This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. This Accepted Manuscript will be replaced by the edited, formatted and paginated article as soon as this is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
The chemistry and bioactivity of Southern African flora I: A bioactivity versus ethnobotanical survey of alkaloid and terpenoid classes

Smith B. Babiaka, Fidele Ntie-Kang, Lydia L. Lifongo, Bakoh Ndingokhar, James A. Mbah, and Joseph N. Yong

As a whole, the African continent is highly endowed with a huge floral biodiversity. Natural products which have been isolated from plants growing in this region have shown interesting chemical structures with diverse biological activities, which could serve as starting point for drug discovery. In this study, a literature survey led to the collection of 864 secondary metabolites from 101 plant species from 57 plant families. A correlation between the known biological activities of isolated compounds and the ethnobotanical uses of the plants has been attempted. This review is a survey of the bioactivities of alkaloids and terpenoids which have been isolated from Southern African flora versus the ethnobotanical uses of the plants used in Southern African traditional medicine. In this study, a literature survey led to the collection of 864 secondary metabolites from 101 plant species from 57 plant families.

1 Introduction

The African continent is highly endowed with a huge floral biodiversity and its plant material contains natural products (NPs) with interesting chemical structures with diverse biological activities, which could serve as starting point for drug discovery programs. Moreover, medicinal plants from Africa have played an important socio-economic role by fulfilling health-care needs and creating business opportunities to the less privileged population of the developing world. In the past centuries, a majority of the local population, especially south of the Sahara have depended on medicinal plants as their main source of treatment of medical disorders and ailments. Thus, several plant species have been used in Africa traditional medicine (ATM) to treat various diseases/ailments. Traditional medicine has been defined by the World Health Organization (WHO) as practices, knowledge and belief systems which use minerals, plants and animal based remedies, spiritual therapies and exercises to prevent, treat and maintain well being. Traditional medical practices are common in Africa, as well as in most undeveloped nations, in which majority of the (mostly poor) population rely on traditional medicines for their health care. In recent years, ATM has gained renewed interest in the health care services throughout the continent despite the advances in Western medicine (WM).

The region of Southern Africa has a rich biological and ethnic diversity. More than three centuries of botanical research and exploration in South Africa and neighbouring countries have revealed promising floristic diversity, with approximately 25,000 plant species and more than 50% endemism in the region. The cultural value of biodiversity and its importance in effective biodiversity conservation planning and ecotourism have also been recognised recently. As a result of the existing account of the importance and uses of flora of Southern Africa, there is growing need for ethnobotanical research.

It has been the objective of the Chemical Bioactivity Information Centre to document knowledge from African flora, relevant for drug discovery programs on the continent. Previous review papers have been focused on the bioactivity versus ethnobotanical survey of medicinal plants from Central, Western and Northern Africa has been done and published by this research group, including the development of natural product databases (CamMedNP, ConMedNP, AfroDb, p-ANAPL) and the pharmacokinetic profiling of natural products from African flora, with the view of drug discovery. Recent review articles have focused on anti-malarial and anti-tubercular principles from African flora, while also focusing on different countries/regions in Africa. This has received significant attention from the readership involved in drug discovery from medicinal plants and thus has prompted the need to explore other regions of the continent, including Southern Africa. To the best of our knowledge there has not been a recent review focusing on the phytochemical and bioactivity of natural products from the Southern Africa region (covering the countries: Angola, Botswana, Madagascar, Malawi, Mozambique, Namibia, South Africa, Swaziland and Zimbabwe), in spite of the rich floral biodiversity and phytochemistry of this region. In this review series, the chemistry and biological activity of Southern Africa flora would be discussed. In the present paper, our main focus would be on alkaloids and terpenoids to highlight the medicinal value and potentials of the isolated phytochemicals by discussing the bioactivity of the isolated principles versus ethnobotanical uses of the plant species.
2 Alkaloids from Southern African flora

In this report, summaries of the most interesting results for alkaloids which exhibit biological activities correlating with the ethnobotanical uses of the plant species of origin have been shown in Tables 1 and 2, while the chemical structures of the isolated compounds are shown in Figure 1.

Boophone disticha (Amaryllidaceae) is a common bulbous plant used traditionally by the local populations of Southern Africa, mostly as a narcotic substance and for the treatment of a host of ailments, including inflammation, wounds, gynaecological conditions and psychosis.3 Cheesman et al. have isolated the crinane alkaloids; buphanidrine (1) and distichamine (2) from the bulbs of this plant, collected in the Mpophomeni area of KwaZulu Natal (South Africa).25 The isolated compounds were novel, broad spectrum moderately active, antibacterial agents with the best MIC value detected at 0.063 mg/mL for Staphylococcus aureus, Escherichia coli and Klebsiella pneumonia.26,27 MIC values for Bacillus subtilis were two-fold less than those observed for the other three bacteria, suggesting that the extract and pure compounds were selective in their interaction with the bacterial pathogens. The close structural similarity of these two compounds (1 and 2) may have bearing on their similar activity profiles. Moreover, the bioactivities of these chemical structures of compounds 1 and 2 may be the basis of the reputed traditional use of the plant for wounds and infections.25

There are several reports on the ethnomedical use of Tabernaemontana elegans (toad tree) pertaining to antibacterial activity, as well as on the screening of the plant extracts.25-31 Some of these reports pertain to the antibacterial activity: a root decoction is applied as a wash to wounds, and drunk for pulmonary disorders and chest pains by the VhaVenda26 and Zulu26 people of South Africa. Other ethnomedical uses of this plant include the treatment of heart diseases with the seeds, stem-bark and roots and the root-bark and properties.27 Extracts of this plant has previously demonstrated antibacterial activity against S. aureus and antymycobacterial activity against M. smegmatis,28 as well as antifungal activity against Candida albicans.29 Extracts from T. elegans, along with those from seven other species of the genus Tabernaemontana have shown antibacterial activity against Gram-positive bacteria.30-31 Pallant et al. have isolated the indole alkaloids; voacangine (3) and dregamine (4) as the active antibacterial components of the plant.32 The study confirms both the antibacterial activity of T. elegans and supports its potential for being investigated further for the development of a novel antibacterial compound. Hypophorine (5) is an indole alkaloid isolated from Erythrina lysistemom, a leguminous plant harvested in Botswana.33 The extracts from this plant have been used in traditional medicine and have also shown antiviral, anticancer and cytotoxic activities.34,35 Although erythrinamine alkaloids36,37 and prenylated flavonoids are known to be prevalent in the plant species, compound 5 is known to contribute to its antimicrobial activities.33

Spirospermum penduliflorum (Menispermaceae) is endemic in Madagascar.38 Moreover, the decoctions of all parts of this plant are traditionally used as anticholinergic and vasorelaxant, among other uses.39 Rafamantananana et al. have isolated two aporphine alkaloids; neolitsine (6) and dicerin (7) from the leaves of this plant.40 Both dicerin and neolitsine are known to possess antiphytotoxic activities, dicerin having an EC50 value of 0.15 ± 0.04 µg/mL on rat aorta relaxation.40 A review on plants traditionally used for the treatment of malaria in Madagascar, showed Vepris ampody as a key component in anti-malarial preparations in Madagascan traditional medicine.41 In Kenya, a decoction of the roots of Vepris glomerata is used traditionally in the treatment of malaria, while the vapour is used to treat eye problems. A decoction of the bark is used in the treatment of cardiac pain while epilepsy, stroke and psychosis is treated using an aqueous root extract of the plant mixed with tea.42,43 The furoquinoline alkaloids; flindersiamine (8) and maculosidine (9) have been isolated from the sister species Vepris uguenensis, harvested in Kenya.44 Compounds 8 and 9 were tested against 3D7 (chloroquine susceptible, CQS) and FC2M9 (chloroquine resistant, CQR) strains of Plasmodium falciparum. It was found that while compound 8 was completely inactive against both strains of the parasite, compound 9 displayed mild activity, with IC50 values of 13.0 ± 11.5 µg/mL and 13.8 ± 1.0 µg/mL against the CQS and CQR strains, respectively.44

The Flaky cherry-orange tree, Teclea gerrardii (Rutaceae), which occurs in riverine thicket and dry forest along the eastern seaboard of Southern Africa (South Africa, Swaziland and Southern Mozambique) has been included in this study. Bark decoctions of the plant are employed traditionally by the Zulus for chest complaints.45 Waffo et al. identified the furoquinoline alkaloids; evoxine (10) and 7-(γ,γ-dimethylallyloxy)γ-fagarine (11), among other compounds including the acridone alkaloids; tegerrardin A (12), tegerrardin B (13), arborinine (14), evoxanthine (15), 1,3-dimethoxy-Nmethylacetamide (16) and tceleine (17) from the stem bark of this plant and tested their antiplasmodial activity against the CQS D10 strain of P. falciparum.46 Compound 10 exhibited an IC50 of 24.5 µM, while arborinine showed the best activity (IC50 = 12.3 µM).46

Secileium tortuosum or Mesembryanthemum tortuosum (Mesembryanthemaceae) is endemic to the Cape Region of South Africa. This plant is one of South Africa’s most popular plants, mainly for its use of this plant as a mood-altering drug can be traced back probably to centuries.47 Due to the popularity of this plant, whole plantations have been established and diverse consumer products are commercially available from the plant. The alkaloids of S. tortuosum (mainly mesembrine alkaloids) exhibit important pharmacological properties and are used for the treatment of psychiatric and psychological conditions, including depression, anxiety, drug dependence, bulimia and obsessive-compulsive disorder.48,49 Four alkaloids from this sub-class; mesembrine (18), mesembrinone (19), mesembranol (20) and mesembranol (21) have been recognized for their remarkable psychoactive properties.47,50 These compounds are currently being used in pharmaceutical formulations for the management of psychiatric and psychological conditions like depression, anxiety, drug dependence, bulimia and obsessive-compulsive disorder.49 Moreover, mesembrine alkaloids have a particular ability to treat conditions of the central nervous system (CNS).50 This has been attributed to their capacity to act as serotonin re-uptake inhibitors, thereby contributing to regulating the balance of neurochemicals in the brain.51-53 Among the uses of Erythrina lysistemom (Leguminoseae), the extracts from this plant have been used in traditional medicine and have shown antiviral, anticancer and cytotoxic activities. The antimicrobial activity of the isoquinoline alkaloid precursor norprotosinomenine (22), isolated from the plant harvested in Botswana, partly justifying its use in ATM.54

3 Terpenoids from Southern African flora
The summary of the most important findings on the bioactive terpenoids from Southern Africa flora have been given in Tables 3 to 7 (according to their subclasses), while the chemical structures are shown in Figures 2 to 8.

3.1 Monoterpeneoids and meroterpenoid

Mujovo et al. isolated the monoterpeneoids (E)-2-(3)-tagetone epoxide (23), myrcenone (24) and piperitenone or 3-methyl-6-(1-methylethylidene)-cyclohex-2-en-1-one (25) in addition to other phytochemicals from Lippia javanica (Verbenaceae).23 An aromatic herb that occurs all over Mozambique. Infusions of its leaves is commonly used in Africa as a tea against various ailments like influenza, measles, rashes, malaria, stomach problems, fever, colds, cough, headaches.34-37 In Botswana it is used as a caffeine-free tea and in Zimbabwe and Malawi as a nerve tonic.38 The compounds were tested against Mycobacterium tuberculosis and HIV reverse transcriptase. It was found that (E)-(23)-tagetone epoxide (23) inhibited the HIV-1 reverse transcriptase enzyme by 91% at 100 µg mL−1. Moreover, the triterpene esculptic acid, also isolated from this plant, was found to exhibit a minimum inhibitory concentration (MIC) of 50 µg mL−1 against sensitive strain of M. tuberculosis, H37Rv, reference strain (27924). This rare monoterpene (compound 23) has also been identified in the Cameroonian Clausena anisata (Rutaceae) essential oil.39 Compound 25 (3-methyl-6-(1-methylethylidene)-cyclohex-2-en-1-one) was also noted to be the major component of the essential oil of L. javanica harvested from Southern Africa.38 The oil was tested for antimicrobial activity on cultures of Escherichia coli, Bacillus subtilis and Staphylococcus aureus, and found to inhibit E. coli and S. aureus at 1% dilution. The oil was also active against P. falciparum in micromolar concentrations.38

Ptaeroxylon obliquum (Rutaceae), also known as sneezewood, grows only in Southern Africa. This plant is traditionally used in Southern Africa for the treatment of various ailments, including headaches and tick control.40,41 Agostinho et al. isolated ptaerobiliquol (26), a new monoterpene-chromone (or meroterpenoid) from the roots of this plant for the first time.42 The compound demonstrated a moderate activity when tested on Toxoplasma gondii replication using CPRG-based colormetric assay,40 inhibiting parasite replication at 5 and 10 µM, with an IC50 of 5.13 µM. Lower concentrations of the compound (0.1 and 1 µM) tested were totally inactive, while cellular toxicity appears at concentration of 25 µM, giving ptaerobiliquol a low therapeutic index.

3.2 Sesquiterpenoids

Vernonia auriculifera (Asteraceae) is a small tree or woody herb that grows between 1 and 7.5 m high and is easily recognizable by its deep purple flowers. This plant has a wide variety of uses in traditional medicine; a drop of the juice squeezed from the crushed stem bark, inserted into the nostrils, is used to relieve headache.43 The Kikuyu people of central Kenya use the leaves of this plant as a wrap for frozen material used as a poultice.45 Cold water infusion of the plant is administered orally in Uganda and Kenya to treat fever associated with viral and bacterial infections.36,56 In Ethiopia, the roots are used to treat toothache46 and snake poison.59 Phytochemical investigation of Vernonia auriculifera by Kiplimo et al. afforded farnesylamine (27), a unique sesquiterpene amine not found previously in plant species.70 The compound could not be screened for antibacterial activity (with the goal of validating its ethnobotanical use) due to sample decomposition. However, in addition to the triterpenoids (lupenyl acetate, oleanolic acid, β-amyrin acetate, β-amyrin, friedelanone, friedelien acetate, α-amyrin and β-sitosterol) present in the plant material, there is potential for synergistic coupling with antimicrobial agents to improve therapeutic efficiency.70

Two sesquiterpeneoids (28 and 29) have also been isolated from Hyenanche globosa (Euphorbiaceae), a narrow endemic poisonous plant restricted to a single flat-topped mountain near Van Rhynsdorp in southern Namaqualand. In vitro studies of the ethanolic extract of the fruits of the plant displayed a significant anti-tyrosinase, antibacterial, and cytotoxic effects. Montaz et al isolated the tumbut (28) and hynanchen or mellitoxin (29) from the ethanolic extract of the fruits of the plant which did not exhibited any significant cytotoxic effects on the on ‘Hela cells’.71 This could be explained by the fact that the compounds responsible for the activity were not isolated and that activity in the crude extract is due to synergy. It has been reported by several studies that compound 28 is the major neurotoxin in the New Zealand shrubs of the genus Coriaria and compound 29 is a major active component in toxic honey.72,74

The shrub Osyris lanceolata (Santalaceae), also called ‘African sandalwood’, is used in traditional medicine in Botswana, South Africa, East Africa, Ethiopia and parts of Asia to treat a wide variety of diseases including; kidney infection, diarrhoea, cholera, coughs, malaria, gynaecological disorders, infertility, venereal diseases, cancer, and insanity. The ethnomedical applications of Osyris species in traditional medicine has been published in different parts of the world, including the NAPRALERT database25 and the Prelude Medicinal Plants Database.76 Yeboah et al. isolated five new dihydro-b-agarofaragin polyesters from the root bark and stem bark of the plant, harvested in Botswana.77 The compounds include 1b-furanoyloxy-9a-benzoyloxy-dihydro-b-agarofuran (30), 1a-furanoyloxy-9b-benzoyloxy-2-oxo-dihydro-b-agarofuran (31), 1b, 9e-difuranoyloxy-8b-acetoxy-2-oxo-3-ene-dihydro-b-agarofuran (32), 1b-furanoyloxy-9a-benzoyloxy-8j-acetoxy-2-oxo-3-ene-dihydro-b-agarofuran (33) and 1b,9a-Difuranoyloxy-2,8-dioxo-3-ene-dihydro-b-agarofuran (34). The compounds have received considerable attention recently and they are considered as ‘privileged structures’ because they typically display multiple pharmacological activities due to their unique framework that can provide ligands to interact with multiple receptors. They have been reported to have insecticidal, anti-HIV, anti-cancer, multidrug resistance (MDR) reversal and acetylcholinesterase (AChE) inhibition activities in literature.78-81

3.3 Sesquiterpene lactones

Dicona anomala (Asteraceae) is a grassland species widely distributed in sub-Saharan Africa. This plant was selected by the national consortium initiative to discover novel anti-plasmodial agents from South African plants based on its ethnomedical profile.32 The EtOAc extract of the plant exhibited an IC50 of 1.4 µg/mL on the chloroquine-sensitive D10 strain on P. falciparum using the pLDH assay.33 The plant also has a wide range of ethnomedical applications, including the treatment of coughs and colds, fevers, ulcers, dermatoses, venereal diseases, labour pains, dysentery, intestinal parasites, stomach pains, toothache and internal worms. D. anomala can also be linked to several pharmacological properties: anti-bacterial, anti-helmintic, anti-viral, anti-plasmodial, anti-spasmodic, wound healing, analgesic and anti-inflammatory.82-86 Becker et al. isolated a eudesmanolide-type sesquiterpene lactone, 3-oxoedusema-1,4(15),11(13)-triene-12,6a-lide (35), commonly named dehydrobrachylaenolide, as the main active constituent of the
extract. The identified compound was previously isolated from the roots of Brachylaena transvaalensis. The compound showed an in vitro IC_{50} of 1.865 µM against a chloroquine-sensitive strain (D10) of P. falciparum. The activity of the compound against the chloroquine-sensitive strain (IC_{50} = 1865 nM) is within an order of magnitude of that of quinine (IC_{50} = 194 nM). In addition, the compound had a therapeutic index of 9.2 against the chloroquine-sensitive strain, which is close to the acceptable value of 10 for potential development. Thus, the compound can be considered as a hit, because it complies with the basic criteria for anti-parasitic drug discovery with an in vitro IC_{50} against whole protozoa of ≤ 1 µg/mL and a selectivity of close to ten-fold more against the chloroquine-sensitive parasites than against the Chinese hamster ovary (CHO) cells.

3.4 Abietane diterpenes

Plectranthus species have found wide applications in African traditional medicine (ATM), for example, in the treatment of gastrointestinal disorders, as anti-microbial agents, for the treatment of wounds, the alleviation of respiratory conditions and for malaria treatment. Zyla et al. isolated the abietane diterpenes; 11-hydroxy-2α-(4-hydroxybenzoxoxy)-abiet-5,7,9(11),13-tetraene-12-one or parviflorone D (36) and 11-hydroxy-2α-(3,4-dihydroxybenzoxoxy)-abiet-5,7,9(11),13-tetraene-12-one or parviflorone F (37) from the leaves Plectranthus ecklonii (Lamiaceae). The compounds were tested for their antiplasmodial activity against a chloroquine-resistant strain of P. falciparum and for their ability to inhibit β-haematin formation. The compounds were less active relative to chloroquine and quinine, but showed significant activity in the inhibition of β-haematin formation. The tritiated hypoxanthine incorporation assay was used to determine antimalarial activity of the isolated compounds, with sodium stibogluconate (IC_{50} = 10.6 nM) as the control drug. When compared to the isolated abietane diterpenes, there was a 15-fold decrease in activity. Compound 37 (IC_{50} = 3.11 µM) had the lowest IC_{50} values and was more effective than quinine, with compound 36 being 62% as active as chloroquine, with IC_{50} = 5.3 µM. Zyla et al. also isolated the known compounds 11-hydroxy-19-(methyl-buten-2-ol)-abiet-5,7,9(11),13-tetraene-12-one (38) and compound 36 from the Plectranthus species; Plectranthus tongaensis (Lamiaceae) cultivated in many household gardens in South Africa. The anti-plasmodial activities were evaluated, compounds 36 and 38 having IC_{50} values of 5.3 µM and 6.0 µM respectively.

Another set of abietane diterpenes isolated by Zyla et al. from Plectranthus tongaensis (Lamiaceae) and tested similarly as above include 11-hydroxy-19-(4-hydroxy-benzoxoxy)-abiet-5,7,9(11),13-tetraene-12-one (39) and 11-hydroxy-19-(3,4-dihydroxy-benzoxoxy)-abiet-5,7,9(11),13-tetraene-12-one (40). Compound 40 was more active than quinine with an IC_{50} value of 4.7 µM compared to compound 39 with an IC_{50} value of 14.7 µM when screened against chloroquine-resistant strain of Plasmodium falciparum. These results justify the use of Plectranthus sp. in the treatment of malaria among other uses.

3.5 Labdane-type diterpenes

Leonotis leonurus (Lamiaceae) commonly known as Wild dagga or Lion’s ear, is a robust perennial shrub which grows usually to 2 m tall and widely distributed in eastern South Africa, growing amongst rocks in grassland. This plant has a wide variety of medicinal uses, for example the treatment of colds, bronchitis, tuberculosis, coughs, asthma, feverish headaches, dysentery and chest infections. Based on its ethnomedicinal profile as a respiratory ailments, and it’s in vitro antibacterial activity, the plant has been identified as a potential source of novel anti-tuberculosis compounds. Naidoo et al. isolated the two new labdane-type diterpenoids; 9,13-Epoxy-6-hydroxy-16, 15-labdanoide (41) and 9, 13, 15, 16-diepoxy-6, 16-labdadienol (42) from the leaves of this plant. The compounds have relevance as chemotaxonomic markers even though they showed no activity against M. Tuberculosis.

The nutritive value of Eragrostis species (Poaceae) has been reported in literature. Eragrostis viscosa (Poaceae) is used in folk medicine as a poison against snakes in Angola but the plant is not eaten by cattle. Phytochemical investigation of the toluene and dichloromethane extracts of the aerial parts of this plant by Sebastião et al. afforded three new 8α,15-epoxylabdananes namely; methyl 8α, 15-epoxylabdan-16β-ol (43), 8α, 15-epoxylabdan-16β-ol (44), 8α, 15-epoxy-16-norlabdan-13β-ol (45) together with other known compounds. Some of the known compounds in this class include 8α, 15-epoxy-16-norlabdan-13-one (46), 8α, 15-epoxylabdan-16β-ol (47) and 16-acetoxy-8α, 15-epoxylabdane (48). The genotoxicity of the compounds isolated from this plant was studied using a cytokinesis-block micronucleus assay and the Ames test was also used to assess mutagenicity. Compounds 44, 46 and 48 gave negative results on both assays and compound 44 was the most cytotoxic of the tested compounds using MTT assay.

3.6 Limonoid diterpenoids

Among medicinal plants growing in Africa, limonoids, having anti-malarial properties, are common a number of plant genera, including Vepris (Rutaceae), Khaya (Meliaceae) and Entandrophragma (Meliaceae). Vepris species are used in ethnomedicine for the treatment of a diverse range of ailments, including pneumonia, lung diseases and kidney disorders, eye troubles, cardiac pains, coughs, colds and influenza, headache, menorrhagia and infertility, and as an aphrodisiac, diuretic and antipyretic, and as an aphrodisiac, diuretic and antipyretic, and as a tonic for angina and rheumatism, and externally as a treatment for malaria. Vepris ugoenensis (Rutaceae), also known as “chemchir” by the Pokot tribe of Kenya, use this plant to treat malaria. Cheplogoi et al. isolated a novel limonoid, methyl ugoenomate (49) together with other compounds from the dichloromethane extract of the roots of this plant. The compound displayed mild activity, with IC_{50} values of 10.4 and 13.8 µg/mL, against the CQS and CQR strains of P. falciparum, respectively, thus partly justifying its use in malaria treatment locally.

3.7 Kaurene diterpenes

Croton pseudoponchellus (Euphorbiaceae), commonly known as the Small Lavender Croton, is a shrub that grows to about 4 m tall and it is widely distributed in drier woodlands of the warmer regions of East, South-central and parts of West Africa. This plant is used in the coastal area of Kenya as a spice when material is burnt and the smoke used to flavour fresh milk. Species of this plant are durable and are used for hut building in Tanzania. A decoction from the roots of this plant is used to treat asthma and the powdered root taken as a snuff for headaches. Leaves are applied by Tanzanians to their chest for chest ailments. Langat et al. isolated two new ent-kauren-19-orientic acid derivatives; ent-14βS-hydroxykaar-16-en-19-orientic (50), ent-14βS,7,15-dihydroxykaar-15-en-19-orientic (51) together with some of the known compounds; ent-kaar-16-en-19-orientic acid (52), ent-kaar-16-en-19-orientic acid (53) ent-12β-hydroxykaar-16-en-19-orientic acid.
isolated compounds showed activity range at 1.0 mg/mL to 0.25mg/mL. Compound 63 was one of the best compounds that showed good antimicrobial activity and the antioxidant activity was done on the compound using the DPPH scavenging method. The result revealed that compound 63 exhibited a decreased scavenging activity with an IC₅₀ of 2.42 µg/mL. Compound 63 showed a smooth trend of non-toxic effects with IC₅₀ value 30.96 of µg/mL. Thus the results obtained in this study confirm the use of this plant in the treatment of microbial infections.

Thiskalange et al. isolated the three known triterpenoids lup-20(30)-ene-3α,29-diol (64), lup-20(29)-ene-30-hydroxy-3-one (65) and Ψ-taraxastanol (66) together with other known compounds from stem bark of Elaeodendron transvaalense (Celastaceae), collected from Venda (Northern Limpopo), South Africa.138 Extracts from this plant have been used in traditional medicine by the Vhavenda people of South Africa (Limpopo province) to treat coughs, diarrhoea, stomach ailments, herpes and sexually associated diseases. The stem bark is mostly used to prepare infusions and decoctions.139 This plant is also used in the treatment of arthritis, cancer, coughs, diarrhoea and stomach ailments and is being prescribed presently to people who are suffering from HIV/AIDS by traditional healers.140

The cytotoxicity of the isolated compounds was determined using XTT colorimetric assay against Vero and MCF-7 breast cancer cell lines.141 Compounds 64 and 66 showed weaker activities with the IC₅₀ ranging from 66.6 to over 100.00 µg/mL in both cell lines, while compound 65 exhibited a good cytotoxicity activity IC₅₀ value of 25.1 µg/mL for Vero cells and 19.4 µg/mL for breast cancer cell line. The cytotoxicities of the isolated compounds (64 to 66) may partly justify the use of E. transvaalense in the treatment of several ailments in ATM, including cancer related problems.139

Some Combretum species have been used in traditional medicine for relieving symptoms that appear to be caused by infective agents like bloody diarrhoea, wounds and conjunctivitis.142 This confirms the preliminary data gathered by Eloff,143 which demonstrated that crude extracts of Combretum padoides (Combretaceae) were active against the four most important nosocomial bacterial pathogens. Angeh et al. isolated a new oleane-type triterpenoid glycoside known as 1α,23β-dihydroxy-12-olean-30-oic-acid (68) and a known steroids from the dichloromethane extract of this plant using antibacterial activity guided fractionation against Staphylococcus aureus.144 Compounds 67 and 68 exhibited a reasonable antibacterial activity with MIC of 0.031 and 0.063 mg/mL against S. aureus and Excherichia coli. This result confirms the antibacterial activity of this plant that the isolated triterpenes are non-cytotoxic.144 Eloff et al. also isolated compounds 67 and 68 from this same plant using bioassay-guided fractionation.145 The compounds demonstrated a reasonable antibacterial activity as described Angeh et al. which could partly justify its use in the treatment of wounds and other infectious diseases.

Terminalia sericea (Combretaceae) stem bark extract showed the best results against a-glucosidase and a-amylase enzymes in an in vitro screening exercise of a number of South African medicinal plants, in an attempt to discover new anti-diabetic agents. A bioassay-guided fractionation of an acetone extract of the stem bark of this plant by Nkobole et al. led to the isolation of lupeol (69) and other known compounds.146 The result demonstrated that compound 69 was one of the secondary metabolite that showed the best inhibitory activity on a-glucosidase with an IC₅₀ value of 66.48 µM. Additionally, bioevaluation of compound 69 inhibitory activity on a-amylase demonstrated that the compound had an IC₅₀ value of

**3.8 Pentacyclic triterpenoids**

*Vernonia* species are known to be rich in triterpenoids, particularly triterpenes and sesquiterpenes.20 *Vernonia auriculifera* (Asteraceae) is a small tree or woody herb that has wide variety of uses in traditional medicine.64-66 Vernonia species extracts have been cited as antimicrobials in traditional medicine.127 Sequential extraction of the leaves, stem bark and root bark of this plant using organic solvents; hexane, dichloromethane, ethyl acetate and methanol by Kiplimo et al. afforded the triterpenoids lupenyl acetate (56), oleanolic acid (57), β-amyrin acetate (58), α-amyrin (59) and β-amyrin (60) friedelanone (61) and friedelin acetate (62) together with some other compounds.70 The antibacterial activities of the isolated compounds were determined using the broth microdilution method as described by Andrews.128 Four strains of gram-negative and five gram-positive bacteria strains were used to determine the antimicrobial activity. The compounds demonstrated moderate antibacterial activity; compounds 59 and 60 had minimum inhibitory concentration (MIC) of 0.25 mg/mL against Staphylococcus aureus, Bacillus subtilis, Enterococcus faecium and Staphylococcus saprophyticus while compounds 56 and 57 exhibited MIC of 0.50 mg/mL against Stenotrophomonas maltophilia. The oleane triterpenoids 57, 58 and 60 displayed better antibacterial activity than the friedelanene triterpenoids 61-62. It is reported that the 28-COOH and ester functionality at C-3 contributes to pharmacological activities of pentacyclic triterpenes129 like lupenyl which has greater antimutagenic activity than compound 56.130 These effects are observed for 61 and 62 where the ketone has higher activity against *B. subtilis* than the ester.

Other triterpenes correlating biological activity and ethnobotanical uses of species from the *Artemisia* genus. As a typical example, the ethnobotanical uses of *A. afra* (Asteraceae) have been investigated by van Wyk et al.131-133 The African wormwood, *A. afra*, is a common species in South Africa with a wide distribution from the Cedarberg Mountains in the Cape, northwards to tropical East Africa and stretching as far north as Ethiopia.131-132 In southern Africa, this plant is used to treat coughs, colds, diabetes, malaria, sore throat, asthma, headache, dental care, gout and intestinal worms.133 In vitro studies of this plant have revealed that the plant is a potential antidepressant, cardiovascular, spasmylic effects, antioxidant, and antimycobacteria.134-136 The crude ethanolic extract of this plant exhibited strong antimicrobial activity by inhibiting the growth of all tested microbial species at concentration range of 1.6 mg/mL to 25 mg/mL thus prompted the further investigation. More et al. isolated compounds 59 and betulinic acid (63) from this plant and other known compounds.137 The compounds were evaluated for antimicrobial activity against gram positive (*Actinomycyes naeslindii, Actinomycyes israelii, and Streptococcus mutans*), gram negative bacteria (*Prevotella intermedia, Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans* previously known as *Actinobacillus actinomycetemcomitans*), and Candida albicans. The

(54) and ent-12β-acetoxykaur-16-en-19-oic acid (55) from the hexane and methylene chloride extracts of the stem bark of this plant.138 Quantitative assessment of anti-plasmodial activity in vitro was determined via the parasite lactate dehydrogenase assay using a modified method described by Makler et al.139 Compound 54, the major constituent was tested in duplicate against the chloroquine sensitive (CQS) strain of *P. falciparum* (D10) and showed weak activity against the *P. falciparum* (CQS) D10 strain. Compounds 50, 52, 54, and 55 were found to be inactive when tested for their effects on Semliki Forest virus replication and for cytotoxicity against human liver tumour cells (Huh-7 strain).
140.72 µM against the enzyme, thus validating the use of the plant in traditional medicine to treat diabetic in South Africa.

Combretaceae species are widely traded in the traditional medicine market in Southern Africa and are used medicinally in several continents in the world. Traditional healers in Eastern and Southern Africa have used Combretum species, for many applications including treating abdominal disorders, backache, bacterial infections, bilharzia, cancer, chest coughs, cleansing the urinary system, colds, conjunctivitis, constipation, diarrhea, dysentery, dysmenorrhea, earache, fever, gastric ulcers, general weakness, gonorrhea, headaches, heart diseases, hookworm, hypertension, jaundice, leprosy, nosebleeds, oedema, pneumonia, skin diseases, sore throats, stomach and gastric problems, swelling caused by mumps, syphilis, toothache, venereal diseases. Extract from Combretum imberbe (Combretaceae) leaves, obtained using intermediate polarity extractants, had reasonable to very good activity with MICs as low as 40 µg/mL, thus validating the use of this plant in the treatment of infectious diseases. Five antibacterial triterpenoids; 1,3,2-dihydroxy-12-olean-29-oic acid (70), 1-hydroxy-12-olean-30-oic acid (71), 3,30-dihydroxyl-12-olean-22-one (72), 1,3,24-trihydroxy-12-olean-29-oic acid (73) and 1,23-dihydroxy-12-olean-29-oic acid-3-4-di-acetylt-1-ramnopyranoside (74) were isolated from the leaves of this plant. The compounds had levels of antibacterial activity MIC values against S. aureus and E. coli ranging from 16 to 62 µg/mL. The antibacterial activity of the isolated compounds was much lower than expected from the activity of the crude extracts this can be due to synergistry. Katererea et al. isolated the two novel derivatives of 1α,3β,23-trihydroxyl-12-29-oic acid; 1α,3β-hydroxyimberbic acid-23-O-acetyl-4-acetylramnopyranoside (75), 1α,3β-hydroxyimberbic acid-23-O-acetyl-3,4 -diacetylramnopyranoside (76) and the known compounds 1α,3β-hydroxyimberbic acid-23-α-L-3,4-diacetylramnopyranosyl)-29-O-a-ramnopyranoside (77), and 1α,3β-Hydroxyimberbic acid (78) form the leaves of the this plant. The antimicrobial activity of the isolated compounds was done using a microtitre dilution assay (MDA), showing compound 77 to have inhibitory activity against P. vulgaris (12.5 µg/mL) and S. aureus (6.25 µg/mL). Compound 75 inhibited S. aureus at 12.5 µg/mL, while compound 76 inhibited S. aureus at 6.25 µg/mL and M. fortuitum at 12.5 µg/mL. Compound 78, the free aglycone, showed activity against Mycobacterium fortuitum at a concentration of 1.56 µg/mL and S. aureus at 3.13 µg/mL, which was a surprising case because the Mycobacterium was generally resistant to the other tests sample. The activity of these compounds validates the use of this plank in folk medicine. Escherichia coli was resistant to these compounds, thus the constituents of these species of Combretaceae may not be active against gram negative bacteria.

Katererea et al. isolated compound 75 and 1α,3β,23-trihydroxyimberbic acid-23-O-acetyl-4-acetylramnopyranosyl]-29-O-a-ramnopyranoside (79) from the stem bark of this plant. Thus, this study established that there is a chemotaxonomic link between the genus Combretum and Terminalia due to the occurrence of the trihydroxy-olean-12-en-29-olate aglycone; compound 75 and 79 in the species which had not been previously reported. The isolated compounds were screened using a microtitre dilution assay (MDA). Compound 79 was active against Candida albicans (12.5 µg/mL) and S. aureus at a lesser extent (25 µg/mL).

In the search for bioactive compounds from the Madagascar forests as part of an International Cooperative Biodiversity Group (ICBG) program, extracts of the roots of Terminalia tropophylla (Combretaceae) were screened and exhibited an activity against the A2780 ovarian cancer cell line, with an IC₅₀ value of 11 µg/mL. Some metabolites isolated from Terminalia species have shown a wide range of biological activities, including antimarial, antifungal, antibacterial, and cytotoxic activities. Cao et al. isolated the new oleane-type triterpenoid saponin terminaliaside A (80), the known triterpenoids saponins; arjunglucone I (81), sericoside (82) and a lignan derivative from the roots of this plant. The compounds were tested in the A2780 assay. Compound 80 was the most active with an IC₅₀ value of 1.2 µM, while compound 81 was weakly active with an IC₅₀ value of 16.5 µM and compounds 82 inactive with IC₅₀ values >30 µM. The antiproliferative activity of compound 80 is enhanced by substriments at the 3-, 16-, 21-, and 28-positions. The activity of the isolated compounds provides the importance of oleane-type saponins as potential anticancer agents for further investigation.

Euclea divinorum (Ebenaceae) root bark is used in traditional medicine for the treatment of diarrhoea, convulsions, cancer, skin diseases and gonorrhea. Previous chemical studies of this plant and other Euclea species revealed the presence of naphthoquinones, triterpenes and flavonoids. Mebe et al. isolated the new triterpenoid; 3β-(5-hydroxyferuloyl) Lup-20(30)-ene (83) with some of the known compounds lupene (84), 7-methyljuglone (85), lupeol (69) and betulin (86) from the chloroform extract of this plant. The isolated compounds were tested for their cytotoxic activity (ED₅₀ < 20 µg/mL) against a panel of cell lines using cell culture systems as described. The results indicate that, the new compound 83 and compound 85 displayed cytotoxic activity, while the other compounds were classed as being inactive. Compound 85 was cytotoxic against all cell lines and its most intense responses were observed with KB (human nasopharyngeal carcinoma), P-388 (murine lymphocytic leukemia), LNCaP (human prostate cancer), ZR-75-1 (human breast cancer) and U373 (human glioblastoma) cells at 4.8, 0.1, 0.8, 2.2 and 2.7 µg/mL, respectively. But, compound 83 was selective, and only showed activity against two cell lines: P-388 and ZR-75-1 at 2.1 and 4.2 µg/mL, respectively. Thus the cytotoxic activities of the isolates correlate with the ethnobotanical use of this plant.

Euclea undulata (Ebenaceae) is used by traditional healers in the Venda area, Limpopo Province in the treatment of diabetes. Previous chemical investigation revealed that naphthoquinones have been isolated from the root, stem and fruit of this plant by van der Vyver and Gerritsma. Deutschländer et al. isolated a new triterpene, α-aminyl-3-O-β-(5-hydroxy) ferulic acid (87), in addition to some of the known compounds; lupeol (69) and betulin (86) from the crude acetone extract of the root bark of this plant. The isolated compounds were evaluated for, their hypoglycaemic activities by executing in vitro assays on C2C12 myocytes, as well as their ability to inhibit the carbohydrate hydrolising enzyme α-glucosidase. The in vitro results on C2C12 myocytes showed that compound 87 has the ability to inhibit α-glucosidase at a concentration of 200.00 µg/mL with an IC₅₀ value of 4.79 µg/mL that correlates with that of the positive control acarbose with an IC₅₀ value 4.75 µg/mL. This study validates the ethnomedicinal use of this plant used by traditional healers for the treatment of diabetes.

The nutritive value of Eragrostis species (Poaceae) has been reported in literature. Sebastião et al. isolated the known triterpenoids 3β-3''4''(dihydroxy)-(E)-cinna maoyloxylup-20(29)-ene (88) in addition to other compounds from the toluene and dichloromethane extracts of aerial parts of Eragrostis viscose. The genotoxicity of the compounds isolated from this plant was studied.
using a cytokinesis-block micronucleus assay and the Ames test was also used to assess mutagenicity. The results revealed that compound 88 was cytotoxic including other compounds from this plant.

Extract from Cassipourea lanceolata (Rhizophoraceae) showed weak antiproliferative activity when tested against the A2780 human ovarian cancer cell line and had an IC50 value of 17 µg/mL. Hou et al. isolated the three new euphane triterpenoids; 1β,3β,11α,26-tetrahydroxy-7,24E-euphadien-11-one (89) and (2S)-1β,3β,24,25-tetrahydroxy-7,9(11)-euphadien (91) from the ethanol extract of the leaves and fruit of this plant collected from Madagascar.169 The isolated compounds were tested using the A2780 ovarian cancer cell line assay as described.159 The compounds 89-91 showed weak antiproliferative activities with IC50 values of 25, 25, and 32 µM, respectively. Compound 89 was found to have IC50 values > 5 µM when tested against the BT-549 and MCF-7 breast cancer, DU 145 prostate cancer, NCI-H460 and H522-TI NSCLC, HCC-2998 and HT-29 colon cancer, OVCAR-5 ovarian cancer, SF-539 CNS cancer, SR and U937 lymphoma, and UACC-257 and MDA-MB-435 melanoma cell lines. The weak antiproliferative activity of the extract can be due to masking or other compounds not isolated in this study.

Garcinia goudotiana (Clusiaceae) is used traditionally for its antiparasitic, antitussive and antimicrobial properties. The crude acetone extract in addition to its dichloromethane and ethyl acetate partitions showed a selective moderate to high antimicrobial activity (100 µg/mL < MIC < 500 µg/mL) against Gram-positive bacteria, in particular against three strains of Enterococcus, six strains of Staphylococcus and M. smegmatis, in addition to the yeast Candida albicans.170 Bioassay-guided fractionation of the crude acetonic extract of the leaves of this plant led to the isolation of two new prenylated benzylophloroglucinol derivatives, in addition to a known xanthone and the known triterpenoid friedelin (100) from the ethanol extract of the leaves and fruit of this plant as previously reported for the structural analog of compound 95 isolated from Pittosporum viridifolium.170

Policarpaea corymbosa (Caryophyllaceae) is a cosmopolitan species, that has been recently studied and the results revealed hepatoprotective activity against two human cancer cell lines (colorectal SW480, and prostate DU145), and one mouse tumour cell line (mammary EMT6) using a XTT assay.171 The results showed that compound 97 was the most active compound exhibiting cytotoxicity against these cell lines with IC50 values ranging from 4.61 to 22.61 µM. This activity level was greater than that of the anticancer drug, etoposide, which was used as positive control. Compounds 99-101 were inactive (IC50 > 10 µM). Compound 98 was tested only against the SW480 cell line and an embryonic rat heart-derived cell line (cardiomyoblast H9c2) by an embryonic rat heart-derived cell line (cardiomyoblast H9c2) by a XTT assay, and was inactive (IC50 > 10 µM).

Croton pseudopulchellus (Euphorbiaceae) commonly known as the Small Lavender Croton is used in the coastal area of Kenya and other parts of Africa to treat various ailments.57,120-124 Langat et al. isolated two new ent-kaurene-19-oxic acid derivatives; compounds 50-51 together with the known compounds; 52-55, 60, eudesm-4(15)-ene-1β,6α-diol (102), (1)7-epi-velularan-4-one (103), gemarcua-4(15), 5,9,10(14)-trien-β-ol (104) and acetyl aleuritic acid (105) from the hexane and methylene chloride extracts of the stem bark of this plant.125 Quantitative assessment of anti-plasmodial activity in vitro was determined via the parasite lactate dehydrogenase assay using a modified method described by Makler et al.126 The activity of some of the compounds was not reported in this study.

Sutherlandia humilis (Fabaceae) commonly known as cancer bush is used traditionally for a myriad of indications, ranging from poor appetite to the prevention and treatment of cancer.127-129 Analysis of...
the methanolic leaf extract of this plant using thin layer chromatography (TLC) revealed the presence of the triterpenoids sutherlandiosides A (106) and Sutherlandiosides B (107).\(^{193}\) Denise \textit{et al}. also isolated the new cycloartane-type triterpene glycoside 24, 25-O-β-D-glucopyranosyl-α-D-hydroxycycloart-3-one (SU3) (108) as the major compound in this plant.\(^{92}\)

\textit{Phyllanthus polyanthus} (Phyllanthaceae) also known as Forest Potato-bush is a rare species of plant in South Africa. A similar species of this plant \textit{P. delpyana} decoctions of the roots are used by the Digo of Kenya in the treatment of sexually transmitted diseases.\(^{184}\) Ndlebe \textit{et al}. isolated two new triterpenoids phyllanthol (109), phyllanthone (110) in addition to the known compounds (20S)-β-acyetoxy-24-methylendammaran-20-0l (111), and (20S)-3α-acyetoxy-24-methylendammaran-20-ol (112), lupenone (113), δ-aminyrin acetate (114) from the stem bark and leaves of this plant.\(^{95}\) Compounds 109-110 has not been isolated previously from a natural source but have been synthesised.\(^{196-200}\)

An ethnomedicinal survey of medicinal plants revealed the wide application of \textit{Mimusops obtusifolia} (Sapotaceae) in the management of malaria in Zulu traditional medicine.\(^{201}\) Crude extracts from the stem bark of this plant showed an \textit{in vitro} anti-plasmodial activity against a CQS of \textit{Plasmodium falciparum} (D10) with an IC\(_{50}\) value of 32.5 µg/mL. Mthokozisi \textit{et al}. isolated the known triterpenoids taxarol (115) and sawamilletin (116) from the stem bark of this plant.\(^{202}\) Quantitative assessment of anti-plasmodial activity \textit{in vitro} was determined.\(^{126}\) The results showed that the compounds had IC\(_{50}\) > 100 µg/mL.

Mthokozisi \textit{et al}. isolated the triterpenoid ursoic acid (117) from the leaves of \textit{Mimusops caffra} (Sapotaceae) collected from Durban, KwaZulu-Natal Province, South Africa. \(^{202,203}\) This plant is used in traditional medicine because of its healing properties against sores and wounds. \(^{204}\) Several triterpenoids isolated from plants have been reported in literature to demonstrate both \textit{in vitro} and \textit{in vivo} anti-plasmodial activity.\(^{205-207}\) Compound 117 has been previously reported to possess anti-plasmodial activity.\(^{208}\) and in this study the compound showed an appreciable anti-plasmodial activity with an IC\(_{50}\) value of 6.8 µg/mL at the tested concentration using CQS of \textit{P. falciparum}. The lower activity of the compound as compared to the crude extract could be due to synergistic effect with other compounds, decomposition during fractionation.

\textit{Morus nigra} (Moraceae) also known as black mulberry extracts have been reported to have antibacterial and fungicidal activity.\(^{209}\) This plant is used commercially for sericulture, as a feed for the domesticated silkworm, the bark of this plant is being used to expel tape worm. Mazimba \textit{et al}. isolated the known compounds 62 and 63 in addition to other compounds from the stem bark of this plant.\(^{70,137,210}\)

### 4 Conclusions

In this review, we present an overview of the results of biological activities of selected NPs (alkaloids and terpenoids) isolated from plants used in traditional medicine in Southern Africa (covering 10 countries). Our focus has been on plants whose ethnomedicinal uses correlate with the biological activities of the derived NPs. The plant sources, geographical collection sites and chemical structures of pure compounds were retrieved from literature sources comprising data collected from articles from major NP peer reviewed journals, spanning the period 1971 to 2014. Thus, the report does not claim to be exhaustive. However, the goal has been to document the baseline knowledge and lay the foundation for subsequent investigations. Our survey consisted in collecting data from the literature sources, mainly from MSc and PhD theses from university libraries within the region. We also used the author queries in major natural product and medicinal chemistry journals. The collected data includes plant sources, uses of plant material in traditional medicine, plant families, region of collection of plant material, isolated metabolites and type (e.g. flavonoid, terpenoid, etc.), measured biological activities of isolated compounds (as commented in the literature). The aim of this study has been to provide a survey of the biological activities of compounds derived from Southern African flora versus the ethnomedicinal uses of the plant species from which the compounds have been isolated. This series of reviews gives dedicated to Southern African flora was also intended to give an in depth coverage of the chemotaxonomy of Southern African flora and a cheminformatics analysis of the derived natural products. In this study, a literature survey led to the collection of 864 secondary metabolites from 101 plant species from 57 plant families. A correlation between the known biological activities of isolated compounds and the ethnomedicinal uses of the plants has been attempted. From the data presented in Tables 1 to 6, the biological activities of 62 out of the 117 plant metabolites commented in the text could be used to validate the ethnomedicinal uses of the plant species. Even though some of the biological activities don’t look famous, the aforementioned activities could be further fine-tuned by chemical modifications. Moreover, virtual screening methods could be used to enhance drug discovery by docking some of the compounds towards specific drug target sites and chemically modifying the NPs, so as to improve binding to the target site. This first part rather focuses of alkaloids and terpenoids. The other compound classes will be examined subsequently.

### 5 Acknowledgements

Financial support is acknowledged from Lhasa Ltd, Leeds, UK through the Chemical and Bioactivity Information Centre (CBIC), University of Buea, Cameroon. Ms. Irene N. Mukoko (Department of Chemistry, University of Buea) assisted in the data analysis. FNK acknowledges a Georg Forster fellowship for postdoctoral researchers from the Alexander von Humboldt Foundation.

### 6 Notes and references

\(^{a}\) Department of Chemistry, Chemical and Bioactivity Information Centre, Faculty of Science, University of Buea, P.O. Box 63, Buea, Cameroon; Tel.: +237 677915473; E-mail: ntiekfidele@gmail.com or fidele.ntiek@ubuea.cm.

\(^{b}\) Department of Chemistry, Faculty of Science, University of Buea, P.O. Box 63, Buea, Cameroon; Phone: +237 677 30 67 42; E-mail: ajeck.james@ubuea.cm (JAM) or Phone: +237 677 53 73 80; E-mail: joseph.yong@ubuea.cm (JNY).

\(^{†}\) These authors contributed equally.


4. S. M. N. Efange, \textit{Natural products: a continuing source of inspiration for the medicinal chemist}. In M. M. Iwu & J. C. Wootton (Eds.), \textit{Advances in Phytomedicine, vol. 1, Ethnomedicine and Drug


52 S. Patnala and I. Kanfer, J. Ethnopharmacol., 2009, 121, 86.


54 A. Hutchings, Zulu medicinal plants, an inventory. Pietermaritzburg: University of Natal Press; 1996

55 A. Hutchings and J. van Staden, J. Ethnopharmacol., 1994, 43, 89.


64 C. Kusamba, Fitoterapia, 2001, 72, 351.

65 J. O. Kokwaro, Medicinal Plants of East Africa, East Africa Education Publishers 1976; pp. 56-70


71 S. Mombat, N. Lall, A. Hussein, S. N. Ostad and M. Abdollahi, Pheco. Mag., 2010, 6, 34.


83 Van der Merwe MM. Bioactive sesquiterpenoids from Dicomia anomala subsp. gerradii MSc thesis, University of KwaZulu-Natal; 2008


86 E. von Koenen, Medicinal, poisonous and edible plants in Namibia, Windhoek, Namibia: Klaus Hess; 2001


90 J. O. Kokwaro, Medicinal Plants of East Africa. Kenya Literature Bureau, Nairobi, Kenya; 1993


94 A. Hutchings, A. H. Scott, G. Lewis and A. Cunningham, Zulu Medicinal Plants – An Inventory, University of Natal Press, Pietermaritzburg, South Africa, 1996


96 P. C. Rwangabo, La médecine traditionnelle au Rwanda, Editions Karthala, ACCT; 1993


Bioactive compounds from natural sources: isolation, characterization and biological properties (379-432), Taylor & Francis: London, UK, 2001


121x33mm (96 x 96 DPI)
<table>
<thead>
<tr>
<th>Compound subclass</th>
<th>Isolated metabolites</th>
<th>Plant species (Country)</th>
<th>Family</th>
<th>Ethnobotanical use</th>
<th>Measured activity</th>
<th>Author, reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crinane alkaloids</td>
<td>Buphanidrine (1) and distichamine (2)</td>
<td>Boophone disticha (South Africa)</td>
<td>Amaryllidaceae</td>
<td>As an arrow poison as well as a narcotic; use decoctions, extracts and infusions of bulbs for numerous ailments including treatment of burns, wounds, pain, inflammation, anxiety, gynaecological conditions and psychosis.</td>
<td>Antibacterial activity</td>
<td>Cheesman et al.</td>
</tr>
<tr>
<td>Indole</td>
<td>Voacangine (3) and dregamine (4)</td>
<td>Tabernaemontana elegans (South Africa)</td>
<td>Apocynaceae</td>
<td>Applied as a wash to wounds, and drunk for pulmonary diseases and chest pains, treatment of heart diseases and cancer.</td>
<td>Antimicrobial activity</td>
<td>Pallant et al.</td>
</tr>
<tr>
<td>Hypophorine (5)</td>
<td>Erythrina lysistemon (Botswana)</td>
<td>Leguminosae</td>
<td>The extracts from this plant have been used in traditional medicine and have also shown antiviral, anticancer and cytotoxic activities.</td>
<td>Antimicrobial activity</td>
<td>Juma et al.</td>
<td></td>
</tr>
<tr>
<td>Aporphine</td>
<td>Neolitsine (6) and dicentrine (7)</td>
<td>Spirospermum penduliflorum (Madagascar)</td>
<td>Menispermacae</td>
<td>Decoction of all parts is traditionally used as anticholinergic and vasorelaxant and the decoction of leaves is also used for the treatment of malaria and as a chloroquine adjuvant; the decoction of roots was taken as cholagogue, tonic and for hepatic disorders.</td>
<td>Antihypertensive activity</td>
<td>Rafamantanana et al.</td>
</tr>
<tr>
<td>Furoquinoline</td>
<td>Flindersiamine (8) and maculosidine (9)</td>
<td>Vepris uguenensis (Kenya)</td>
<td>Rutaceae</td>
<td>Treatment of malaria.</td>
<td>Anti-malarial activity</td>
<td>Cheplogoi et al.</td>
</tr>
<tr>
<td></td>
<td>Evoxine (10) and 7-(γ,γ-dimethylallyloxy)-γ-fagarine (11)</td>
<td>Teclea gerrardii (South Africa).</td>
<td></td>
<td>Bark decoctions are taken for chest complaints.</td>
<td>Antiplasmodial activity</td>
<td>Waffo et al.</td>
</tr>
<tr>
<td>Compound subclass</td>
<td>Isolated metabolites</td>
<td>Plant species (Country)</td>
<td>Family</td>
<td>Ethnobotanical use</td>
<td>Measured activity</td>
<td>Author, reference</td>
</tr>
<tr>
<td>-------------------</td>
<td>----------------------</td>
<td>-------------------------</td>
<td>--------</td>
<td>-------------------</td>
<td>-------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Acridone alkaloids</td>
<td>Tegerrardin A (12), tegerrardin B (13), arboritine (14), evoxanthine (15), 1,3-dimethoxy-N-methylacridone (16) and tecleanone (17)</td>
<td><strong>Teclea gerrardii</strong> (South Africa)</td>
<td>Rutaceae</td>
<td>Bark decoctions are taken for chest complaints.46</td>
<td>Antiplasmodial activity</td>
<td>Waflo et al.46</td>
</tr>
<tr>
<td>Mesembrine</td>
<td>Mesembrine (18), mesebrenone (19), mesembranol (20) and mesembranol (21)</td>
<td><strong>Sceletium tortuosum</strong> (South Africa)</td>
<td>Mesembryanthemaceae</td>
<td>Used for centuries as a mood-altering drug, used also in the management of psychiatric and psychological conditions including depression, anxiety, drug dependence, bulimia and obsessive-compulsive disorder.47-49</td>
<td>Psychoactive activity</td>
<td>Shikanga et al.50</td>
</tr>
<tr>
<td>Isoquinoline</td>
<td>Norprotosinomenine (22)</td>
<td><strong>Erythrina lysistemon</strong> (Botswana)</td>
<td>Leguminosae</td>
<td>The extracts from this plant have been used in traditional medicine and have also shown antiviral, anticancer and cytotoxic activities.51-52</td>
<td>Antimicrobial activity</td>
<td>Juma et al.53</td>
</tr>
</tbody>
</table>
Table 3: Summary of the bioactivity of derived (monoterpenes, meroterpenoid and sesquiterpenes) versus ethnobotanical uses of plant species derived from Southern Africa flora

<table>
<thead>
<tr>
<th>Compound subclass</th>
<th>Isolated metabolites</th>
<th>Plant species (Country)</th>
<th>Family</th>
<th>Ethnobotanical use</th>
<th>Measured activity</th>
<th>Author, reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monoterpenes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(E)-2(3)-Tagetenone epoxide (23), myrcenone (24), piperitenone or 3-methyl-6-(1-methylethylidene)-cyclohex-2-en-1-one (25)</td>
<td>Lippia javanica (Mozambique)</td>
<td>Verbenaceae</td>
<td>Its infusion is commonly used in Africa as a tea against various ailments like influenza, measles, rashes, malaria, stomach problems, fever, colds, <strong>cough</strong>, headaches, in Botswana it is used as a caffeine-free tea and in Zimbabwe and Malawi as a nerve tonic.</td>
<td><strong>Antitubercular and anti-HIV activity</strong></td>
<td>Mujovo et al.14</td>
<td></td>
</tr>
<tr>
<td>Piperitenone or 3-methyl-6-(1-methylethylidene)-cyclohex-2-en-1-one (25), major component of the essential oil</td>
<td>Lippia javanica (South Africa)</td>
<td>Verbenaceae</td>
<td>Used in South Africa against various chest ailments, influenza, measles, rashes, stomach problems and headaches, depending on the traditional healer, and is therefore known as <strong>fever tea</strong> or <strong>musudzungwane</strong> in Tshivenda, its essential oil has also been found to have good insect repellent activity. In Botswana it is used as a caffeine free tea. In Zimbabwe and Malawi it is used mainly as a nerve tonic.</td>
<td><strong>Antimicrobial and antimalarial activity</strong></td>
<td>Manenzhe et al.53</td>
<td></td>
</tr>
<tr>
<td><strong>Meroterpenoid</strong></td>
<td>7a,8,9a,9b,10b-Heptahydro-4H-10,10-dimethyl-1,7-dioxa-5-hydroxy-2-hydroxymethylcyclobuty [1,2,3,3a,4]indenol[5,6-a]naphthalen-4-one or ptaerobliquol (26)</td>
<td>Ptaeroxylon obliquum (Mozambique)</td>
<td>Rutaceae</td>
<td>Used in southern Africa for the treatment of various diseases, from headaches to tick control.</td>
<td><strong>Antiprotozoan activity</strong></td>
<td>Agostinho et al.62</td>
</tr>
<tr>
<td><strong>Sesquiterpenes</strong></td>
<td>Farnesylamine (27)</td>
<td>Vernonio auriculifera (South Africa)</td>
<td>Asteraceae</td>
<td>Used as a poultice, to relieve headache, to treat conjunctivitis, to treat fever associated with viral and bacterial infections, treat toothache and snake poison.</td>
<td><strong>Antibacterial activity</strong></td>
<td>Kiplimo et al.70</td>
</tr>
<tr>
<td>Tutin (28) and hyenanchin (29)</td>
<td>Hyaenancha globosa (South Africa)</td>
<td>Euphorbiaceae</td>
<td>Fruits were formerly used to poison carcases in order to destroy hyenas and other vermin.</td>
<td><strong>Antibacterial activity, cytotoxicity and antioxidant activity</strong></td>
<td>Montaz et al.71</td>
<td></td>
</tr>
<tr>
<td>1β-Furanoyloxy-9a-benzoyloxy-β-dihydroagarofuran (30), 1α-furanoyloxy-9β-benzoyloxy-2-oxo-dihydro-β-agarofuran (31), 1β,9α-difuranoyloxy-8β-acetoxy-2-oxo-3-ene-dihydro-β-agarofuran (32), 1β-furanoyloxy-9α-benzoyloxy-8β-acetoxy-2-oxo-3-ene-dihydro-β-agarofuran (33) and 1β,9α-Difuranoyloxy-2,8-dioxo-3-ene-dihydro-β-agarofuran (34)</td>
<td>Osyris lanceolata (Botswana)</td>
<td>Santalaceae</td>
<td>To treat a wide variety of kidney infection, <strong>diarrhoea, cholera, coughs, malaria</strong>, gynaecological disorders, infertility, <strong>venereal diseases</strong>, cancer, and insanity.</td>
<td><strong>Antimicrobial activity</strong></td>
<td>Yeboah et al.77</td>
<td></td>
</tr>
<tr>
<td>3-Oxoeudesma-1,4(15),11(13)-triene-12,6a-lide (35)</td>
<td>Dicoma anomala (South Africa)</td>
<td>Asteraceae</td>
<td>Treatment of coughs and colds, fevers, ulcers, dermatosis, venereal diseases, labour pains, dysentery, intestinal parasites, stomach pains, toothache and internal worms.</td>
<td><strong>Antimalarial activity</strong></td>
<td>Becker et al.87</td>
<td></td>
</tr>
</tbody>
</table>
Table 4: Summary of the bioactivity of derived (abietane diterpenes, labdane-type diterpenes, limnoid diterpenes and kaurene diterpenes) versus ethnobotanical uses of plant species derived from Southern Africa flora

<table>
<thead>
<tr>
<th>Compound subclass</th>
<th>Isolated metabolites</th>
<th>Plant species (Country)</th>
<th>Family</th>
<th>Ethnobotanical use</th>
<th>Measured activity</th>
<th>Author, reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abietane diterpenes</td>
<td>Parviflorone D (36) and parviflorone F (37)</td>
<td>Plectranthus ecklonii (South Africa)</td>
<td>Lamiaceae</td>
<td>For treatment of gastrointestinal disorders, as antimicrobial agents for the treatment of wounds, the alleviation of respiratory conditions and for malaria.</td>
<td>Antiplasmodial activity.</td>
<td>van Zyl et al.</td>
</tr>
<tr>
<td></td>
<td>11-Hydroxy-19-(methyl-but-2-en-oyloxy)-abieta-5,7,9 (11),13-tetraene-12-one (38)</td>
<td>Plectranthus lucidus (South Africa)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>11-Hydroxy-19-(4-hydroxy-benzoyloxy)-abieta-5,7,9(11),13-tetraene-12-one (39) and 11-hydroxy-19- (3,4-dihydroxy -benzoyloxy)-abieta-5,7,9(11),13-tetraene-12-one (40)</td>
<td>Plectranthus tongaensis (South Africa)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labdane-type diterpenes</td>
<td>9,13-Epoxy-6-hydroxy-16,15-labdanolide (41) and 9,13:15,16-Diepoxy-6,16-labdanediol (42)</td>
<td>Leonotis leonurus (South Africa)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limnoid diterpenoid</td>
<td>Methyl uguenesonate (49)</td>
<td>Vepris uguenensis (Kenya)</td>
<td>Rutaceae</td>
<td>Treatment of malaria.</td>
<td>Antimalarial activity.</td>
<td>Cheplogoi et al.</td>
</tr>
<tr>
<td>kaurene diterpene</td>
<td>Ent-14S*-hydroxykaur-16-en-19-oic (50), ent-14S*,17-dihydroxykaur-13-en-19-oic (51), ent-kaur-16-en-19-oic acid (52), ent-kaur-16-en-19-al (53), ent-12β-hydroxykaur-16-en-19-oic acid (54), ent-12β-acetoxykaur-16-en-19-oic acid (55)</td>
<td>Croton pseudopulchellus (South Africa)</td>
<td>Euphorbiaceae</td>
<td>A decoction from the roots is used to treat asthma, the powdered root taken as a snuff for headaches and leaves are applied by Tanzanians to their chest for chest ailments.</td>
<td>Antiviral, cytotoxicity and antiplasmodial activity.</td>
<td>Langat et al.</td>
</tr>
</tbody>
</table>
Table 5: Summary of the bioactivity of derived pentacyclic triterpenoids versus ethnobotanical uses of plant species derived from Southern Africa flora

<table>
<thead>
<tr>
<th>Compound subclass</th>
<th>Isolated metabolites</th>
<th>Plant species (Country)</th>
<th>Family</th>
<th>Ethnobotanical use</th>
<th>Measured activity</th>
<th>Author, reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentacyclic triterpenoids</td>
<td>Lupenyl acetate (56), oleanolic acid (57), β- amyrin acetate (58), α-amyrin (59) and β- amyrin (60), friedelanone (61) and friedelin acetate (62).</td>
<td>Vernonia auriculifera (Kenya)</td>
<td>Asteraceae</td>
<td>Used as a poultice, to relieve headache, to treat conjunctivitis, to treat fever associated with viral and bacterial infections, treat toothache and snake poison.</td>
<td>Antibacterial activity.</td>
<td>Kiplimo et al.</td>
</tr>
<tr>
<td></td>
<td>α-αAmyrin (59) and betulinic acid (63)</td>
<td>Artemisia afra (South Africa)</td>
<td></td>
<td>To treat coughs, colds, diabetes, malaria, sore throat, asthma, headache, dental care, gout and intestinal worms.</td>
<td>antimicrobial activity.</td>
<td>More et al.</td>
</tr>
<tr>
<td></td>
<td>Lup-20(30)-ene-3α,29-diol (64), lup-20(29)-ene-30-hydroxy-3-one (65) and Ψ – taraxastanonol (66)</td>
<td>Elaeodendron transvaalense (South Africa)</td>
<td>Celastraceae</td>
<td>To treat coughs, diarrhoea, stomach ailments, herpes and sexually associated diseases, treatment of arthritis, cancer and prescribed presently for HIV/AIDS.</td>
<td>Cytotoxicity activity.</td>
<td>Tshikalange et al.</td>
</tr>
<tr>
<td></td>
<td>1α,23β-dihydroxy-12-oleanen-29-oic-acid-23β-O-α-4-acetylrhamnopyranoside (67) and 1,22-dihydroxy-12-oleanen-30-oic acid (68)</td>
<td>Combretum padoides (South Africa)</td>
<td>Combretaceae</td>
<td>Use in traditional medicine for relieving symptoms that appear to be caused by infective agents e.g. bloody diarrhoea, wounds and conjunctivitis.</td>
<td>antibacterial activity.</td>
<td>Angeh et al.</td>
</tr>
<tr>
<td></td>
<td>67 and 68</td>
<td>Combretum padoides (South Africa)</td>
<td></td>
<td></td>
<td></td>
<td>Eloff et al.</td>
</tr>
<tr>
<td></td>
<td>Lupeol (69)</td>
<td>Terminalia sericea (South Africa)</td>
<td></td>
<td>Use traditional in South Africa to treat diabetic.</td>
<td>Antidiabetic activity.</td>
<td>Nkobole et al.</td>
</tr>
<tr>
<td></td>
<td>1,3-Dihydroxy-12-oleanen-29-oic (70), 1-Hydroxy-12-oleanen-30-oic acid (71), 3,30-Dihydroxyl-12-oleanen-22-one (72), 1,3,24-Trihydroxy-12-oleanen-29-oic acid (73) and 1,23-Dihydroxy-12-oleanen-29-oicacid-3-O-2,4-di-acetyl-1-rhamnopyranoside (74)</td>
<td>Combretum imberbe (Zimbabwe)</td>
<td></td>
<td>Treating abdominal disorders, backache, bacterial infections etc.</td>
<td>antimicrobial activity.</td>
<td>Eloff et al.</td>
</tr>
</tbody>
</table>
Figures and captions

Fig. 1 Chemical structures of alkaloids from Southern African flora (1 to 22).
Fig. 2 Chemical structures of monoterpenes, meroterpenoid and sesquiterpenes from Southern African flora (23 to 35 and 102 to 104).
Fig. 3 Chemical structures of abietane diterpenes, labdane-type diterpenes, limnoid diterpenes and kaurene diterpenes from Southern African flora (36 to 48).
Fig. 4 Chemical structures of abietane diterpenes, labdane-type diterpenes, limnoid diterpenes and kaurene diterpenes from Southern African flora (49 to 55).
Fig. 5 Chemical structures of triterpenoids from Southern African flora (56 to 66).
Fig. 6 Chemical structures of triterpenoids from Southern African flora (67 to 73).
1,23-Dihydroxy-12-oleanen-29-oicacid-3-O-2,4-di-acetyl-1-rhamnopyranoside (74)

1α,3,β-Hydroxyimberbic acid or 1α,3,β-dihydroxy-olean-12-en-29-oate-23-O-L-4-acetylrhamnopyranoside (75)

1α,3,β-Hydroxyimberbic acid-23-O-α-L-4-acetylrhamnopyranoside or 1α,3,β-trihydroxy-olean-12-en-29-oate-23-O-L-3, 4-acetyl-rhamnopyranoside (76)

1α,3,β-Hydroxyimberbic acid-23-O-α-L-3,4-diacetyl-rhamnopyranosyl]-29-O-α-rhamnopyranoside (77)

1α,3,β-Hydroxyimberbic acid or 1α,3,β-dihydroxyolean-12-en-29-oic acid (78)

1α,3,β-Hydroxyimberbic acid-23-O-α-L-3,4-diacetylrhamnopyranosyl]-29-O-α-rhamnopyranoside (79)

Terminaliaside A (80)

Arjunglucoside I (81) R₁ = OH, R₂ = H
Sericoside (82) R₁ = H, R₂ = OH

3β-(5-hydroxyferuloyl)Lup-20(30)-ene (83) R = OH
Lupene (84)
Betulin (86)

Fig. 7 Chemical structures of triterpenoids from Southern African flora (74 to 84 and 86).

Methyljuglone (85)

Fig. 8 Chemical structure of methyljuglone.
Fig. 9 Chemical structures of triterpenoids from Southern African flora (87 to 95).
Fig. 10 Chemical structures of a triterpenoids from Southern African flora (96 to 101).
Fig. 11 Chemical structures of a sesquiterpene and triterpenoids from Southern African flora (105 to 117).
<table>
<thead>
<tr>
<th>Compound subclass</th>
<th>Isolated metabolites</th>
<th>Plant species (Country)</th>
<th>Family</th>
<th>Ethnobotanical use</th>
<th>Measured activity</th>
<th>Author, reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentacyclic triterpenoids</td>
<td>1α,3, β-Hydroxyimberbic acid-23-O-α-L-4-acetylrhamnopyranoside (75), 1α,3, β-Hydroxyimberbic acid-23-0-Oα-L-3,4-diacetylrhamnopyranoside (76), 1α,3, β-Hydroxyimberbic acid-23-α-[L-3, 4-diacetyl-rhamnopyranosyl]-29-Oα-L-rhamnopyranoside (77), and 1,3, -Hydroxyimberbic acid (78)</td>
<td>Combretum imberbe (Zimbabwe)</td>
<td>Combretaceae</td>
<td>Used in African traditional medicine for diverse uses. 23,27,148-150</td>
<td>antimicrobial activity</td>
<td>Katererea et al.151</td>
</tr>
<tr>
<td></td>
<td>Terminalia stuhlmannii (Zimbabwe)</td>
<td>Terminalia tropophylla (Madagascar)</td>
<td>Terminaliaceae</td>
<td>Used in African traditional medicine for diverse uses. 154-158</td>
<td>Antimicrobial activity</td>
<td>Katererea et al.151</td>
</tr>
<tr>
<td></td>
<td>Euclea divinorum (Zimbabwe)</td>
<td>Euclea undulata (Madagascar)</td>
<td>Ebenaceae</td>
<td>Treatment of diabetes. 165-166</td>
<td>Cytotoxicity</td>
<td>Mebe et al.163</td>
</tr>
<tr>
<td></td>
<td>Eragrostis viscosa (Angola)</td>
<td>Cassipourea lanceolata (Madagascar)</td>
<td>Poaceae</td>
<td>Not specified</td>
<td>Antiproliferative activity</td>
<td>Hou et al.166</td>
</tr>
<tr>
<td></td>
<td>Garcinia goudotiana (Madagascar)</td>
<td>Pittosporum verticillatum (Madagascar)</td>
<td>Clusiaceae</td>
<td>Used for antiparasitic, antitussive and antimicrobial properties. 171</td>
<td>Antimicrobial and cytotoxic activity</td>
<td>Sania et al.171</td>
</tr>
<tr>
<td></td>
<td>Pittosporum verticillatum (Madagascar)</td>
<td>Some species are used in traditional medicine as anti-inflammatory, antimicrobial and antispasmodic agents. 173</td>
<td>Pittosporaceae</td>
<td>cytotoxicity</td>
<td>Mahenina et al.175</td>
<td></td>
</tr>
</tbody>
</table>