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REVIEW

The chemistry and bioactivity of Southern African flora I: A bioactivity *versus* ethnobotanical survey of alkaloid and terpenoid classes

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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.[1,2] 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.[3] 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.[4] 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.[5,6] 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).[7]

The region of Southern Africa has a rich biological and ethnic diversity.[8] 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.[9,10] The cultural value of biodiversity and its importance in effective biodiversity conservation planning and ecotourism have also been recognised recently.[11] 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,[3,7,12-13] including the development of natural product databases (CamMedNP, ConMedNP, AfroDb, p-ANAPL)[14-17] and the pharmacokinetic profiling of natural products from African flora,[17-19] with the view of drug discovery. Recent review articles have focused on anti-malarial and anti-tubercular principles from African flora,[19-21] while also focusing on different countries/regions in Africa.[3,20-22] 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.[8] 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 ethnobtanical 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.[23] 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).[24] 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.*[24] 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.[24]

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 diseases and chest pains by the VhaVenda[25] and Zulu[26] 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 antimycobacterial activity against *M. smegmatis*,[28] as well as anti-fungal activity against *Candida albicans*.[30] Extracts from *T. elegans*, along with those from seven other species of the genus *Tabernaemontana* have shown antibacterial activity against Gram-positive bacteria.[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 lysistemon*, 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 erythrinaline alkaloids[36,37] and prenylated flavonoids are known to be prevalent in the plant species,[33,38] compound **5** is known to contribute to its antimicrobial activities.[33]

Spirospermum penduliflorum (Menispermaceae) is endemic in Madagascar.[39] Moreover, the decoctions of all parts of this plant are traditionally used as anticholinergic and vasorelaxant, among other uses.[39] Rafamantanana *et al*. have isolated two aporphine alkaloids; neolitsine (**6**) and dicentrine (**7**) from the leaves of this plant.[40] Both dicentrine and neolitsine are known to possess antihypertensive activities, dicentrine having an EC_{50} 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 FCM29 (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 IC_{50} 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-*N*-methylacridone (**16**) and tecleanone (**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 IC_{50} of 24.5 μM, while arborinine showed the best activitity (IC_{50} = 12.3 μM).[46]

Sceletium 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.[47-49] Four alkaloids from this sub-class; mesembrine (**18**), mesembrenone (**19**), mesembrenol (**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.[51-52] Among the uses of *Erythrina lysistemon* (Leguminosae), 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.[33]

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 Monoterpenoids and meroterpenoid

Mujovo *et al*. isolated the monoterpenes (*E*)-2(3)-tagetenone 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),[53] 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.[54-57] In Botswana it is used as a caffeine-free tea and in Zimbabwe and Malawi as a nerve tonic.[58] The compounds were tested against *Mycobacterium tuberculosis* and HIV reverse transcriptase. It was found that (*E*)-2(3)-tagetenone epoxide (**23**) inhibited the HIV-1 reverse transcriptase enzyme by 91% at100 μgmL^{-1}. Moreover, the triterpene euscaphic acid, also isolated from this plant, was found to exhibit a minimum inhibitory concentration of 50 $\mu g\ mL^{-1}$ against sensitive strain of *M. tuberculosis*, H37Rv, reference strain (27294). This rare monoterpene (compound **23**) has also been also identified in the Cameroonian *Clausena anisata* (Rutaceae) essential oil.[59] Compound **25** (3-methyl-6-(1-methylethylidene)-cyclohex-2-en-1-one) was also noted to be the major component of the essential oil from *L. javanica* harvested from South Africa.[58] 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.[58]

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.[60,61] Agostinho *et al*. isolated ptaerobliquol (**26**), a new monoterpene-chromone (or meroterpenoid) form the roots of this plant for the first time.[62] The compound demonstrated a moderate activity when tested on *Toxoplasma gondii* replication using CPRG-based colorimetric assay,[63] inhibiting parasite replication at 5 and 10 μM, with an IC_{50} 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 ptaerobliquol a low therapeutic index.

3.2 Sesquiterpenes

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.[64] The Kikuyu people of central Kenya use the leaves of this plant as a wrap for pounded material used as a poultice,[65] cold water infusion of the plant is administered orally in Uganda and Kenya to treat fever associated with viral and bacterial infections.[66,67] In Ethiopia, the roots are used to treat toothache[68] and snake poison.[69] 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, friedelin 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 sesquiterpenes (**28** and **29**) have also been isolated from *Hyaenanche globosa* (Euphorbeaceae), a narrow endemic poisonous plant restricted to a single flat-topped mountain near Van Rhynsdrop 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. Momtaz *et a*l isolated the tutin (**28**) and hyenanchin 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 ethnomedicinal applications of *Osyris* species in traditional medicine has been published in different parts of the world, including the NAPRALERT database[75] and the Prelude Medicinal Plants Database.[76] Yeboah *et al*. isolated five new dihydro-*β*-agarofuran polyesters from the root bark and stem bark of the plant, harvested in Botswana.[77] The compounds include 1*β*-furanoyloxy-9*α*-benzoyloxy-dihydro-*β*-agarofuran (**30**), 1*α*-furanoyloxy-9*β*-benzoyloxy-2-oxo-dihydro-*β*-agarofuran (**31**), 1*β*, 9*α*-difuranoyloxy-8*β*-acetoxy-2-oxo-3-ene-dihydro-*β*-agarofuran (**32**), 1*β*-furanoyloxy-9*α*-benzoyloxy-8*β*-acetoxy-2-oxo-3-ene-dihydro-*β*-agarofuran (**33**) and 1*β*,9*α* –Difuranoyloxy-2,8-dioxo-3-ene-dihydro-*β*-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

Dicoma 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 ethnomedicinal profile.[82] The EtOAc extract of the plant exhibited an IC_{50} of 1.4 μg/mL on the chloroquine-sensitive D10 strain on *P. falciparum* using the *pLDH assay*.[83] The plant also has a wide range of ethnomedicinal applications, including the treatment of coughs and colds, fevers, ulcers, dermatosis, 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.[83-86] Becker *et al*. isolated a eudesmanolide-type sesquiterpene lactone, 3-oxoeudesma-1,4(15),11(13)-triene-12,6a-lide (**35**), commonly named dehydrobrachylaenolide, as the main active constituent of the

extract.[87] 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).[88] 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.[89] Thus the compound can be considered as a hit, because it complies with the basic criteria for anti-parasitic drug discovery[89] 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 gastro-intestinal disorders,[90] as anti-microbial agents,[91] for the treatment of wounds,[92] the alleviation of respiratory conditions[93] and for malaria treatment.[92,94-97] Zyla *et al*. isolated the abietane diterpenes; 11-hydroxy-2α-(4-hydroxybenzoyloxy)-abieta-5,7,9(11),13-tetraene-12-one or parviflorone D (**36**) and 11-hydroxy-2α-(3,4-dihydroxybenzoyloxy)-abieta-5,7,9(11),13-tetraene-12-one or parviflorone F (**37**) from the leaves *Plectranthus ecklonii* (Lamiaceae).[98] 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[99] was used to determined 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).[98] Zyla *et al*. also isolated the known compounds 11-hydroxy-19-(methyl-buten-2-oyloxy)-abieta-5,7,9(11),13-tetraene-12-one (**38**) and compound **36** from the *Plectranthus* species; *Plectranthus tongaensis* (Lamiaceae)[98] 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-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**).[98] 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.[100] This plant has a wide variety of medicinal uses, for example the treatment of cold,[101] bronchitis, tuberculosis,[57] coughs, asthma,[102] feverish headaches,[103] dysentery and chest infections.[104] Based on its ethnomedicinal profile as a respiratory ailments, and it's *in vitro* antibacterial activity,[105] 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-labdanolide (**41**) and 9, 13:15, 16-diepoxy-6, 16-labdanediol (**42**) from the leaves of this plant.[106] The compounds have relevance as chemotaxonomic markers even though they showed no activity against *M. Tuberculosis*.[106]

The nutritive value of *Eragrostis* species (Poaceae) has been reported in literature.[107,108] *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 8*α*,15-epoxylabdanes namely; methyl 8*α*,15-epoxylabdan-16*β*-oate (**43**), 8*α*,15-epoxylabdan-16*β*-ol (**44**), 8*α*,15-epoxy-16-norlabdan-13*β*-ol (**45**) together with other known compounds.[109] Some of the known compounds in this class include 8*α*,15-epoxy-16-norlabdan-13-one (**46**), 8*α*,15-epoxylabdan-16*β*-oic acid (**47**) and 16-acetoxy-8*α*,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).[20] *Vepris* species are used in ethnomedicine for the treatment of a diverse range of ailments, including pneumonia, lung diseases and kidney disorders,[110] eye troubles, cardiac pains, coughs, colds and influenza,[111,112] headache,[113] menorrhegia and infertility,[114] and as an aphrodisiac,[115] diuretic and antipyretic,[116] astringent and fortifier,[117] tonic for angina and rheumatism,[112] and both orally and externally as a treatment for malaria.[118] *Vepris uguenensis* (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 uguenesonate (**49**) together with other compounds from the dichloromethane extract of the roots of this plant.[119] 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 pseudopulchellus (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.[120,121] 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.[122] Species of this plant are durable and are used for hut building in Tanzania.[123] A decoction from the roots of this plant is used to treat asthma[57,124] and the powdered root taken as a snuff for headaches.[120] Leaves are applied by Tanzanians to their chest for chest ailments.[120] Langat *et al*. isolated two new ent-kauren-19-oic acid derivatives; *ent*-14*S**-hydroxykaur-16-en-19-oic (**50**), *ent*-14*S**,17-dihydroxykaur-15-en-19-oic (**51**) together with some of the known compounds; *ent*-kaur-16-en-19-oic acid (**52**), *ent*-kaur-16-en-19-al (**53**) *ent*-12*β*-hydroxykaur-16-en-19-oic acid

(**54**) and *ent*-12*β*-acetoxykaur-16-en-19-oic acid (**55**) 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] 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).

3.8 Pentacyclic triterpenoids

Vernonia species are known to be rich in terpenoids, particularly triterpenes and sesquiterpenes.[20] *Vernonia auriculifera* (Asteraceae) is a small tree or woody herb that has wide variety of uses in traditional medicine.[64-69] *Vernoni*a 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 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 determined 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 0.25 mg/mL against *Stenotrophomonas maltophilia*. The oleanane triterpernoids **57**, **58** and **60** displayed better antibacterial activity than the friedelane triterpenoids **61**-**62**. It is reported that the 28-COOH and ester functionality at *C*-3 contributes to pharmacological activities of pentacyclic triterpenes[129] 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 Cederberg 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, spasmolytic 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 compound **59** and betulinic acid (**63**) from this plant and other known compounds.[137] The compounds were evaluated for antimicrobial activity against gram positive (*Actinomyces naeslundii*, *Actinomyces israelii*, and *Streptococcus mutans*), gram negative bacteria (*Prevotella intermedia*, *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* previously known as *Actinobacillus actinomycetemcomitans*), and *Candida albicans*. The 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 IC_{50} of 2.42 µg/mL. Compound **63** showed a smooth trend of non-toxic effects with IC_{50} 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.

Tshikalange *et al.* isolated the three known triterpenoids lup-20(30)-ene-3*α*,29-diol (**64**), lup-20(29)-ene-30-hydroxy-3-one (**65**) and *Ψ*–taraxastanonol (**66**) together with other known compounds from stem bark of *Elaeodendron transvaalense* (Celastraceae), 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 ailaments 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 IC_{50} ranging from 66.6 to over 100.00 µg/mL in both cell lines, while compound **65** exhibited a good cytotoxicity activity IC_{50} 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 oleanene-type triterpenoid glycoside known as 1*α*, 23*β*-dihydroxy-12-oleanen-29-oic-acid-23*β*-O-*α*-4-acetylrhamnopyranoside (**67**), 1,22-dihydroxy-12-oleanen-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 *Escherichia 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.*,[144] 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 *α*-glucosidase and *α*-amylase enzymes in an *in vitro* screening exercise of a number of South African medicinal plants, in an attempt to discover new antidiabetic 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 *α*-glucosidase with an IC_{50} value of 66.48 µM. Additonally, bio-evaluation of compound **69** inhibitory activity on α-amylase demonstrated that the compound had an IC_{50} value of

140.72 μM against the enzyme, thus validating the use of the plant in tradional 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.[147] 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, diarrhoea, dysentery, dysmenorrhoea, earache, fever, gastric ulcers, general weakness, gonorrhoea, 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.[23,27,148-150] 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 traditional use of the plant in the treatment of infectious diseases. Five antibacterial triterpenoids; 1,3-dihydroxy-12-oleanen-29-oic (**70**), 1-hydroxy-12-olean-30-oic acid (**71**), 3,30-dihydroxyl-12-oleanen-22-one (**72**), 1,3,24-trihydroxyl-12-olean-29-oic acid (**73**) and 1,23-dihydroxy-12-oleanen-29-oicacid-3-*O*-2,4-di-acetyl-1-rhamnopyranoside (**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.[145,147] The antibacterial activity of the isolated compounds was much lower than expected from the activity of the crude extracts this can be due to synergy. Katererea *et al*. also isolated the two novel derivatives of 1*α*,3*β*,23-trihydroxyolean-12-en-29-oic acid; 1*α*,3,*β*-hydroxyimberbic acid-23-O-*α*-*L*-4-acetylrhamnopyranoside (**75**), 1*α*,3,*β*-hydroximberbic acid-23-*O*-*α*-*L*-3,4-diacetylrhamnopyranoside (**76**) and the known compounds 1*α*,3,*β*-hydroxyimberbic acid-23-*α*-[*L*-3,4-diacetyl-rhamnopyranosyl]-29-*O*-*α*-rhamnopyranoside (**77**), and 1,3, -Hydroxyimberbic acid (**78**) form the leaves of the this plant.[151] The antimicrobial activity of the isolated compounds was done using a microtitre dilution assay (MDA),[152] 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* at12.5 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 test samples. 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 1*α*,3,*β*-hydroxyimberbic acid-23-*O*-*α*-[*L*-4-acetyl-rhamnopyranosyl]-29-*O*-*α*-rhamnopyranoside (**79**) from the stem bark of this plant.[151] 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-oate 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).[152] Compound **79** was active against *Candida albicans* (12.5 μg/mL) and *S. aureus* to 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 IC_{50} value of 11 μg/mL.[153] Some metabolites isolated from *Terminalia* species have shown a wide range of biological activities, including antimalarial,[154] antifungal,[154-156] antibacterial,[155-157] and cytotoxic activities.[156,158] Cao *et al*. isolated the new oleanane-type triterpenoid saponin terminaliaside A (**80**), the known triterpenoids saponins; arjunglucoside I (**81**), sericoside (**82**) and a lignan derivative form the roots of this plant.[153] The compounds were tested in the A2780 assay. Compound **80** was the most active with an IC_{50} value of 1.2 μM, while compound **81** was weakly active with an IC_{50} value of 16.5 μM and compounds **82** inactive with IC_{50} values >30 μM. The antiproliferative activity of compound **80** is enhanced by substituents at the 3-, 16-, 21-, and 28-positions.[159] The activity of the isolated compounds provides the importance of oleanane-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 gonorrhoea.[26,85] Previous chemical studies of this plant and other *Euclea* species revealed the presence of naphthoquinones, triterpenes and flavonoids.[160-162] Mebe *et al*. isolated the new triterpenoid; 3*β*-(5-hydroxyferuloyl) Lup-20(30)-ene (**83**) with some of the known compounsds lupene (**84**), 7-methyljuglone (**85**), lupeol (**69**) and betulin (**86**) from the chloroform extract of this plant.[163] The isolated compounds were tested for their cytotoxic activity (ED_{50} < 20 μg/mL) against a panel of cell lines using cell culture systems as described.[164] 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.[165-166] Deutschländer *et al*. isolated a new triterpene, *α*-amyrin-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.[167] 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.[168] 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 IC_{50} value of 4.79 μg/mL that correlates with that of the positive control acarbose with an IC_{50} 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.[107-108] Sebastião *et al*. isolated the known triterpenoids 3β-(3'',4''-dihydroxy)-(*E*)-cinnamoyloxylup-20(29)-ene (**88**) in addition to other compounds from the toluene and dichloromethane extracts of aerial parts of *Eragrostis viscose.*[109] 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 IC_{50} value of 17 μg/mL. Hou *et al.* isolated the three new euphane triterpenoids; 1*β*,3*β*,11*α*,26-tetrahydroxy-7,24*E*-euphadiene (**89**), 3*β*,26-dihydroxy-8,24*E*-euphadien-11-one (**90**) and (24*S*)- 1*β*,3*β*,24,25-tetrahydroxy-7,9(11)-euphadiene (**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 IC_{50} values of 25, 25, and 32 μM, respectively. Compound **89** was found to have IC_{50} values > 5 μM when tested against the BT-549 and MCF-7 breast cancer, DU 145 prostate cancer, NCI-H460 and H522-T1 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 acetonic extract in addition to its dichloromethane and ethyl acetate partitions showed a selective moderate to high antimicrobial activity (100 μg/mL < MIC < 500 μg mg/mL or MIC ≤ 100 μg/mL) against Gram-positive bacteria, in particular against three strains of *Enteroccocus*, six strains of *Staphyloccocus* 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 benzoylphloroglucinol derivatives, in addition to a known xanthone and the known triterpenoid friedelin (**92**).[171] Human colon carcinoma HT29 and human fetal lung fibroblast MRC5 cells was also used to evaluate the cytotoxic activities of the extracts and isolated compounds. The prenylated compounds showed a high antimicrobial activity against some Gram-positive bacteria with a moderate cytotoxicity while the activity of compound **92** was not reported.

The *Pittosporum* is the only genus of the Pittosporaceae family found in Malagasy flora.[172] Some of the species are used in traditional medicine as anti-inflammatory, antimicrobial and antispasmodic agents.[173] In the search for biologically active triterpenoids saponins from Pittosporaceae,[174] phytochemical investigation of the ethanol extract from the root barks of *Pittosporum verticillatum* (Pittosporaceae) led to the isolation of three new triterpene saponins, 3-*O*-[*β*-*D*-glucopyranosyl-(1→2)]-[*α*-*L*-arabinopyranosyl-(1→3)]-[*α*-*L*-arabinofuranosyl-(1→4)]-*β*-*D*-glucuronopyranosyl-21-*O*-(2-acetoxy-2-methylbutanoyl)-*R*1-barrigenol (**93**), 3-*O*-[*β*-*D*-glucopyranosyl-(1→2)]-[*α*-*L*-arabinopyranosyl-(1→3)]-[*α*-*L*-arabinofuranosyl-(1→4)]-*β*-*D*-glucuronopyranosyl-21-*O*-(2-acetoxy-2-methylbutanoyl)-28-*O*-acetyl-*R*1-barrigenol (**94**), 3-*O*-[*β*-*D*-glucopyranosyl-(1→2)]-[*α*-*L*-arabinopyranosyl-(1→3)]-[*α*-*L*-arabinofuranosyl-(1→4)]-*β*-*D*-glucuronopyra-nosyl-21-*O*-*β*,*β*-dimethylacryloyl-22-*O*-angeloyl-*R*1-barrigenol (**95**) and senaciapittoside *B* (**96**).[175] Saponins have been reported to possess cytotoxic activity.[176,177] Thus, the isolated compounds **93-96** were tested for cytotoxicity against one human cancer cell line, SW480 (colorectal adenocarcinoma), and one embryonic heart-derived cell line H9c2 (rat cardiomyoblast), using the XTT method as described.[178] Doxorubicin (IC_{50} 1.00 μM on SW480 and 0.50 μM on H9c2) and methotrexate (IC_{50} N 20.00 μM on SW480 and 5.00 μM on H9c2) were used as positive controls. The result showed that, compound **95** exhibited a moderate cytotoxicity on SW480 cell line, which was however higher than the positive control methotrexate, whereas a weak activity was observed on the H9c2 cell line. Compounds **93**, **94** and **96** were found to be inactive on both cell types. All the isolated compounds **93-96** were inactive in comparison with the positive control doxorubicin. The results displayed a marginal cytotoxicity of triterpenoids saponins of this plant as previously reported for the structural analog of compound 95 isolated from *Pittosporum viridifolium*.[179]

Polycarpaea corymbosa (Caryophyllaceae) is a cosmopolite species, that has been recently studied and the results revealed hepatoprotective activity after administration of the whole plant extract to mammals.[180,181] This plant has wide applications in traditional medicine in some part of the world. It is used to treat cough in traditional Chinese medicine,[182] the leaves are used in Indian to treat inflammatory swellings and jaundice.[183] Previous chemical investigation of this plant revealed the presence of triterpenes, steriods[184] and flavonoids.[183] In the search for biologically active triterpenoid saponins from the Caryophyllaceae family.[185-186] Mahenina *et al*. isolated four new triterpenoids saponins (**97**–**100**) and a known triterpenoid saponins (**101**) from the methanolic extracts of leaves and roots of this plant.[187] The compounds were 3*β*-*O*-(*β*-*D*-xylopyranosyl-(1→2)-*β*-*D*-glucopyranosyl-(1→4)-[*β*-*D*-glucopyranosyl-(1→2)]-*α*-*L*-arabinopyranosyl)-13*β*,28-epoxyolean-11-en-16*α*-ol (**97**), 3*β*-*O*-(*β*-*D*-xylopyranosyl-(1→2)-*β*-*D*-glucopyranosyl-(1→4)-[*β*-*D*-glucopyranosyl-(1→2)]-*α*-*L*-arabinopyranosyl)-oleana-11,13(18)-diene-16*α*,28-diol (**98**), 3*β*-*O*-(*β*-*D*-xylopyranosyl-(1→2)-*β*-*D*-glucopyranosyl-(1→4)-[*β*-*D*-glucopyranosyl-(1→2)]-*α*-*L*-arabinopyranosyl)-camelliagenin A (**99**),16*α*,22*α*-diacetoxy-3*β*-*O*-(*β*-*D*-xylopyranosyl-(1→2)-*β*-*D*-glucopyranosyl-(1→4)-[*β*-*D*-gluco-pyranosyl-(1→2)]-*α*-*L*-arabinopyranosyl)-olean-12-*en*-28-ol (**100**) and apoanagallosaponin IV (**101**). Triterpenoid saponins have been known to possess cytotoxic activity.[176-177] Thus, the isolated compounds **97**, **99**–**101** were evaluated for their cytotoxic activities against two human cancer cell lines (colorectal SW480, and prostate DU145), and one mouse tumour cell line (mammary EMT6) using a XTT assay.[178] The results showed that compound **97** was the most active compound exhibiting cytotoxicity against these cell lines with IC_{50} 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 (IC_{50} > 10 μM). Compound **98** was tested only against the SW480 cell line and an embryonic rat heart-derived cell line (cardiomyoblast H9c2) by a XTT assay, and was inactive (IC_{50} > 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-kauren-19-oic acid derivatives; compounds **50-51** together with the known compounds; **52-55, 60**, eudesm-4(15)-ene-1*β*,6*α*-diol (**102**), (-)-7-epivaleran-4-one (**103**), germacra-4(15), 5*E*,10(14)-trien-9*β*-ol (**104**) and acetyl aleuritolic 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.[188-190] 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**).[191] Denise *et al*. also isolated the new cycloartane-type triterpene glycoside 24, 25-*O*-*β*-*D*-diglucopyranosyl-6*α*-hydroxycycloart-3-one (SU3) (**108**) as the major compound in this plant.[192]

Phyllanthus polyanthus (Phyllanthaceae) also known as Forest Potato-bush is a rare species of plant in South Africa.[193] A similar species of this plant *P. delpyanus* decocotions of the roots are used by the Digo of Kenya in the treatment of sexually transmitted diseases.[194] Ndlebe *et al*. isolated two new triterpenoids phyllanthol (**109**), phyllanthone (**110**) in addition to the known compounds (20*S*)-3*β*-acetoxy-24-methylenedammaran-20-ol (**111**), and (20*S*)-3*α*-acetoxy-24-methylenedammaran-20-ol (**112**), lupenone (**113**), *δ*-amyrin acetate (**114**) from the stem bark and leaves of this plant.[195] Compounds **109**-**110** has not been isolated previously from a natural source but have been synthesised.[196-200]

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

Mthokozisi *et al*. isolated the triterpenoid ursolic acid (**117**) from the leaves of *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 *in vitro* and *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 *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.

Morus nigra (Moraceae) also known as black mulberry extracts have been reported to have antibacterial and fungicidal activity.[209] This plant is used economically for sericulture, as a feed for the domesticated silkworm, the bark of this plant is being used to expel tape worm. Mazimba *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 Sothern Africa (covering 10 countries). Our focus has been on plants whose ethnobotanical 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 ethnobotanical 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 ethnobotanical 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 ethnobotanical uses of the plant species. Even though some of the biological activies 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.

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6 Notes and references

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Table 1: Summary of the bioactivity of derived alkaloids (crinane, indole, bisindole, aporphine and furoquinoline) *versus* ethnobotanical uses of plant species

Compound subclass	Isolated metabolites	Plant species (Country)	Family	Ethnobotanical use	Measured activity	Author,reference
Crinane alkaloids	Buphanidrine (**1**) and distichamine (**2**)	*Boophone disticha* (South Africa)	Amaryllidaceae	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.[23]	**Antibacterial** activity	Cheesman *et al.*[24]
Indole	Voacangine (**3**) and dregamine (**4**)	*Tabernaemontana elegans* (South Africa)	Apocynaceae	Applied as a wash to **wounds**, and drunk for pulmonary diseases and chest pains, treatment of heart diseases and cancer.[25,26]	**Antimicrobial** activity	Pallant *et al.*[32]
	Hypophorine (**5**)	*Erythrina lysistemon* (Botswana)	Leguminosae	The extracts from this plant have been used in traditional medicine and have also shown **antiviral**, anticancer and cytotoxic activities.[34,35]	**Antimicrobial** activity	Juma *et al.*[33]
Aporphine	Neolitsine (**6**) and dicentrine (**7**)	*Spirospermum penduliflorum* (Madagascar)	Menispermaceae	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.[39]	**Antihypertensive** activity	Rafamantanana *et al.*[40]
Furoquinoline	Flindersiamine (**8**) and maculosidine (**9**)	*Vepris uguenensis* (Kenya)	Rutaceae	Treatment of **malaria.**[41]	**Anti-malarial** activity	Cheplogoi *et al.*[44]
	Evoxine (**10**) and 7-(γ,γ-dimethylallyloxy)-γ-fagarine (**11**)	*Teclea gerrardii* (South Africa).		Bark decoctions are taken for chest complaints.[45]	Antiplasmodial activity	Waffo *et al.*[46]

Table 2: Summary of the bioactivity of derived alkaloids (acridone, mesembrine and isoquinoline) *versus* ethnobotanical uses of plant species derived from Southern Africa flora

Compound subclass	Isolated metabolites	Plant species (Country)	Family	Ethnobotanical use	Measured activity	Author, reference
Acridone alkaloids	Tegerrardin A (**12**), tegerrardin B (**13**), arborinine (**14**), evoxanthine (**15**), 1,3-dimethoxy- *N*-methylacridone (**16**) and tecleanone (**17**)	*Teclea gerrardii* (South Africa)	Rutaceae	Bark decoctions are taken for chest complaints.[45]	Antiplasmodial activity	Waffo *et al.*[46]
Mesembrine	Mesembrine (**18**), mesembrenone (**19**), mesembrenol (**20**) and mesembranol (**21**)	*Sceletium tortuosum* (South Africa)	Mesembryanthemaceae	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]	**Psychoactive** activity	Shikanga *et al.*[50]
Isoquinoline	Norprotosinomenine (**22**)	*Erythrina lysistemon* (Botswana)	Leguminosae	The extracts from this plant have been used in traditional medicine and have also shown **antiviral**, anticancer and cytotoxic activities. [51-52]	**Antimicrobial** activity	Juma *et al.*[33]

Table 3: Summary of the bioactivity of derived (monoterpenes, meroterpenoid and sesquiterpenes) *versus* ethnobotanical uses of plant species derived from Southern Africa flora

Compound subclass	Isolated metabolites	Plant species (Country)	Family	Ethnobotanical use	Measured activity	Author, reference
Monoterpenes	(*E*)-2(3)-Tagetenone epoxide (**23**), myrcenone (**24**), piperitenone or 3-methyl-6-(1-methylethylidene)-cyclohex- 2-en-1-one (**25**)	*Lippia javanica* (Mozambique)	Verbenaceae	Its infusion is commonly used in Africa as a tea against various ailments like influenza, measles, rashes, malaria, stomach problems, fever, colds, **cough**, headaches , in Botswana it is used as a caffeine-free tea and in Zimbabwe and Malawi as a nerve tonic.[54-57]	**Antitubercular** and anti-HIV activity	Mujovo *et al.*[53]
	Piperitenone or 3-methyl-6-(1-methylethylidene)-cyclohex- 2-en-1-one (**25**), major component of the essential oil	*Lippia javanica* (South Africa)		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 **fever** tea or musudzungwane 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.[54-57]	**Antimicrobial** and **antimalarial** activity	Manenzhe *et al.*[58]
Meroterpenoid	7*a*,8,9,9*a*,9b,10*b*-Heptahydro-4*H*-10,10-dimethyl-1,7-dioxa-5-hydroxy-2-hydroxymethylcyclobutyl[1,2,3:3,3*a*,4]indeno[5,6-*a*]naphtalen-4-one or ptaerobliquol (**26**)	*Ptaeroxylon obliquum* (Mozambique)	Rutaceae	Used in southern Africa for the treatment of various diseases, from headaches to tick control.[60,61]	Antiprotozoan activity	Agostinho *et al.*[62]
Sesquiterpenes	Farnesylamine (**27**)	*Vernonia auriculifera* (South Africa)	Asteraceae	Used as a poultice, to relieve headache, to treat conjunctivitis, to treat fever associated with viral and **bacterial infections**, **treat toothache** and snake poison.[65-68]	**Antibacterial** activity	Kiplimo *et al.*[70]
	Tutin (**28**) and hyenanchin (**29**)	*Hyaenanche globosa* (South Africa)	Euphorbiaceae	Fruits were formerly used to poison carcasses in order to destroy hyenas and other vermin.[71]	Antibacterial activity, cytotoxicity and antioxidant activity	Momtaz *et al.*[71]
Dihydro-β-agarofuran sesquiterpene polyesters	1β-Furanoyloxy-9α-benzoyloxy-dihydro-β-agarofuran (**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 *1*β,9α –Difuranoyloxy-2,8-dioxo-3-ene-dihydro-β-agarofuran (**34**)	*Osyris lanceolata* (Botswana)	Santalaceae	To treat a wide variety of kidney infection, **diarrhoea, cholera, coughs**, **malaria**, gynaecological disorders, infertility, **venereal diseases**, cancer, and insanity.[75,76]	**Antimicrobial** activity	Yeboah *et al.*[77]
Sesquiterpene lactones	3-Oxoeudesma-1,4(15),11(13)-triene-12,6*a*-lide (**35**)	*Dicoma anomala* (South Africa)	Asteraceae	Treatment of coughs and colds, **fevers**, ulcers, dermatosis, venereal diseases, labour pains, dysentery, intestinal parasites, stomach pains, toothache and internal worms.[82]	**Antimalarial** activity	Becker *et al.*[87]

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

Compound subclass	Isolated metabolites	Plant species (Country)	Family	Ethnobotanical use	Measured activity	Author,reference
Abietane diterpenes	Parviflorone D (**36**) and parviflorone F (**37**)	*Plectranthus ecklonii* (South Africa)	Lamiaceae	For treatment of gastro-intestinal disorders, as anti-microbial agents for the treatment of wounds, the alleviation of respiratory conditions and **for malaria**.[90-97]	**Antiplasmodial** activity.	van Zyl *et al.*[98-99]
	11-Hydroxy-19-(methyl-buten-2-oyloxy)-abieta-5,7,9 (11),13-tetraene-12-one (**38**)	*Plectranthus lucidus* (South Africa)				
	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**)	*Plectranthus tongaensis* (South Africa)				
Labdane-type diterpenes	9,13-Epoxy-6-hydroxy-16,15-labdanolide (**41**) and 9,13:15,16-Diepoxy-6,16-labdanediol (**42**)	*Leonotis leonurus* (South Africa)		Treating **colds, bronchitis**, **tuberculosis**, **coughs**, **asthma, feverish headaches, dysentery and chest infections**.[101-104]	**Antimycobacterial** activity.	Naidoo *et al.*[106]
	Methyl 8α,15-epoxylabdan-16β-oate (**43**), 8*α*,15-epoxylabdan-16*β*-ol (**44**), 8*α*,15-epoxy-16-norlabdan-13*β*-ol (**45**), 8*α*,15-epoxy-16-norlabdan-13-one (**46**), 8*α*,15-epoxylabdan-16*β*-oic acid (**47**) and 16-acetoxy-8*α*,15-epoxylabdane (**48**)	*Eragrostis viscosa* (Angola)	Poaceae	Used in folk medicine as a poison against snakes.[107,108]	Mutagenic activity, cytotoxic activity and genotoxicity.	Sebastião *et al.*[109]
Limonoid diterpenoid	Methyl uguenesonate (**49**)	*Vepris uguenensis* (Kenya)	Rutaceae	Treatment of **malaria**.[118]	**Antimalarial** activity.	Cheplogoi *et al.*[119]
kaurene diterpene	Ent-14*S**-hydroxykaur-16-en-19-oic (**50**), ent-14*S**,17-dihydroxykaur-15-en-19-oic (**51**), ent-kaur-16-en-19-oic acid (**52**), en*t*-kaur-16-en-19-al (**53**), ent-12*β*-hydroxykaur-16-en-19-oic acid (**54**), ent-12*β*-acetoxykaur-16-en-19-oic acid (**55**)	*Croton pseudopulchellus* (South Africa)	Euphorbiaceae	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.[57,120-124]	Antiviral, cytotoxicity and antiplasmodial activity.	Langat *et al.*[125]

Table 5: Summary of the bioactivity of derived pentacyclic triterpenoids versus ethnobotanical uses of plant species derived from Southern Africa flora

Compound subclass	Isolated metabolites	Plant species (Country)	Family	Ethnobotanical use	Measured activity	Author,reference
Pentacyclic triterpenoids	Lupenyl acetate (**56**), oleanolic acid (**57**), *β*- amyrin acetate (**58**), *α*-amyrin (**59**) and *β*- amyrin (**60**), friedelanone (**61**) and friedelin acetate (**62**).	*Vernonia auriculifera* (Kenya)	Asteraceae	Used as a poultice, to relieve headache, to treat conjunctivitis, to treat fever associated with viral and **bacterial infections**, **treat toothache** and snake poison.[64-69]	**Antibacterial** activity.	Kiplimo *et al.*[70]
	α-Amyrin (**59**) and betulinic acid (**63**)	*Artemisia afra* (South Africa)		To treat **coughs**, **colds**, diabetes, **malaria**, **sore throat**, asthma, **headache**, **dental care**, **gout** and **intestinal worms**.[131-133]	**antimicrobial** activity.	More *et al.*[137]
	Lup-20(30)-ene-3α,29-diol (**64**), lup-20(29)-ene-30-hydroxy-3-one (**65**) and *Ψ* – taraxastanonol (**66**)	*Elaeodendron transvaalense* (South Africa)	Celastraceae	To treat coughs, diarrhoea, stomach ailments, herpes and sexually associated diseases, treatment of arthritis, **cancer** and precbribed presently for HIV/AIDS.[139]	**Cytotoxicity** activity.	Tshikalange *et al.*[138]
	1*α*,23*β*-dihydroxy-12-oleanen-29-oic-acid-23*β*-*O*-*α*-4-acetylrhamnopyranoside (**67**) and 1,22-dihydroxy-12-oleanen-30-oic acid (**68**)	*Combretum padoides* (South Africa)	Combretaceae	Use in traditional medicine for relieving symptoms that appear to be caused by infective agents e.g. bloody **diarrhoea**, **wounds** and **conjunctivitis**.[142]	**antibacterial** activity.	Angeh *et al.*[144]
	67 and **68**	*Combretum padoides* (South Africa)				Eloff *et al.*[145]
	Lupeol (**69**)	*Terminalia sericea* (South Africa)		Use traditional in South Africa to treat **diabetic**.[146]	**Antidiabetic** activity.	Nkobole *et al.*[146]
	1,3-Dihydroxy-12-oleanen-29-oic (**70**), 1-Hydroxy-12-olean-30-oic acid (**71**), 3,30-Dihydroxyl-12-oleanen-22-one (**72**), 1,3,24-Trihydroxyl-12-olean-29-oic acid (7**3**) and 1,23-Dihydroxy-12-oleanen-29-oicacid-3-O-2,4-di-acetyl-1-rhamnopyranoside (**74**)	*Combretum imberbe* (Zimbabwe)		Treating abdominal disorders, backache, **bacterial infections** etc.[147]	**antimicrobial** activity.	Eloff *et al.*[145]

Figures and captions

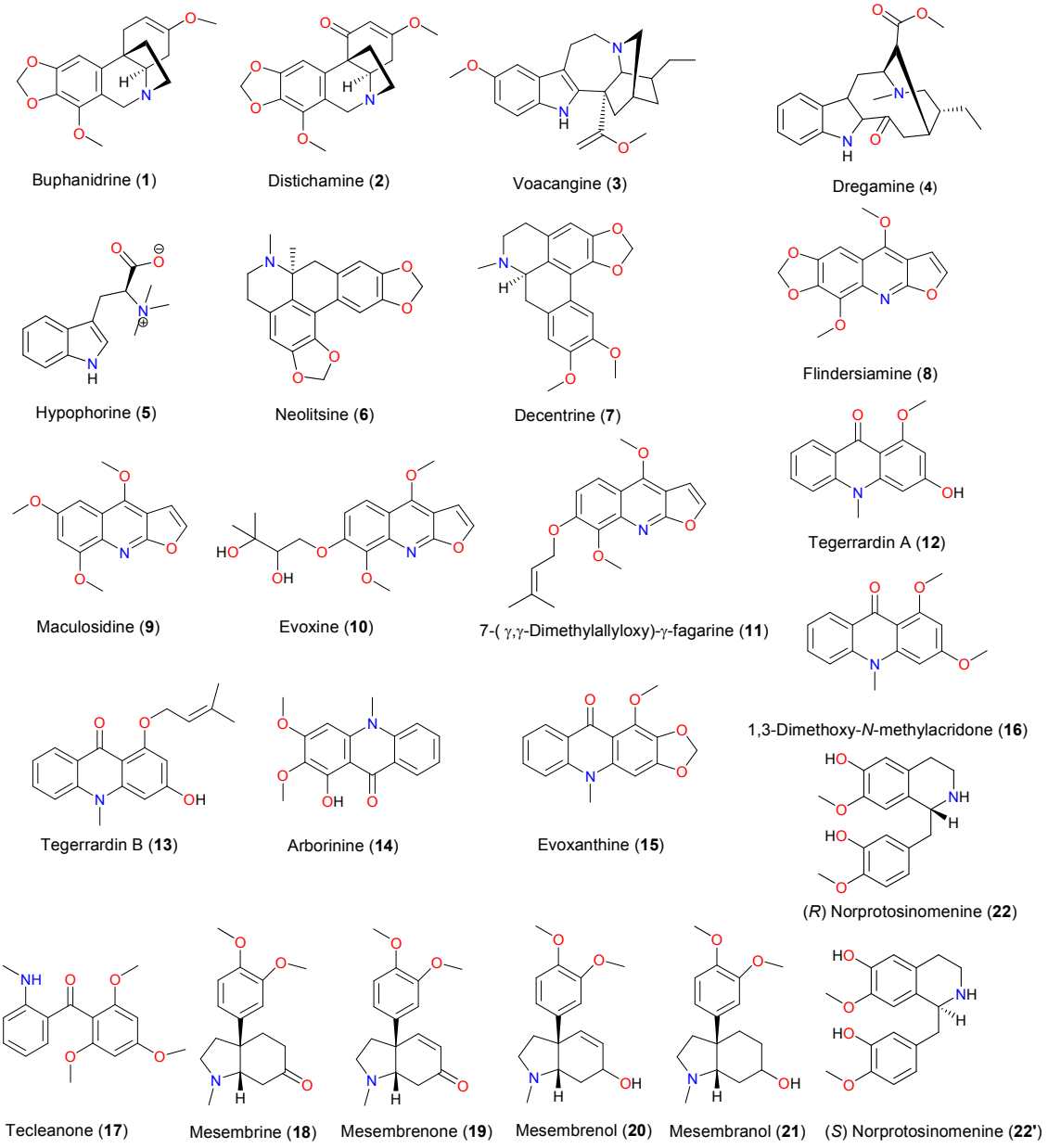


Fig. **1** Chemical structures of alkaloids from Southern African flora (**1** to **22**).

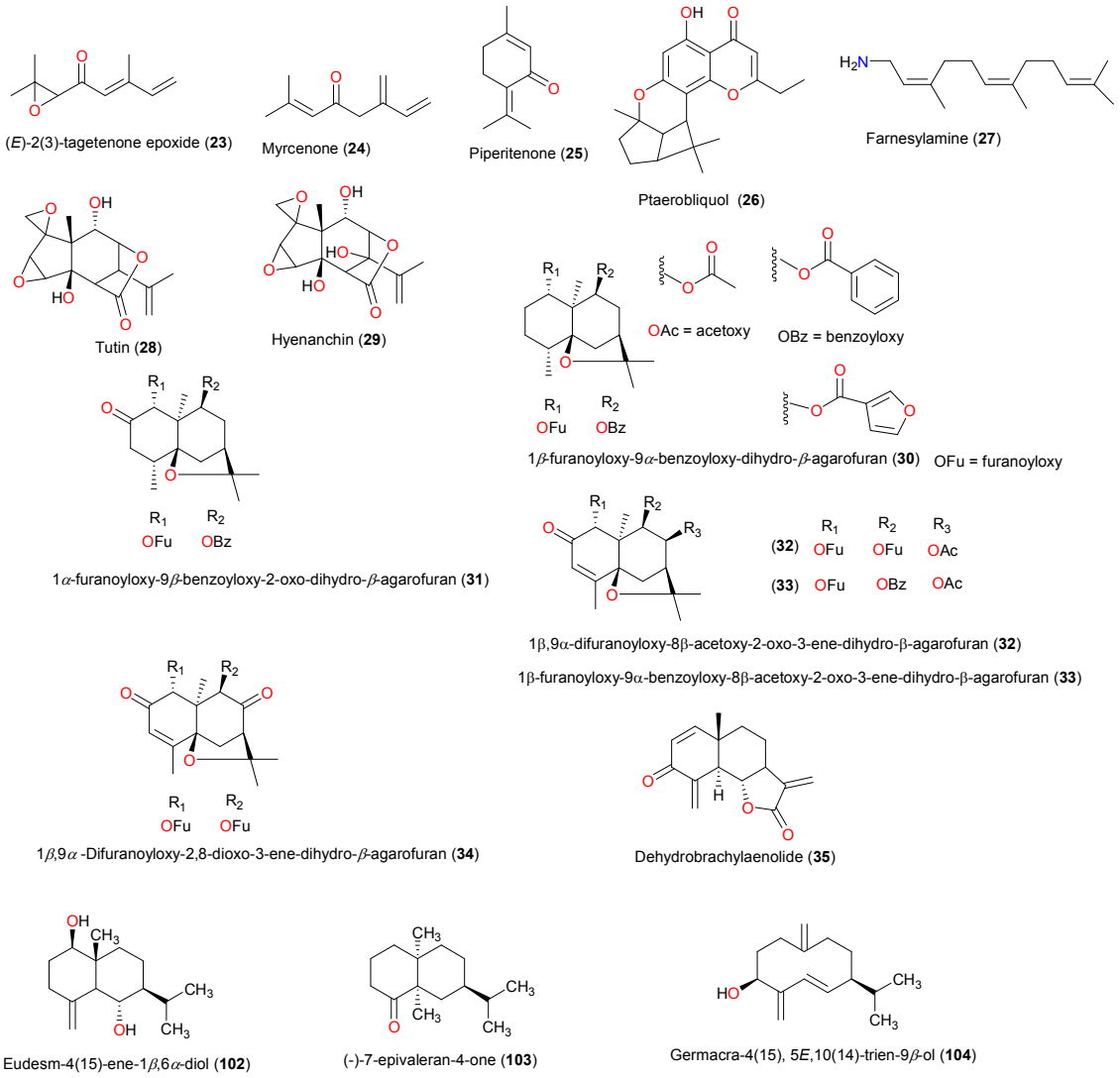


Fig. **2** Chemical structures of monoterpenes, meroterpenoid and sesquiterpenes from Southern African flora (**23** to **35** and **102** to **104**).

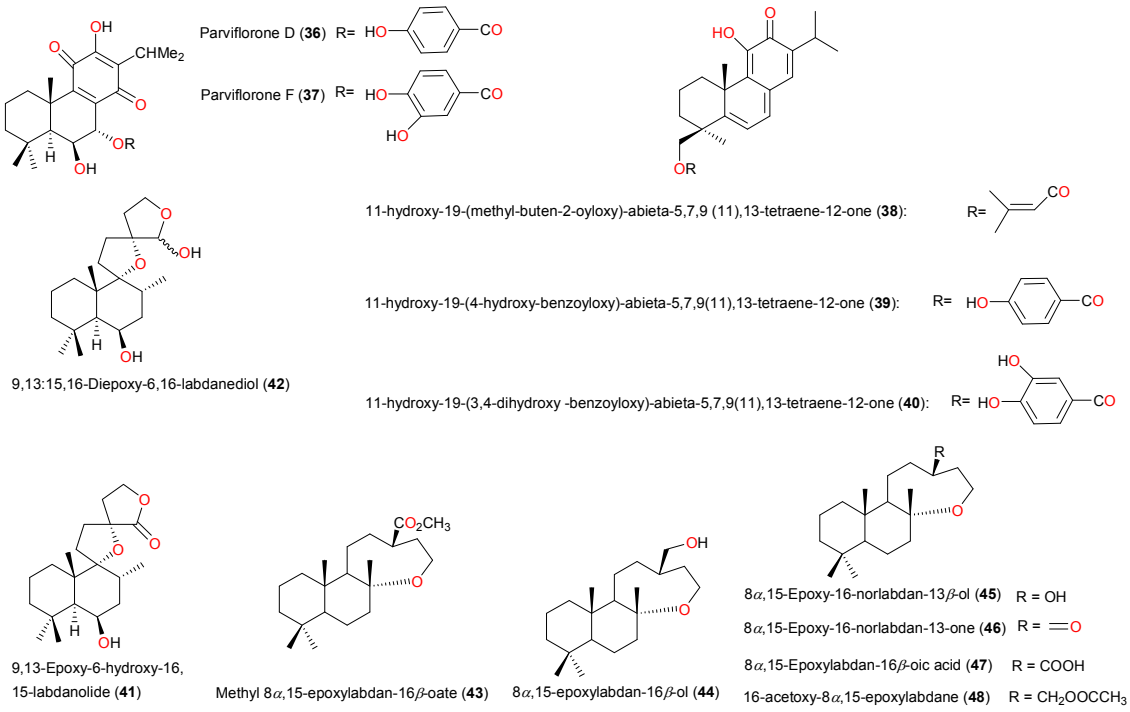


Fig. **3** Chemical structures of abietane diterpenes, labdane-type diterpenes, limnoid diterpenes and kaurene diterpenes from Southern African flora (**36** to **48**).

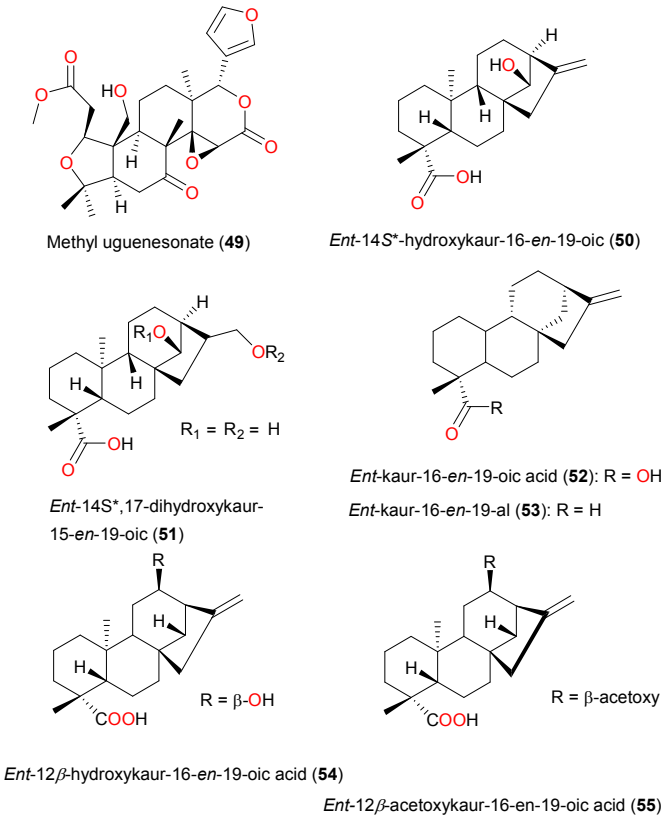
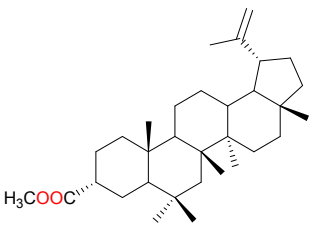
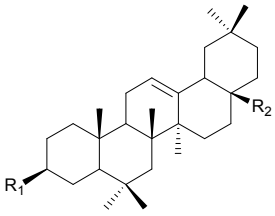


Fig. **4** Chemical structures of abietane diterpenes, labdane-type diterpenes, limnoid diterpenes and kaurene diterpenes from Southern African flora (**49** to **55**).



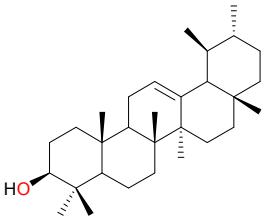
Lupenyl acetate (**56**)



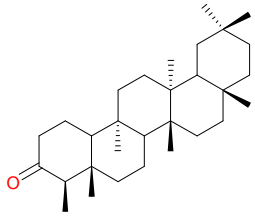
Oleanolic acid (**57**): R_1 = OH, R_2 = CO_2H

β- amyrin acetate (**58**): R_1 = OAc, R_2 = CH_3

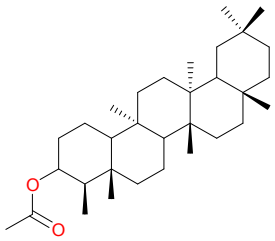
β- amyrin (**60**): R_1 = OH, R_2 = CH_3



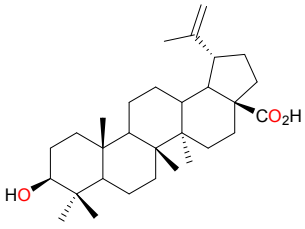
α-amyrin (**59**)



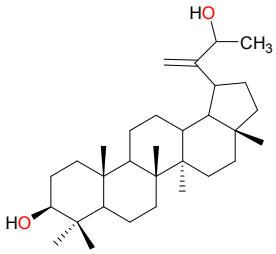
Friedelanone (**61**)



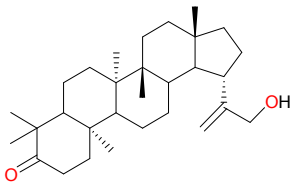
Friedelin acetate (**62**)



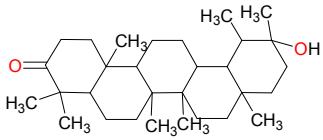
Betulinic acid (**63**)



Lup-20(30)-ene-3α,29-diol (**64**)



Lup-20(29)-ene-30-hydroxy-3-one (**65**)



Ψ- taraxastanonol (**66**)

Fig. **5** Chemical structures of triterpenoids from Southern African flora (**56** to **66**).

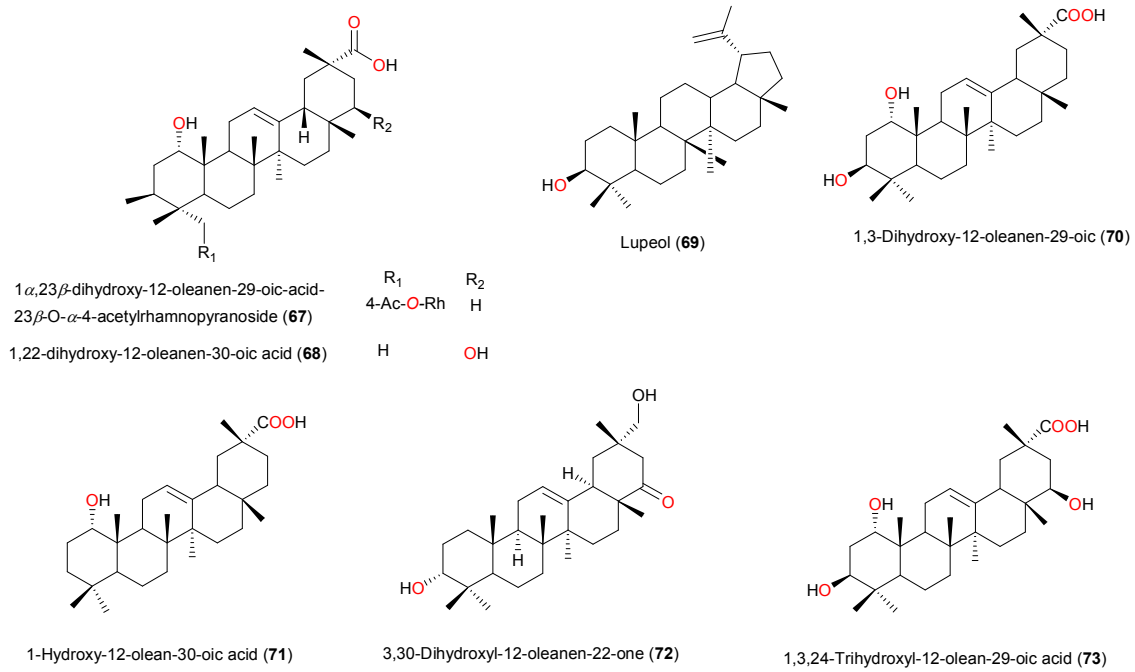
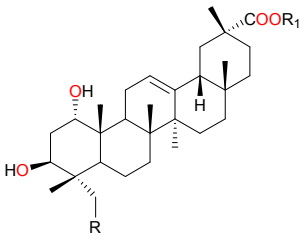
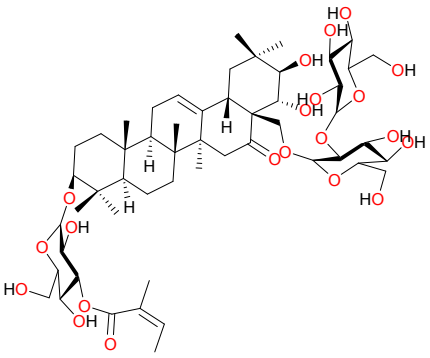


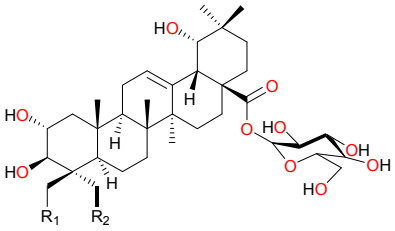
Fig. **6** Chemical structures of triterpenoids from Southern African flora (**67** to**73**).



	R	R_1
1,23-Dihydroxy-12-oleanen-29-oicacid-3-O-2,4-di-acetyl-1-rhamnopyranoside (**74**)	4-Ac-*O* -Rh	H
1α,3, β-Hydroxyimberbic acid-23-O-α-L-4-acetylrhamnopyranoside or ,1α,3, β –23-trihvdroxv-olean-12-en-29-oate-23-O-α-*L*-4-acetylrhamnopyranoside (**75**)	3,4-Ac-*O*-Rh	H
1α,3, β-Hydroximberbic acid-23-*O*-α-*L*-3,4-diacetylrhamnopyranoside or 1α,3, β-trihydroxy-olean-12-en-29-oate-23-O-α-*L*-3, 4-acetyl-rhamnopyranoside (**76**)	3,4-Ac-*O*-Rh	Rh
1α ,3, β -Hydroxyimberbic acid-23- α-[*L*-3, 4-diacetyl- rhamnopyranosyl]-29-*O*-α- rhamnopyranoside (**77**)	H	H
1α,3,β -Hydroxyimberbic acid or1α,3,β–dihydroxyolean-12-*en*-29-oic acid (**78**)		
1α,3, β -Hydroxyimberbic acid-23-*O*- α -[*L*-4- acetyl- rhamnopyranosyl]-29-*O*- α -rhamnopyranoside (**79**)		

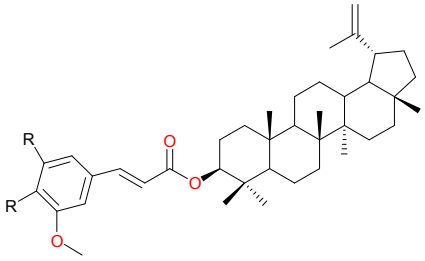


Terminaliaside A (**80**)

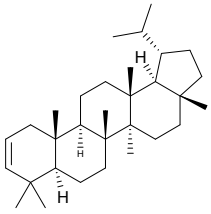


Arjunglucoside I (**81**) R_1 = OH, R_2 = H

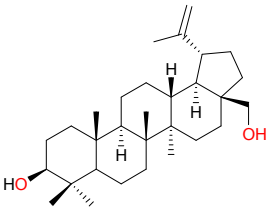
Sericoside (**82**) R_1 = H, R_2 = OH



3β-(5-hydroxyferuloyl)Lup-20(30)-ene (**83**) R = OH

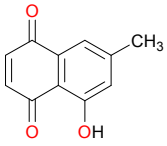


Lupene (**84**)



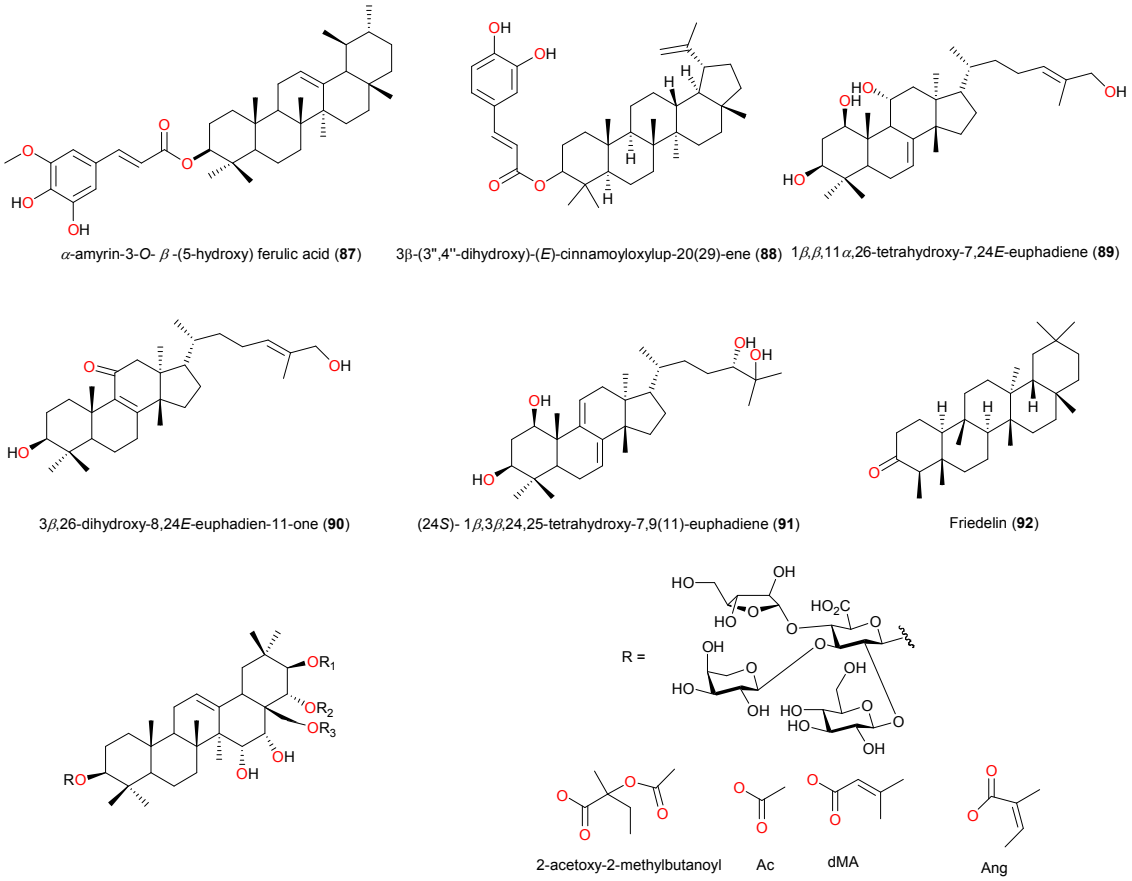
Betulin (**86**)

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



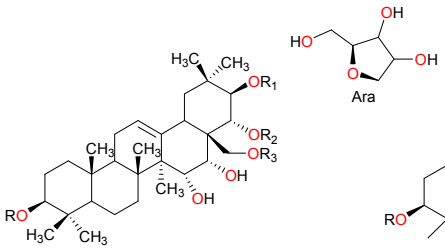
Methyljuglone (**85**)

Fig. **8** Chemical structure of methyljuglone.



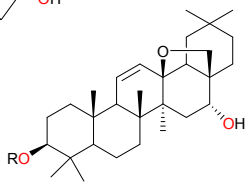
	R_1	R_2	R_3
3-*O*-[*β*-*D*-glucopyranosyl-(1 → 2)]-[α-*L*-arabinopyranosyl-(1 → 3)]-[α-*L*-arabinofuranosyl-(1 → 4)]-*β*-*D*-glucuronopyra-nosyl-21-*O*-(2-acetoxy-2-methylbutanoyl)-*R*1-barrigenol (**93**)	2-acetoxy-2-methylbutanoyl	H	H
3-*O*-[*β*-*D*-glucopyranosyl-(1 →2)]-[*α*-*L*-arabinopyranosyl-(1 → 3)]-[*α*-*L*-arabinofuranosyl-(1 → 4)]-*β*-*D*-glucuronopyranosyl-21-*O*-(2-acetoxy-2-methylbutanoyl)-28-*O*-acetyl-R1-barrigenol (**94**)	2-acetoxy-2-methylbutanoyl	H	Ac
3-*O*-[*β*-D-glucopyranosyl-(1 →2)]-[α-L-arabinopyranosyl-(1 → 3)]-[*α*-*L*-arabinofuranosyl-(1 → 4)]-*β*-*D*-glucuronopyra-nosyl-21-*O*-*β*,*β*-dimethylacryloyl-22-*O*-angeloyl-R1-barrigenol (**95**)	dMA	Ang	H

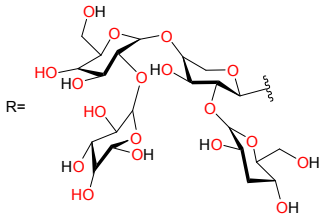
Fig. **9** Chemical structures of triterpenoids from Southern African flora (**87** to **95**).



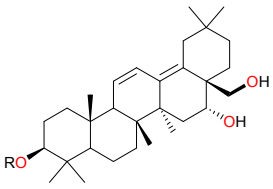
R_1 = Ac, R_2 = Ara, R_3 = H

Senaciapittoside B (**96**)

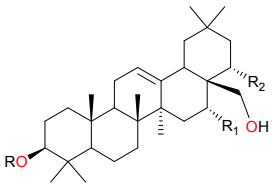




3β-*O*-(β-*D*-xylopyranosyl-(1→2)-β-*D*-glucopyranosyl-(1→ 4)-[β-*D*-glucopyranosyl-(1→2)]-α-*L*-arabinopyranosyl)-13β,28-epoxyolean-11-en-16α-ol (**97**)



3β-*O*-(β-*D*-xylopyranosyl-(1→2)-β-*D*-glucopyranosyl-(1→4)-[β-*D*-glucopyranosyl-(1→2)]-α-*L*-arabinopyranosyl)-oleana-11,13(18)-diene-16α,28-diol (**98**)



	R_1	R_2
3β-*O*-(β-*D*-xylopyranosyl-(1→2)-β-*D*-glucopyranosyl-(1→4)-[β-*D*-glucopyranosyl-(1→2)]-α-*L*-arabinopyranosyl)-camelliagenin A (**99**)	OH	OH
16α,22α-diacetoxy-3β-*O*-(β-*D*-xylopyranosyl-(1→2)-β-*D*-glucopyranosyl-(1→4)-[β-*D*-gluco-pyranosyl-(1→2)]-α-*L*-arabinopyranosyl)-olean-12-*en*-28-ol (**100**)	OAc	OAc
Apoanagallosaponin IV (**101**)	OAc	OH

Fig. **10** Chemical structures of a triterpenoids from Southern African flora (**96** to **101**).

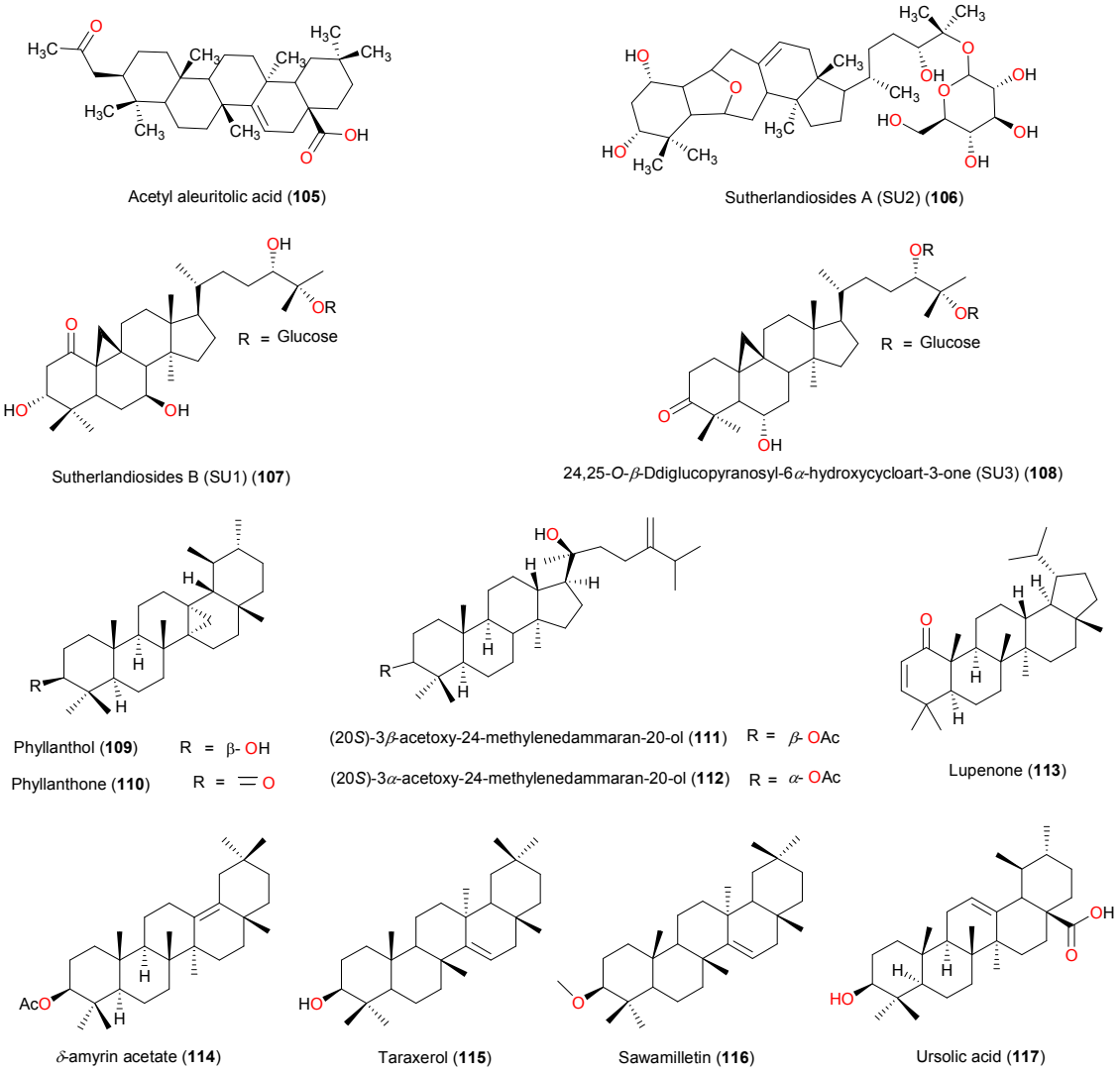


Fig. **11** Chemical structures of a sesquiterpene and triterpenoids from Southern African flora (**105** to **117**).

Table 6: Summary of the bioactivity of derived pentacyclic triterpenoids versus ethnobotanical uses of plant species derived from Southern Africa flora

Compound subclass	Isolated metabolites	Plant species (Country)	Family	Ethnobotanical use	Measured activity	Author,reference
Pentacyclic triterpenoids	1*α*,3, *β*-Hydroxyimberbic acid-23-O-*α*-*L*-4-acetylrhamnopyranoside (**75**), 1*α*,3, *β*-Hydroximberbic acid-23-*O*-*α*-*L*-3,4-diacetylrhamnopyranoside (**76**), 1*α* ,3, *β* -Hydroxyimberbic acid-23- *α*-[*L*-3, 4-diacetyl- rhamnopyranosyl]-29-*O*-*α*-rhamnopyranoside (**77**), and 1,3, -Hydroxyimberbic acid (**78**)	*Combretum imberbe* (Zimbabwe)	Combretaceae	Used in African traditional medicine for diverse uses. [23,27,148-150]	antimicrobial activity	Katererea *et al.*[151]
	75 and 1*α*,3, *β* -Hydroxyimberbic acid-23-*O*- *α* -[*L*-4- acetyl-rhamnopyranosyl]-29-*O*- *α* -rhamnopyranoside (**79**)	*Terminalia stuhlmannii* (Zimbabwe)		Used in African traditional medicine for diverse uses.[154-158]	Antimicrobial activity	Katererea *et al.*[151]
	Terminaliaside A (**80**), arjunglucoside I (**81**) and sericoside (**82**)	*Terminalia tropophylla* (Madagascar)		Used in African traditional medicine for diverse uses. [154-158]	Antiproliferative activity	Cao *et al.*[153]
	3*β*-(5-hydroxyferuloyl)Lup-20(30)-ene (**83**), lupene (**84**), **69** and betulin (**86**)	*Euclea divinorum* (Zimbabwe)	Ebenaceae	Bark of the roots is used in the treatment of diarrhoea, convulsions, **cancer**, skin diseases and gonorrhoea.[26,85]	**Cytotoxicity**	Mebe *et al.*[163]
	69 , **86** and *α*-amyrin-3-*O*- *β* -(5-hydroxy) ferulic acid (**87**)	*Euclea undulata* (South Africa)		Treatment of **diabetes**.[165-166]	**hypoglycaemic** activity	Deutschländer *et al.*[167]
	3*β*-(3'',4''-dihydroxy)- (*E*)-cinnamoyloxylup-20(29)-ene (**88**)	*Eragrostis viscosa* (Angola)	Poaceae	Used in folk medicine as a poison against snakes.[107-108]	mutagenic activity, cytotoxic activity, genotoxicity activity	Sebastião *et al.*[109]
	1*β*,3*β*,11α,26-tetrahydroxy-7,24*E*-euphadiene (**89**), 3*β*,26-dihydroxy-8,24*E*-euphadien-11-one (**90**) and (24*S*)- 1*β*,3*β*,24,25-tetrahydroxy-7,9(11)-euphadiene (**91**)	*Cassipourea lanceolata* (Madagascar)	Rhizophoraceae	Not specified	Antiproliferative activity	Hou *et al.*[169]
	Friedelin (**92**)	*Garcinia goudotiana* (Madagascar)	Clusiaceae	Used for **antiparasitic**, antitussive and **antimicrobial** properties.[171]	**Antimicrobial** and cytotoxic activity	Sania *et al.*[171]
	3-*O*-[*β*-*D*-glucopyranosyl-(1 → 2)]-[*α*-*L*-arabinopyranosyl-(1 → 3)]-[*α*-*L*-arabinofuranosyl-(1 → 4)]-*β*-*D*-glucuronopyra-nosyl-21-*O*-(2-acetoxy-2-methylbutanoyl)-R1-barrigenol (**93**), 3-*O*-[*β*-*D*-glucopyranosyl-(1 →2)]-[*α*-*L*-arabinopyranosyl-(1 → 3)]-[*α*-*L*-arabinofuranosyl-(1 → 4)]-*β*-*D*-glucuronopyranosyl-21-*O*-(2-acetoxy-2-methylbutanoyl)-28-*O*-acetyl-*R*1-barrigenol (**94**), 3-*O*-[*β*-*D*-glucopyranosyl-(1 → 2)]-[*α*-*L*-arabinopyranosyl-(1 → 3)]-[*α*-*L*-arabinofuranosyl-(1 → 4)]-*β*-*D*-glucuronopyra-nosyl-21-*O*-*β*,*β*-dimethylacryloyl-22-*O*-angeloyl-*R*1-barrigenol (**95**) and senaciapittoside B (**96**)	*Pittosporum verticillatum* (Madagascar)	Pittosporaceae	Some species are used in traditional medicine as anti-inflammatory, antimicrobial and antispasmodic agents.[173]	cytotoxicity	Mahenina *et al.*[175]