africa.
Smith, M.T., Crouch, N.R., Gericke, N., Hirst, M., 1996. Psychoactive constituents of the genus *Sceletium* N.E.Br. and other Mesembryanthemaceae: a review. Journal of Ethnopharmacology 50, 119–130.
Standards South Africa, 2007. National Standard SANS 368. Aloe Raw Material. South African Bureau of Standards, Pretoria.
Stewart, K.M., Cole, D., 2005. The commercial harvest of devil's claw (*Harpagophytum* spp.) in southern Africa: the devil's in the details. Journal of Ethnopharmacology 100, 225–236.
Street, R.A., Stirk, W.A., Van Staden, J., 2008. South African traditional medicinal plant trade — challenges in regulating quality, safety and efficacy. Journal of Ethnopharmacology 119, 705–710.
Thring, T.S.A., Weitz, F.M., 2006. Medicinal plant use in the Bredasdorp/Elim region of the Southern Overberg in the Western Cape Province of South Africa. Journal of Ethnopharmacology 103, 261–275.
Van der Stel, S., 1685. Simon Van der Stel's Journey to Namaqualand in 1685. Facsimile Edition, 1979. Human and Rossouw, Cape Town.
Van Heerden, F.R., 2008. *Hoodia gordonii*: a natural appetite suppressant. Journal of Ethnopharmacology 119, 434–437.
Van Heerden, F.R., Vleggaar, R., Horak, R.M., Learmonth, R.A., Maharaj, V., Whittal, R.D., 1998. Pharmaceutical compositions having appetite suppressant activity. International Patent PCT/GB98/01100, filed 15 April 1998.
Van Wyk, B.-E., 2008a. A broad review of commercially important southern African medicinal plants. Journal of Ethnopharmacology 119, 342–355.
Van Wyk, B.-E., 2008b. A review of Khoisan and Cape Dutch medical ethnobotany. Journal of Ethnopharmacology 119, 331–341.
Van Wyk, B.-E., Albrecht, C., 2008. A review of the taxonomy, ethnobotany, chemistry and pharmacology of *Sutherlandia frutescens* (Fabaceae). Journal of Ethnopharmacology 119, 620–629.
Van Wyk, B.-E., Gericke, N., 2000. People's Plants: A Guide to Useful Plants of Southern Africa. Briza Publications, Pretoria.
Van Wyk, B.-E., Wink, M., 2004. Medicinal Plants of the World. Briza Publications, Pretoria.
Van Wyk, B.-E., Van Oudtshoorn, M.C.B.V., Smith, G.F., 1995. Geographical variation in the major compounds of *Aloe ferox* leaf exudate. Planta Medica 61, 250–253.
Van Wyk, B.-E., Van Oudtshoorn, B., Gericke, N., 1997. Medicinal plants of South Africa. Briza Publications, Pretoria.
Van Wyk, B.-E., De Wet, H., Van Heerden, F.R., 2008. An ethnobotanical survey of medicinal plants in the southeastern Karoo, South Africa. South African Journal of Botany 74, 696–704.
Van Wyk, B.-E., Van Oudtshoorn, B., Gericke, N., 2009. Medicinal plants of South Africa. Revised and expanded edition. Briza Publications, Pretoria.
Vermaak, I., Hamman, J.H., Viljoen, A.M., 2011. *Hoodia gordonii*: an up-to-date review of a commercially important anti-obesity plant. Planta Medica 77, 1149–1160.
Viljoen, A.M., Demirci, B., Başer, K.H.C., Van Wyk, B.-E., 2002. The essential oil composition of the roots and rhizomes of *Siphonochilus aethiopicus*. South African Journal of Botany 68, 115–116.
Viljoen, A.M., Subramoney, S., Van Vuuren, S.F., Başer, K.H.C., Demirci, B., 2005. The composition, geographical variation and antimicrobial activity of *Lippia javanica* (Verbenaceae) leaf essential oils. Journal of Ethnopharmacology 96, 271–277.
Viljoen, A.M., Van Vuuren, S.F., Gwebu, T., Demirci, B., Başer, K.H.C., 2006. The geographical variation and antimicrobial activity of African wormwood (*Artemisia afra* Jacq.) essential oil. Journal of Essential Oil Research 18, 19–25.
Vleggaar, R., Ackerman, L.G.J., Steyn, P.S., 1992. Structure elucidation of monatin, a high-intensity sweetener isolated from the plant *Schlerochiton ilicifolius*. Journal of the Chemical Society, Perkin Transactions 1, 3095–3098.
Von Ahlefeldt, D., Crouch, N.R., Nichols, G., Symmonds, R., McKean, S., Sibiya, H., Cele, M.P., 2003. Medicinal Plants Traded on South Africa's Eastern Seaboard. Porcupine Press, Johannesburg.
Von Koenen, E., 2001. Medicinal, Poisonous and Edible Plants in Namibia. Klaus Hess Publishers, Windhoek and Göttingen.
Watt, J.M., 1935. The uses and actions of *Xysmalobium undulatum*. South African Journal of Medical Science 1, 4–11.
Watt, J.M., 1967. African plants potentially useful in mental health. Lloydia 30, 1–22.
Watt, J.M., Breyer-Brandwijk, M.G., 1962. The Medicinal and Poisonous Plants of Southern and Eastern Africa, 2nd ed. Livingstone, London.
Wegener, T., 2000. Devil's claw: from African traditional remedy to modern analgesic and anti-inflammatory. HerbalGram 50, 47–54.
Wichtl, M., Bisset, N.G. (Eds.), 2000. Herbal Drugs and Phytopharmaceuticals. CRC Press, Boca Raton.
Widgerow, A.D., Chait, L.A., 1998. Treatment of post operative scars with a tape containing a gel from *Bulbine frutescens*. United States Patent No. 6159494.
Widgerow, A.D., Chait, L.A., Stals, R., Stals, P.J., 2000. New innovations in scar management. Aesthetic Plastic Surgery 24, 227–234.
Williams, V.L., Balkwill, K., Witskowski, E.T.F., 1997. *Muthi* traders on the Witwatersrand, South Africa — an urban mosaic. South African Journal of Botany 63, 378–381.

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