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Chemistry of South African Lamiaceae: Structures and Biological Activity of Terpenoids

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Abstract

South Africa flora is one of the most important mega floras with high endemic species percentage. Lamiaceae is an important family in South Africa with ± 308 species in 41 genera and contains many important plants (~23%) traditionally used for treatment of different human diseases. The chemical profile of Lamiaceae is very rich in terpenoids in general and more specifically diterpenes. Genera like *Leonotis* and *Plectranthus* are well studied, while on the other hand, genus like *Stachys* (~41 species, ~50% endemic) didn't receive any attention. Different classes of diterpenes were identified and some of them demonstrating important biological activities.

Keywords: South African flora, Lamiaceae, *Leonotis*, *Plectranthus*, chemical constituents, terpenoids

This work is dedicated to Prof. Benjamin Rodriguez (Instituto de Quimica Organica General, CSIC, Spain) for his contributions in the field of natural products and specially in the chemistry of Lamiaceae family.

1. Introduction

The Green economy concept has been driven as an urgent need for addressing global challenges in vital fields like energy, environment, and health. Green economy is expected to play a very important role in changing the way that society manages the interaction of the environmental and economic domains. Consequently, a new paradigm has been established and shifted toward green economy or green growth. Natural products represent one of the most important elements required to build safe and effective economy especially in health sector. South Africa (SA) is recognized as one of the most biodiverse

country in the world with 20,456 indigenous vascular plant taxa recorded where 13,265 (65%) are endemic [1, 2].

The Lamiaceae (formerly Labiateae, mint family) is a cosmopolitan family with ~7136 species in 236 genera. Most species are shrubby or herbaceous and trees are extremely rare [3]. The Lamiaceae family has great economic value, as it contains several horticultural species, most of which are used as culinary herbs like salvia, rosemary, oicum, mint, *Leonotis*, etc. Lamiaceae species are known to contain pharmacologically active terpenoids with a wide spectrum of bioactivity and expected to play more important roles in the process of drug discovery as well as cosmetic, food, and pesticides industries [4–6]. In the Sub-Saharan region, ~60 genera with ±980 species were reported [7]. SA considers as a diversity spot of Lamiaceae with ±308 species in 41 genera [8]. The species occur predominantly in the summer and/or winter rainfall areas. The habitats are different and vary to a great extent [9].

However, the South African flora is one of the most important mega floras for its unique diversity and endemism, it receives low attention in terms of bioprospecting, and the number of research paper every year dealing with chemical/biological profiling is still beyond the required level. This review serves as a background for the chemistry of all species belonging to the family Lamiaceae growing in SA and it covers publications till 2017. The articles information's abstracted from Sci-finder database [10] and includes all species growing in SA as well as other places. This chapter doesn't cover the essential oils and *Plectranthus barbatus*, which recently reviewed by others [11, 12].

2. Terpenoids of different genera of South African Lamiaceae

Different classes of secondary metabolites have been identified from Lamiaceae, the majority of the isolated compounds are terpenoids (~71%), and additionally other classes of compounds like flavonoids, α -pyrone derivatives, phenolic acids, and alkaloids were reported. Mono-, sesqui-, and tri-terpenoids are relatively small in number (~15%) when compared to diterpenoids and it was reported that more than 100 of different diterpene skeletons were identified which indicate the high evolutionary index of Lamiaceae [13]. According to the literature, the genera *Leonotis* (known as wild dagga) and *Plectranthus* have received the highest attention where 70 (*Leonotis*) and 94 (*Plectranthus*) compounds were identified so far, the majority of the isolated compounds are labdane diterpenes. In this chapter, the different genera have been listed alphabetically and the trivial names have been retained in the cases where they were given by authors and/or chemical abstracts.

2.1. *Aeollanthus* genus

Aeollanthus genus represented by 43 species globally and 7 in SA. From *A. buchnerianus*, an abietan diterpene, [(rel)-14 α -acetoxyabiet-7-en-18-oic acid](1)[14], 3 β -acetoxy-7,15-isopimaradiene

(2), 3 β -acetoxy-7,15-isopimaradien-19-ol (3) and 19-acetoxy-7,15-isopimaradien-3 β -ol (4), 7,15-isopimaradien-19-ol (5, akhdarenol) and 7,15-isopimaradien-3 β ,19-diol (6, virescenol), a mixture of 19-isobutyryloxy- and 19-butyryloxy-8 β -hydroxy-15-isopimarene (7), and a 3:1 mixture of 5-stigmasten-3 β -ol and β -sitosterol were isolated from the aerial parts of *A. rydingianus*. 5 and 6 showed activity against *S. aureus* and *Enterococcus hirae* [15].

2.2. *Ballota* genus

Ballota is represented by one species in SA viz *B. africana*. Hispanolone (8) was isolated from the aerial parts [16].

2.3. *Cedronella* genus

Cedronella genus is represented by only one species in SA viz *C. canariensis*. The phytochemical studies of the aerial parts resulted in isolation of a dimer of *d*-pinocarvone (9), cedronellone (10), and ursolic acid (11) [17].

2.4. *Clerodendrum* genus

Seven species were recorded in SA and clerodendrumic acid (12) was isolated from *C. glabrum* var. *glabrum* and showed weak antifungal, antibacterial, and cytotoxic activities [18].

2.5. *Hoslundia* genus

Hoslundia genus is represented by one species in SA viz *H. opposita*. The phytochemical studies of the aerial parts yielded an interesting and rare pyrano and furanoflavonoid derivatives in addition to euscaphic and (13) ursolic acid (11) [19, 20]; four abietane-type esters, 3-*O*-cinnamoylhosloppone (14), 3-*O*-benzoylhosloppone (15), 3-*O*-benzoylhosloquinone (16), and 3-*O*-benzoylhinokiol (17); 13 was found to exhibit MIC of 50 μ g/mL against *M. tuberculosis*, while 14 inhibits the growth of the MDR strain K₁ of *Plasmodium falciparum* in vitro with an IC₅₀-value of 0.4 μ g/mL [21].

2.6. *Hyptis* genus

Three species were recorded in SA. The triterpenes 3 α ,19 α -dihydroxyurs-12-en-28-oic acid (18) and 3 β -acetoxyoleanan-13 β ,28-olide (19), Me betulinate (20), oleanolic acid/acetate (21/22), and ursolic (11) and maslinic acids (23) were isolated from *H. mutabilis* [22].

From *H. spicigera*, seven labdane diterpenes; 19-acetoxy-2 α ,7 α ,15-trihydroxy-labda-8(17),(13Z)-diene (24); 15,19-diacetoxy-2 α ,7 α -dihydroxy-labda-8(17),(13Z)-diene (25); 7 α ,15,19-triacetoxy-2 α -hydroxy-labda-8(17),(13Z)-diene (26); 19-acetoxy-2 α ,7 α -dihydroxy-labda-8(17),(13Z)-dien-15-al (27); 19-acetoxy-7 α ,15-dihydroxy-labda-8(17),(13Z)-dien-2-one (28); 2 α ,7 α ,15,19-tetrahydroxy-ent-labda-8(17), (13Z)-diene (29); and 19-acetoxy-2*R*,7*R*-dihydroxy-labda-14,15-dinorlabd-8(17)-en-13-one (30) were isolated from the aerial parts [23].

2.7. *Leonotis* genus

Seven species were recorded in SA and two of them were extensively studied. Traditionally, this genus is used to substitute hemp and called as wild dagga; however, there is no much scientific biological evidences supporting such claim. The chemistry was started in early 60s of the last century by South African researchers. Many labdane diterpenes have been

isolated. The chemistry of the genus was covered previously by a review published by Piozzi et al.[24].

2.7.1. *Leonotis leonurus*

The chemistry of *Leonotis* was commenced in 1962 and some compounds were identified; marrubiin (**31**) compounds, X (**32**) and Y (**33**), the stereoisomers of premarrubiin (**34**) and (**35**) (the C-13 epimeric forms of premarrubiin). Leonurun (**36**) has been isolated and the relative stereochemistry was determined using single-crystal X-ray diffraction analysis [24, 25]. After two years, labdane (13S)-9 α ,13 α -epoxylabda-6 β (19),15(14)-dioldilactone (**37**) was isolated, this compound caused significant changes in blood pressure of anesthetized normotensive rats, and also was found to exhibit a negative chronotropic effect [26].

The organic extract of *L. leonurus* showed 99% growth inhibition against *M. tuberculosis* at 1.0 mg/mL, subsequent phytochemical studies resulted in the identification of three labdane-type diterpenoids: 9,13:15,16-diepox-6,16-labdanediol (**38**), 6-acetoxy-9,13-epoxy-15-methoxy-labdan-16,15-olide (**39**), and 9,13-epoxy-6-hydroxylabdan-16,15-olide (**40**). None of the isolated compounds were active against *M. tuberculosis* [27].

Recently, Fang et al. [28] identified leonurenones A–C (**41–43**), in addition to 9,13:15,16-diepox-6,16-labdanediol (**38**) and nepetifolin (**44**). The leonurenones contain an uncommon α,β -unsaturated enone moiety in ring B. Compound **38** was isolated as epimeric form, (at C-16, ratio 3:1). Compound **41** was isolated from aqueous extract of the leaves and the authors proposed the possible formation of **43** as an artefact *via* oxidation and lactonization of the more polar intermediate (**41**) during the isolation process. The total aqueous extract, at concentration of 1.0 g/mL, showed an 81% inhibition in a binding assay at the GABAA site. Compounds **41** and **43** did not show activity (<50% inhibition) in this assay [28].

In the following year, Wu and co-workers (2013) were successful to isolate and identify eleven labdanoides, *viz* leoleorins D–J (**41–43**, **45–48**) and 16-*epi*-leoleorin F (**49**), leoleorin A [corresponding to compound Y (**33**)], leoleorin B (**50**) (anhydro derivative of compound Y), and leoleorin C [9,13-epoxy-6-hydroxylabdan-15,16-olide (**40**)]. The absolute configurations of leoleorin A (**33**) and D (**41**) were established by X-ray crystallographic analyses. It is important to indicate that new compounds “leoleorins G–I”, which were isolated in this study, were reported in the previous work under the names of leonurenones A–C (**41–43**) (¹³C data showed exchange positions C₁₂ and C₁₄ for leonurenones C/leoleorin H between the two references) [29].

From *L. leonurus*' flowers, an acyclic diterpene ester, 1,2,3-trihydroxy-3,7,11,15-tetramethyl-hexadecan-1-yl-palmitate (**51**), along with geniposidic acid (**52**) were isolated, the compounds exhibited neither cytotoxicity on mammalian kidney fibroblasts (Vero cells) nor antimicrobial activities [30].

2.7.2. *Leonotis nepetaefolia*

The chemistry of *L. nepetaefolia* started almost simultaneously with *L. leonurus*. Leonotin (**53**), nepetaefuran (**54**), nepetaefuranol (**55**), nepetaefolin (**44**) methoxynepetaefolin (**56**), nepetaefolinol (**57**) and leonotinin (**58**) the dilactone (8 β ,17,9,13-diepoxyabdane-16,15,19,6 β -diolactone, **59**) were characterized [31–36].

From the species collected from India, nepetaefolinol (**57**), dehydrated nepetaefolinol (**60**) and isomeric tetrol (**61**) (15,16-epoxy-labda-13(16),14-diene-6 β ,9,17,19-tetrol: the reduction product of leonotinin) were identified [37]. Leonitinic acid (**62**) with free C-17 carboxyl group was also isolated [38].

From a commercially material, originally collected from Peru, five inseparable epimeric mixtures of bis-spirolabdane diterpenoids, resulted from biosynthetic epimerization of three different structures around C-13 and C-15, have been isolated and identified as leonepetaefolin A (**63**) and its epimeric isomer 15-epi-leonepetaefolin A (**64**) (ratio 1:1), leonepetaefolin B (**65**)/15-epi-leonepetaefolin B (**66**) (2:3), leonepetaefolin C (**67**)/15-epi-leonepetaefolin C (**68**) (1,1), leonepetaefolin D (**69**)/15-epi-leonepetaefolin D (**70**) (7,10), leonepetaefolin E (**71**)/15-epi-leonepetaefolin E (**72**) (2,3) [39]. Additionally, methoxynepetaefolin (**56**), nepetaefolin (**44**), nepetaefuran (**54**), dubiin (**73**), 19 chlroro derivative of nepetaefolin (**74**), leonotinin (**58**), leonotin (**53**), and LS-1 (**75**) were isolated. The absolute configuration of the epimeric mixture **63** and **64** was determined by X-ray crystallographic analysis [39].

The isolated compounds were evaluated for their binding activities to a panel of CNS G-protein-coupled receptors including adrenergic, dopaminergic, histaminic, muscarinic, opioid, and serotonergic receptors and neurotransmitter transporters and showed no interesting activity.[39]. From the material collected from Japan, five iridoid glycosides: 10-*O*-(*trans*-3,4-dimethoxycinnamoyl) geniposidic acid (76), 10-*O*-(*p*-hydroxybenzoyl) geniposidic acid (77), geniposidic acid (52), mussaenoside (78), and ixoside (79) were isolated [40].

2.7.3. *Leonotis ocymifolia*

L. ocymifolia was studied under different synonyms viz; *L. dubia* (*L. ocymifolia*, var. *ocymifolia*), *L. leonitis*; *L. leonitis* var. *hirtifolia* (*L. ocymifolia*, var. *ocymifolia*) and *L. dysophylla* Benth. (*L. ocymifolia* var. *raineriana*) and *L. ocymifolia* var. *raineriana* (Burm f) Iwarsson var. *raineriana* (Visiani) Iwarsson. The chemical studies resulted in the isolation of dubiin (73), 9 α ,13(*S*)-epoxy-8 β -hydroxylabdane-6 β ,19;16,15-diolide (80), and leonitin (81). 20-acetoxy-9 α ,13-dihydroxy-15(16)-epoxylabd-14-en-6 β (19)-lactone (82) and 6 β -acetoxy-9 α ,13 α -epoxylabda-20(19),16(15)-diol-dilactone (83) are from the leaves, in addition to compound X (32)[24, 41] Finally, nepetaefolin (44), leonotin (58), and leonotin (53) were identified from the material collected from Pretoria (South Africa) [42].

2.8. *Neophyptis* genus

Neophyptis genus is represented by *N. paniculata* in SA. Isonocembrene-A (84), β -caryophyllene oxide (85), α -himachalene (86), the isolates showed weak to moderate antibacterial activity against five strains of *S. aureus* [43].

2.9. *Ocimum* genus

Ocimum genus comprises 65 aromatic species, distributed in tropical and subtropical regions worldwide. Species belonging to this genus are popularly used in Africa and Asia for treating diabetic symptoms. The genus is represented by 16 species in SA and the phytochemical

study of *O. amercanium* afforded four compounds of the copane series (copan-3-ol (**87**), cop-11(12)-en-3-ol (**88**), cop-3(15)-en-11-ol (**89**), and cop-10(11)-en-3,12-diol(**90**)) [44].

2.10. *Orthosiphon* genus

Orthosiphon genus comprises 40 species recorded from the old world: in tropical and subtropical regions including Southern Africa and Madagascar. Three species were found in SA. Three labdanoids (+)-*trans*-ozic acid (**91**), labda-8(17),12*E*,14-trien-2 α ,18-diol (**92**), and 2 α -hydroxylabda-8(17),12*E*,14-trien-18-oic acid (**93**) have been isolated from an ethanol extract. Compound **93** exhibited activity against *M. tuberculosis*, while **92** showed cytotoxic activity against MCF-7 and decreased the production of all the pro-inflammatory cytokines. From the same source, pheophytin a, the acidic degradation product of chlorophyll a, was isolated and showed inhibition of HIV-1 protease [45, 46].

2.11. *Paltstoma* genus

Only one species was recorded in SA. From the ethyl acetate extract of *P. rotundifolium*, casipourol (**94**), β -sitosterol, and α -amyrin were identified [47].

2.12. *Plectranthus* genus

About 300 species distributed in tropical and warm regions of the old World, 45 species recorded in SA, from which 19 species were studied for their chemical and/or biological constituents. The genus is characterized by the presence of orange glands that distributed in the aerial parts and contain highly oxygenated (and modified) abietane-type diterpenoids. Others, e.g., kaurane, labdane, phyllocladane as well as the rare skeleton halimane diterpenoids were described.

2.12.1. *Plectranthus ambiguus*

The plant afforded a series of tetracyclic phyllocladane-type (= 13 β -kaurane) diterpenoids: (16*R*)-2 α -seneciyoxy-3 α -acetoxypyllocladan-16,17-diol (**95**), (16*R*)-2 α -seneciyoxy-3 α ,17-diacetoxy-16-hydroxypyllocladane (**96**), (16*R*)-2 α -isovaleroyloxy-3 α -acetoxypyllocladan-16,17-diol (**97**), (16*R*)-2 α -isovaleroyloxy-3 α ,17-diacetoxy-16-hydroxypyllocladane (**98**), (16*R*)-3 α -acetoxypyllocladan-16,17-diol (**99**), (16*R*)-2 α -seneciyoxy-16,17-dihydroxypyllocladan-3-one (**100**), and (16*R*)-2 α ,3 α -diacetoxypyllocladan-16,17-diol (**101**). The authors discriminated between phyllocladane and *ent*-kaurane tetracyclic skeletons after extensive spectroscopic investigation as well as chemical transformations [48, 49].

2.12.2. *Plectranthus amboinicus*

Thymoquinone (**105**) was identified as an active nonpolar ingredient to suppress the expression of lipopolysaccharide-induced tumor necrosis factor- α (TNF- α) [50]. The total extract showed cytotoxic activity against MCF-7, using HPLC-based metabolomics approach, and 7 α -acetoxy-6 β -hydroxyroyleanone (**102**) was identified as the main active constituent. Other minor compounds like coleon E (**103**) and royleanone (**104**) were also identified [51].

2.12.3. *Plectranthus caninus*

Plectranthus caninus afforded coleons M (**106**), N (**107**), P (**108**), Q (**109**), R (**110**), S (**111**), and T (**112**) and barbatusin (**113**) [52, 53].

2.12.4. *Plectranthus ecklonii*

Plectranthus ecklonii is traditionally used in South Africa for treating stomach aches, nausea, vomiting, and meningitis. Ecklonoquinone A (**114**) and B (**115**) and parviflorons D (**116**) and F (**117**) were isolated [54, 55]. Compound **117** showed potent activity against *Listeria monocytogenes* and *M. tuberculosis* and both **116** and **117** were found to be very toxic against vero cell lines. The potency of parvifloron D (**116**) was further confirmed and showed fast and potent apoptotic inducer in leukemia cells [56].

2.12.5. *Plectranthus ernstii*

Two pimaranes rel-15(ζ),16-epoxy-7α-hydroxypimar-8,14-ene (**118**): rel-15(ζ),16-epoxy-7-oxopimar-8,14-ene (**119**) and a labdane 1R,11S-dihydroxy-8R,13R-epoxylabd-14-ene (**120**) were isolated. The three compounds showed activity against *M. tuberculosis* and different strains of *S. aureus* [57].

2.12.6. *Plectranthus fruticosus*

Plectranthus fruticosus cultivated in Portugal afforded 4 labdanes, ent-labda-8(17),12Z,14-trien-2β-ol (**121**), ent-2α-acetoxylabda-8(17),12Z,14-trien-3β-ol (**122**), ent-3β-acetoxylabda-8(17),

2.12.7. *Plectranthus grandidentatus*

Fatty acid esters of 7 α -acyloxy-6 β -hydroxyroyleanone (**152**) showed moderate antibacterial activity [62]; coleon U exhibited potent cytotoxicity against a panel of human cancer cell lines [63, 65] also showed potent inhibition of mouse splenocyte proliferation induced by ConA or LPS mitogens [64]. Coleons U **141** is considered as a promising compound and deserves further evaluation as an anti-cancer drug [68]. Coleon U (**141**), 7 α -acetoxy-6 β -hydroxyroyleanone (**102**), and horminone (**150**) showed activity against methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant *Enterococcus faecalis* (VRE). Recently, the biological activity of **102** was reported and showed selective cytotoxicity against MCF-7. Other derivatives of the same compound showed potent cytotoxic [69, 70] and antimicrobial [66] activities.

Horminone (**150**), 16-acetoxy-7 α ,12-dihydroxy-8,12-abietadiene-11,14-dione (**153**) and 7 α -12-dihydroxy-17(15 $\rightarrow$ 16)-abieta-8,12,16-triene-11,14-dione (**157**); 3 β -acetoxy-6 β ,7 α -12-trihydroxy-17(15 $\rightarrow$ 16)18(4 $\rightarrow$ 3)bisabeo-abieta-4(19)8,12,16-triene-11,14-dione (**158**) were isolated [13, 66, 71], on the other hand, the structure of an aristolane sesquiterpene aldehyde (**159**) have been revised [72], all compounds showed moderate antimicrobial activity [13, 66, 71, 72], while **158** showed antiviral activity [73].

Plectranthus madagascariensis is used as a traditional medicine in Southern Africa. Three constituents were isolated and identified as 6 β ,7 β -dihydroxyroyleanone (**154**), 7 β -acetoxy-6 β -hydroxyroyleanone (**155**), and coleon U (**141**). The compounds exhibited inhibitory activity on α -glucosidase, *S. aureus* and *Enterococcus faecalis* [74].

2.12.10. *Plectranthus ornatus*

Traditionally, the plants were used for treatment of stomach and liver diseases and as a substitute of *P. barbatus*. The phytochemical studies resulted in the isolation of 11 neoclerodanes (plectronatins A (**160**) [75], 11*R**-acetoxykolavenic acid (**161**), 11*R**-acetoxy-2-oxokolavenic acid (**162**), 11*R**-acetoxy-3 β -hydroxyneocleroda-4(18),13*E*-dien-15-oic acid (**163**) [76], ornatins A–E (**164**–**168**), 3 β -hydroxyneocleroda-4(18),13*E*-dien-15-oic acid (**169**) [77]; 7 labdanes (plectronatins B (**170**), C (**171**), [75], 6-*O*-acetylforskolin (**172**); 1,6-di-*O*-acetylforskolin (**173**), 1,6-di-*O*-acetyl-9-deoxyforskolin (**174**) [76, 78], rhinocerotinoic acid (**175**) [66], 8 β -hydroxylabd-13-en-15-oic acid (**176**) [77]); 2 abietanes (14-*O*-acetyl-coleon U (**177**), coleon R (**110**)) and a halimane derivative, (11*R**-acetoxyhalima-5,13*E*-dien-15-oic acid (**178**) [79]) in addition to β -sitosterol and stigmasterol, 3 β -acetyl- α -amyrin, and friedelin. Inversion at C-13 of 1,6-di-*O*-acetyl-9-deoxyforskolin (**174**) was carried out based on correlations between ^{13}C NMR experimental data and HF/6-31G*

calculation [80]. **160**, **161** showed moderate antimicrobial. **178** exhibited growth inhibitory activity against five *Staphylococcus* and five *Enterococcus* strains [75]. Ornatin C, D, E and three related diterpenes displayed marginal bactericidal or bacteriostatic effects against the Gram-positive strains [77].

2.12.11. *Plectranthus porcatus*

(13*S*,15*S*)-6 β ,7 α ,12 α ,19-tetrahydroxy-13 β ,16-cyclo-8-abietene-11,14-dione (**179**) has been isolated and showed weak antibacterial activity against *S. aureus* [81].

2.12.12. *Plectranthus saccatus*

Ent-7 α -acetoxy-15-beyerene-18-oic acid (**180**), *ent*-3 β -(3-methyl-2-butenoyl) oxy-15-beyerene-19-oic acid (**181**), and *ent*-3 β -(3-methylbutanoyl) oxy-15-beyerene-19-oic acid (**182**). Both **181** and **182** showed insect antifeedant activity against *Spodopteralittoralis*, while **180** showed no antibacterial activity [81, 82].

2.12.13. *Plectranthus strigosus*

9 abietanes (parviflorones A (**183**), B (**184**), C (**185**), D (**114**), E (**186**), F (**115**), G (**187**), and H (**188**) [83], and hinokiol (**189**) [84]), 3 kauranes (*ent*-16-kauren-19-ol (**190**), *ent*-16-kauren-19-oic acid (**191**), xylopic acid (**192**), xylopinic acid (**193**)), and 2 sesquiterpens (4 β ,6 β -dihydroxy-1 α ,5 β (H)-guai-9-ene (**194**) 4 β ,6 β -dihydroxy-1 α ,5 β (H)-guai-10(14)-ene (**195**)), were isolated [84]. A bioactivity study revealed herpetic inhibitory properties for (**190**) and (**191**) [84].

2.13. *Salvia* genus

The genus *Salvia* is known as sage and is the largest genus in Lamiaceae, comprising over 900 species distributed throughout the world. *Salvia* is represented by 30 species in SA, distributed mainly in great cape region. The chemistry of *Salvia* is rich in diterpenoids and different skeletons have been reported, also, many members of this genus is well known for its curative and medicinal properties like *S. officinalis* and *S. miltiorrhiza*.

2.13.1. *Salvia africana-lutea*

Carnosol (**196**), rosmadial (**197**), and carnosic acid (**198**-characterized as its methyl ester) were isolated. Compound **198** exhibited potent activity against *M. tuberculosis* and cytotoxic activity against a breast (MCF-7) human cancer cell line [45].

2.13.2. *Salvia chamelaeagnea*

Four compounds were isolated: carnosol (**196**), 7-O-methylepirosmanol (**200**), oleanolic and ursolic acids as the active principles against *S. aureus* [85].

2.13.3. *Salvia coccinea*

Momordic acid, methyl ester (**201**) [86], salviacoccin (**202**) [87], dehydrouvaol (**203**), and uvaol (**204**) [88] were isolated.

2.13.4. *Salvia disermas*

The aerial parts afforded ocotillol II (**205**) [89].

2.13.5. *Salvia radula*

Betulafolientriol oxide (**206**) was isolated [90].

2.13.6. *Salvia reflexa*

Four neoclerodanes were isolated and identified as salviarin (**207**), 6 β -hydroxysalviarin(**208**), 15,16-epoxy-8 α -hydroxyneocleroda-2,13(16),14-triene-17,12R:18,19-diolide (**209**), and 5,6-seco-clerodane, 7,8-didehydrorhyacophiline (**210**) [91].

2.13.7. *Salvia repens*

The whole plant extract yielded 12-methoxycarnosic acid (**199**) with antiprotozoal activity against *Leishmania donovani* amastigotes and cytotoxicity against the L6-cells [92].

2.13.8. *Salvia verbenaca*

The plant yielded β -sitosterol, ursolic acid, dehydroursolic acid, sitosteryl-3- β -D-glucoside [93], taxodione (**211**), horminone (**150**) and 7 α -acetoxy-6 β -hydroxyroyleanone (**102**) [94], verbenacine (**212**) and salvinine (**213**) [95].

2.14. *Solenostemon* genus

Solenostemon genus is from *S. rotundifolius*; oleanolic acid was isolated as a major component [96].

2.15. *Tetradenia* genus

Seven species were recorded in SA, one of them *T. riparia* is widely distributed in Africa and showed interesting chemical profile. Several compounds have been isolated from the leaves of this plant, including 8(14),15-sandaracopimaradiene-7 α ,18-diol (**214**) [97], 8(14),15-sandaracopimaradiene-2 α ,18-diol (**215**) [98], 9 β ,13 β -epoxy-7-abietene (**216**), 6,7-dehydro-royleanone (**136**) [99], and ibozol (**217**) [100].

Compound (**214**) exhibited antimicrobial activity (**213**). Compound (**215**) showed papaverine-like antispasmodic activity on guinea pig ileum contracted by methacholine, histamine, or BaCl₂ and on the noradrenaline-induced contractions of rabbit aorta [101]. It also showed activities against *Trichomonasvulgaris* with MIC of 20–40 μ g/mL [102], wheat rootlets inhibition activity (MIC7.81 μ g/mL) [103], and *M. tuberculosis*[104].

2.16. *Teucrium* genus

Three species were recorded in SA. From *T. africanum* tafricanins A (218) and B(219), teutridin (220) and 4 α ,18-epoxytafricanin A (221) were isolated [105].

2.17. *Vitex* genus

Vitex genus is represented by 12 species in SA. The fraction responsible for antimicrobial activity of *V. rehmannii* was purified to give a labdane diterpene as an inseparable epimeric mixture of 12*S*,16*S*/*R*-dihydroxy-*ent*-labda-7,13-dien-15,16-olide (222). The extract and the labdane diterpene exhibited good antimalarial activity, with the labdane diterpene being the most active IC₅₀: 2.39 $\pm$ 0.64 μ g/mL [106].

3. Conclusion

South African flora characterized by high endemism and unique floral kingdom is only located in the great cape region. Lamiaceae is represented by ~308 species widely distributed all over the country. In general, the bioprospecting of SA flora including Lamiaceae is not reached; yet the required level and more attention are required to explore the potential of their chemical constituents. The present work shades the light on the isolated terpenoids of all listed species in updated SA flora checklist. It is interesting to indicate that *Plectranthus* genus contains mostly abietane diterpenes and shows potent activity as demonstrated by coleon U and parviflorons F and D. On the other hand, leoleorin C from *L. Leonurus* showed moderate binding affinity (K_i = 2.9 μ M) to the Sigma 1 receptor. These compounds and others may be considered as a model for drug discovery for human benefits.

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Conflict of interest

The author declares no conflict of interest to disclose.

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References

- [1] Domitilla R. The Red List of South African plants—A global first. *African Journal of Science*. 2011;**107**:3-4. DOI: 10.4102/sajs.v107i3/4.653
- [2] Domitilla CR, von Staden L, John SD. Lessons from the conservation assessment of the South African mega flora. *Annals of the Missouri Botanical Garden*. 2013;**99**:221-230. DOI: 10.3417/2011111
- [3] Heywood VH. *Flowering Plants of the World*. Oxford: Oxford University Press; 1978. pp. 239-240
- [4] Lee CJ, Chen LJ, Chang TL, Ke WM, Lo YF, Wang CC. The correlation between skin-care effects and phytochemical contents in *Lamiaceae* plants. *Food Chemistry*. 2011;**124**:833-841
- [5] Khaled-Khodja N, Boulekbache-Makhlouf L, Madan K. Phytochemical screening of antioxidant and antibacterial activities of methanolic extracts of some *Lamiaceae*. *Industrial Crops and Products*. 2014;**61**:41-48
- [6] Ramos M, Jiménez A, Peltzer M, Garrigós MC. Characterization and antimicrobial activity studies of polypropylene films with carvacrol and thymol for active packaging. *Journal of Food Engineering*. 2012;**109**:513-519
- [7] Klopper RR, Chatelain C, Bänninger V, Habashi C, Steyn, HM, De Wet BC, Arnold TH, Gautier L, Smith GF, Spichiger R. Checklist of the flowering plants of Sub-Saharan Africa. An index of accepted names and synonyms. Southern African Botanical Diversity Network Report No. 42. SABONET, Pretoria; 2006
- [8] <https://peerj.com/preprints/2277v1.pdf>
- [9] <http://posa.sanbi.org/searchspp.php> [Accessed: January 2018]
- [10] <https://www.cas.org/products/scifinder> [Accessed: November–December 2017]
- [11] Alasbahi RH, Melzig MF. *Plectranthus barbatus*: A review of phytochemistry, ethnobotanical uses and pharmacology—Part 2. *Planta Medica*. 2010;**76**:753-765. DOI: 10.1055/s-0029-1240898
- [12] Alasbahi RH, Melzig MF. *Plectranthus barbatus*: A review of phytochemistry, ethnobotanical uses and pharmacology—Part 1. *Planta Medica*. 2010;**76**:653-661. DOI: 10.1055/s-0029-1240898
- [13] Batista O, Duarte A, Nascimento J, Simoes MF, de laTorre MC, Rodriguez B. Structure and antimicrobial activity of diterpenes from the roots of *Plectranthus hereroensis*. *Journal of Natural Products*. 1994;**57**:588-561. DOI: 10.1021/np50108a031
- [14] Dellar JE, Cole MD, Waterman PG. Unusual antimicrobial compounds from *Aeollanthus buchnerianus*. *Experientia*. 1996;**52**:175-179
- [15] Rijo P, Simoes M-F, Duarte A, Rodriguez B. Isopimarane diterpenoids from *Aeollanthus rydingianus* and their antimicrobial activity. *Phytochemistry*. 2009;**70**:1161-1165. DOI: 10.1016/j.phytochem.2009.06.008

- [16] Davies-Coleman MT, Rivett DE. Transformation of hispanolone from *Ballota africana* into 15,16-epoxy-9-hydroxylabda-13(16),14-diene. *South African Journal of Chemistry*. 1990;**43**:117-119
- [17] Carreiras MC, Rodriguez B, Lopez-Garcia RE, Rabanal RM. A dimer of d-pinocarvone from *Cedronella canariensis*. *Phytochemistry*. 1987;**26**:3351-3353
- [18] Masevhe NA, Awouafack MD, Ahmed AS, McGaw LJ, Eloff JN. Clerodendrumic acid, a new triterpenoid from *clerodendrum glabrum* (verbenaceae), and antimicrobial activities of fractions and constituents. *Helvetica Chimica Acta*. 2013;**96**:1693-1703. DOI: 10.1002/hlca.201200552
- [19] Mujovo SF, Hussein AA, Meyer JJM, Fourie B, Muthivhi T, Lall N. Bioactive compounds from *Lippia javanica* and *Hoslundia opposita*. *Natural Product Research*. 2008;**22**:1047-1054. DOI: 10.1080/14786410802250037
- [20] Annan K, Jackson N, Dickson RA, Sam GH, Komlaga G. Acaricidal effect of an isolate from *Hoslundia opposita* vahl against *Amblyomma variegatum* (Acari: Ixodidae). *Pharmacognosy Research*. 2011;**3**:185-188
- [21] Achenbach H, Waibel R, Nkunya MHH, Weenen H. Antimalarial compounds from *Hoslundia opposita*. *Phytochemistry*. 1992;**31**:3781-3784
- [22] Perptiseda-Miranda R, Gascon-Figueroa M. Chemistry of *Hyptis mutabilis*: New penta cyclic triterpenoids. *Journal of Natural Products*. 1988;**51**(5):996-998. DOI: 10.1021/np50059a035
- [23] Fragoso-Serrano M, Gonzalez-Chimeo E, Pereda-Miranda R. Novel labdane diterpenes from the insecticidal plant *Hyptis spicigera*. *Journal of Natural Products*. 1999;**62**:45-50. DOI: 10.1021/NP980222Z
- [24] Piozzi F, Bruno M, Rosselli S, Maggio A. Structure and biological activity of the furan-diterpenoids from the genera *Leonotis* and *Leonurus*. *Heterocycles*. 2007;**74**:31-52
- [25] McKenzie JM, Green IR, Mugabo P. Leonurun, a novel labdane diterpenoid from *Leonotis leonurus*. *South African Journal of Chemistry*. 2006;**59**:114-116
- [26] Obikeze KC, McKenzie JM, Green IR, Mugabo P. Characterization and cardiovascular effects of (13S)-9 α ,13 α -epoxylabda-6 β (19),15(14)dioldilactone, a diterpenoid isolated from *Leonotis leonurus*. *South African Journal of Chemistry*. 2008;**61**:119-122
- [27] Naidoo D, Maharaj V, Crouch NR, Ngwane A. New labdane-type diterpenoids from *Leonotis leonurus* support circumscription of *Lamiaceae*. *Biochemical Systematics and Ecology*. 2011;**39**:216-219. DOI: 10.1016/j.bse.2010.12.021
- [28] Fang H, Charlotte L, Wayne WH. Leonurenones A–C: Labdane diterpenes from *Leonotis leonurus*. *Phytochemistry*. 2012;**83**:168-172. DOI: 10.1016/j.phytochem.2012.07.014
- [29] Wu H, Li J, Fronczek FR, Ferreira D, Burandt CL Jr, Setola V, Roth BL, Zjawiony JK. Labdane diterpenoids from *Leonotis leonurus*. *Phytochemistry*. 2013;**91**:229-235. DOI: 10.1016/j.phytochem.2012.02.021

- [30] Agnihotri VK, El Sohly HN, Smillie TJ, Khan IA, Walker LA. Constituents of *Leonotis leonurus* flowering tops. *Phytochemistry Letters*. 2009;**2**:103-105. DOI: 10.1016/j.phytol.2009.02.001
- [31] White JD, Manchand PS, Whalley WB. The structure of leonotin, a novel furanoid diterpene. *Journal of Chemical Society D*. 1969;**0**:1315-1316. DOI: 10.1039/C29690001315
- [32] White JD, Manchand PS, Whalley WB. Structure of nepetaefolin, a prefuranoid diterpene. *Journal of the American Chemical Society*. 1972;**92**:5527-5528. DOI: 10.1021/ja00721a046
- [33] Blount JF, Manchand PS. X-ray structure determination of methoxynepetaefolin and nepetaefolinol, labdane diterpenoids from *Leonotis nepetaefolia* R.Br. *Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry*. 1980;**1**:264-268. DOI: 10.1039/P19800000264
- [34] Manchand PS. Methoxynepetaefolin, a new labdane diterpene from *Leonotis nepetaefolia*. *Tetrahedron Letters*. 1973;**21**:1907-1908. DOI: 10.1016/S0040-4039(01)96273-2
- [35] Purushothaman KK, Vasanth S, Connolly JD. Nepetaefolinol and two related diterpenoids from *Leonotis nepetaefolia*. *Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry*. 1974;**23**:2661-2663. DOI: 10.1039/p19740002661
- [36] Von Dreele RB, Pettit GR, Ode RH, Perdue RE, Jr, White JD, Manchand PS. The crystal and molecular structure of the unusual spiro dihydrofuran diterpene nepetaefolin. *Journal of the American Chemical Society*. 1975;**97**:6236-6240. DOI: 10.1021/ja00854a049
- [37] Govindasamy L, Rajakannan V, Velmurugan D, Banumathi S, Vasanth S. Structural studies on three plant diterpenoids from *Leonotis nepetaefolia*. *Crystal Research and Technology*. 2002;**37**:896-909. DOI: 10.1002/1521-4079(200208)37:8<896:AID-CRAT896>3.0.CO;2-F
- [38] Boalino DM, Tinto WF. A new diterpene of *Leonotis nepetaefolia*. *Heterocycles*. 2004;**63**:383-387
- [39] Li J, Fronczek FR, Ferreira D, Burandt CL, Setola V, Roth BL, Zjawiony JK. Bis-spirolabdane diterpenoids from *Leonotis nepetaefolia*. *Journal of Natural Products*. 2012;**75**:728-734. DOI: 10.1021/np3000156
- [40] Takeda T, Narukawa Y, Hada N. Studies on the constituents of *Leonotis nepetaefolia*. *Chemical and Pharmaceutical Bulletin*. 1999;**47**:284-286. DOI: 10.1248/cpb.47.284
- [41] Habtemariam S, Gray AI, Waterman PG. Diterpenes from the leaves of *Leonotis ocymifolia* var. *Raineriana*. *Journal of Natural Products*. 1994;**57**:1570-1574. DOI: 10.1021/np50113a017
- [42] Hussein AA, Meyer MJJ, Rodriguez B. Complete ¹H and ¹³C NMR assignments of three labdane diterpenoids isolated from *Leonotis ocymifolia* and six other related compounds. *Magnetic Resonance in Chemistry*. 2003;**41**:147-151
- [43] Rahman MM, Gibbons S. Antibacterial constituents of *Neohyptis paniculata*. *Fitoterapia*. 2015;**105**:269-272. DOI: 10.1016/j.fitote.2015.07.012

- [44] Upadhyay RK, Misra LN, Singh G. Sesquiterpene alcohols of the copane series from essential oil of *Ocimum americanum*. *Phytochemistry*. 1991;**30**(2):691-693. DOI: 10.1016/0031-9422(91)83755-A
- [45] Hussein AA, Meyer JJM, Jimeno ML, Rodriguez B. Bioactive diterpenes from *Orthosiphon labiatus* and *Salvia africana-lutea*. *Journal of Natural Products*. 2007;**70**(2):293-295. DOI: 10.1021/np0680376
- [46] Kapewangolo P, Omolo JJ, Bruwer R, Fonteh P, Meyer D. Antioxidant and anti-inflammatory activity of *Ocimum labiatum* extract and isolated labdane diterpenoid. *Journal of Inflammation (London United Kingdom)*. 2015;**12**:1-28
- [47] Rasamiravaka T, Jaziri M, Rasamiravaka T, Ngezahayo J, Pottier L, Oliveira RS, Florence S, Caroline S, Pierre D, Jeremie N, et al. Terpenoids from *Platostoma rotundifolium* (Briq.) A. J. Paton Alter the expression of quorum sensing-related virulence factors and the formation of biofilm in *Pseudomonas aeruginosa* PAO1. *International Journal of Molecular Sciences*. 2017;**18**(6):1270
- [48] Liu G, Ruedi P. Phyllocladanes (13 β -kauranes) from *Plectranthus ambiguus*. *Phytochemistry*. 1996;**41**:1563-1568. DOI: 10.1016/0031-9422(95)00816-0
- [49] Liu G, Muller R, Ruedi P. Chemical transformations of phyllocladane (=13 β -kaurane) diterpenoids. *Helvetica Chimica Acta*. 2003;**86**:420-438. DOI: 10.1002/hlca.200390043
- [50] Chen Y-S, Yu H-M, Shie J-J, Cheng T-JR, Wu C-Y, Fang J-M, Wong C-H. Chemical constituents of *Plectranthus amboinicus* and the synthetic analogs possessing anti-inflammatory activity. *Bioorganic and Medicinal Chemistry*. 2014;**22**:1766-1772. DOI: 10.1016/j.bmc.2014.01.009
- [51] Yulianto W, Andarwulan N, Giriwono PE, Pamungkas J. HPLC-based metabolomics to identify cytotoxic compounds from *Plectranthus amboinicus* (Lour.) Spreng against human breast cancer MCF-7Cells. *Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences*. 2016;**1039**:28-34. DOI: 10.1016/j.jchromb.2016.10.024
- [52] Arihara S, Ruedi P, Eugster CH. New spirocyclopropylcyclohexenedione diterpene type compounds: Coleons M, N, P, Q, and R and barbatusin from *Plectranthus caninus* and coleon O from *Coleus somaliensis*. *Helvetica Chimica Acta*. 1975;**58**:343-356. DOI: 10.1002/hlca.19750580203
- [53] Arihara S, Ruedi P, Eugster CH. Diterpenoid leaf-gland pigments: coleons S and T from *Plectranthus caninus* Roth (Labiatae), a new diosphenol-*trans*-A/B-6,7-diketone pair of the abietane series. *Helvetica Chimica Acta*. 1977;**60**:1443-1447. DOI: 10.1002/hlca.19770600436
- [54] Uchida M, Ruedi P, Eugster CH. Leaf-gland pigments from Labiatae: ecklonoquinones A and B, two novel dibenzo-*p*-dioxin-*O*-quinones from *Plectranthus ecklonii* Benth. *Helvetica Chimica Acta*. 1980;**63**:225-231. DOI: 10.1002/hlca.19800630122
- [55] Nyila MA, Leonard CM, Hussein AA, Lall N. Bioactivities of *Plectranthus ecklonii* constituents. *Natural Product Communications*. 2009;**4**:1177-1180

- [56] Burmistrova O, Perdomo J, Simoes MF, Rijo P, Quintana J, Estevez F. The abietane diterpenoid parvifloron D from *Plectranthus ecklonii* is a potent apoptotic inducer in human leukemia cells. *Phytomedicine*. 2015;**22**:1009-1016. DOI: 10.1016/j.phymed.2015.06.013
- [57] Stavri M, Paton A, Skelton BW, Gibbons S. Antibacterial diterpenes from *Plectranthus ernstii*. *Journal of Natural Products*. 2009;**72**:1191-1194. DOI: 10.1021/np800581s
- [58] Gaspar-Marques C, Simoes MF, Duarte A, Rodriguez B. Labdane and kaurane diterpenoids from *Plectranthus fruticosus*. *Journal of Natural Products*. 2003;**66**(4):491-496. DOI: 10.1021/np020493g
- [59] Gaspar-Marques C, Simoes MF, Rodriguez B. Further labdane and kaurane diterpenoids and other constituents from *Plectranthus fruticosus*. *Journal of Natural Products*. 2004;**67**:614-621. DOI: 10.1021/np030490j
- [60] Purushothaman KK, Sarada A, Saraswathy A. Some rare chemical constituents of a traditional drug of doubtful origin. *Indian Drugs*. 1986;**23**:579-580
- [61] Uchida M, Miyase T, Yoshizaki F, Bieri JH, Ruedi P, Eugster CH. 14-Hydroxytaxodione as major diterpenoid in *Plectranthus grandidentatus* Gurke; isolation of seven new dimeric diterpenoids from *P. grandidentatus*, *P. myrianthus* Briq. and *Coleus carnosus* Hassk.: Structures of grandidones A, 7-epi-A, B, 7-epi-B, C, D and 7-epi-D. *Helvetica Chimica Acta*. 1981;**64**:2227-2250. DOI: 10.1002/hlca.19810640729
- [62] Antonio P, Batista O, Simoes MF, Nascimento J, Duarte A, de la Torre MC, Rodriguez B. Abietane diterpenoids from *Plectranthus grandidentatus*. *Phytochemistry*. 1996;**44**:325-327. DOI: 10.1016/S0031-9422(96)00467-0
- [63] Marque CC, Pedro M, Simoes MFA, Nascimento MSJ, Pinto MMM, Rodriguez B. Effect of abietane diterpenes from *Plectranthus grandidentatus* on the growth of human cancer cell lines. *Planta Medica*. 2002;**68**:839-840. DOI: 10.1055/s-2002-34407
- [64] Cerqueira F, Cordeiro-Da-Silva A, Gaspar-Marques C, Simoes F, Pinto MMM, Nascimento MSJ. Effect of abietane diterpenes from *Plectranthus grandidentatus* on T- and B-lymphocyte proliferation. *Bioorganic and Medicinal Chemistry*. 2004;**12**:217-223. DOI: 10.1016/j.bmc.2003.10.006
- [65] Gaspar-Marques C, Simoes MF, Rodriguez B. A Trihomo abietane diterpenoid from *Plectranthus grandidentatus* and an unusual addition of acetone to the ortho-quinone system of crypto tanshinone. *Journal of Natural Products*. 2005;**68**:1408-1411. DOI: 10.1021/np0580457
- [66] Gaspar-Marques C, Rijo P, Simoes MF, Duarte MA, Rodriguez B. Abietanes from *Plectranthus grandidentatus* and *P. hereroensis* against methicillin- and vancomycin-resistant bacteria. *Phytomedicine*. 2006;**13**:267-271. DOI: 10.1016/j.phymed.2005.06.002
- [67] Rijo P, Gaspar-Marques C, Simoes MF, Jimeno ML, Rodriguez B. Further diterpenoids from *Plectranthus ornatus* and *P. grandidentatus*. *Biochemical Systematics and Ecology*. 2007;**35**:215-221. DOI: 10.1016/j.bse.2006.10.011

- [68] Coutinho I, Pereira G, Simoes MF, Corte-Real M, Goncalves J, Saraiva L. Selective activation of protein kinase C- δ and - ϵ by 6, 11,12,14-tetrahydroxy-abieta-5,8,11,13-tetraene-7-one (coleon U). *Biochemical Pharmacology*. 2009;**78**:449-459. DOI: 10.1016/j.bcp.2009.04.026
- [69] Burmistrova O, Simoes MF, Rijo P, Quintana J, Bermejo J, Estevez F. Antiproliferative activity of abietane diterpenoids against human tumor cells. *Journal of Natural Products*. 2013;**76**:1413-1423. DOI: 10.1021/np400172k
- [70] Rijo P, Duarte A, Francisco AP, Semedo-Lemsaddek T, Simoes MF. *In vitro* antimicrobial activity of royleanone derivatives against gram-positive bacterial pathogens. *Phytotherapy Research*. 2014;**28**:76-81. DOI: 10.1002/ptr.4961
- [71] Batista O, Simoes MF, Nascimento J, Riberio S, Duarte A, Rodriguez B, de la Torre MC. A rearranged abietane diterpenoid from *Plectranthus hereroensis*. *Phytochemistry*. 1996;**41**:571-573. DOI: 10.1016/0031-9422(95)00646-X
- [72] Rodriguez B, de la Torre MC, Simoes F, Batista O, Nascimento J, Duarte A, Mayer R. Revision of the structure of an aristolane sesquiterpene aldehyde isolated from the root of *Plectranthus hereroensis* and *Aristolochia debilis*. *Phytochemistry*. 1995;**38**:905-907. DOI: 10.1016/0031-9422(94)00741-B
- [73] Batista O, Simoes MF, Duarte A, Valdeira ML, de la Torre MC, Rodriguez B. An antimicrobial abietane from the root of *Plectranthus hereroensis*. *Phytochemistry*. 1995;**38**:167-169. DOI: 10.1016/0031-9422(94)00586-I
- [74] Kubinova R, Porizkova R, Navratilova A, Farsa O, Hanakova Z, Bacinska A, Cizek A, Valentova M. Antimicrobial and enzyme inhibitory activities of the constituents of *Plectranthus madagascariensis* (Pers.) Benth. *Journal of Enzyme Inhibition and Medicinal Chemistry*. 2014;**29**:749-752. DOI: 10.3109/14756366.2013.848204
- [75] Rijo P, Gaspar-Marques C, Simoes MF, Duarte A, Apreada-Rojas MC, Cano FH, Rodriguez B. Neoclerodane and labdane diterpenoids from *Plectranthus ornatus*. *Journal of Natural Products*. 2002;**65**:1387-1390. DOI: 10.1021/np020203w
- [76] Oliveira PM, Ferreira AA, Silveira D, Alves RB, Rodrigues GV, Emerenciano VP, Raslan DS. Diterpenoids from the aerial parts of *Plectranthus ornatus*. *Journal of Natural Products*. 2005;**68**:588-591. DOI: 10.1021/np049827
- [77] Avila FN, Pinto FCL, Sousa TS, Torres MCM, Costa-Lotufo LV, Rocha DD, de Vasconcelos MA, Cardoso-Sa N, Teixeira EH, Albuquerque MRJR, et al. Miscellaneous diterpenes from the aerial parts of *Plectranthus ornatus* codd. *Journal of the Brazilian Chemical Society*. 2017;**28**:1014-1022. DOI: 10.21577/0103-5053.20160255
- [78] Rijo P, Simoes MF, Rodriguez B. Structural and spectral assignment of three forskolin-like diterpenoids isolated from *Plectranthus ornatus*. *Magnetic Resonance in Chemistry*. 2005;**43**:595-598. DOI: 10.1002/mrc.1600/pdf
- [79] Rijo P, Rodriguez B, Duarte A, Simoes MF. Antimicrobial properties of *Plectranthus ornatus* extracts, 11-acetoxylalima-5,13-dien-15-oic acid metabolite and its derivatives. *Natural Products Journal*. 2011;**1**:57-64. DOI: 10.2174/2210315511101010057

- [80] Oliveira PM, Pacheco AG, Alves RB, Pilo-Veloso D, Raslan DS, de Carvalho Alcantara AF. A new configurational analysis of 1,6,7-triacetoxy-8,13-epoxy-14-labden-11-one isolated from *Plectranthus ornatus* based on NMR and theoretical calculations. *Open Natural Products Journal*. 2009;**2**:1-5
- [81] Simoes MF, Rijo P, Duarte A, Barbosa D, Matias D, Delgado J, Cirilo N, Rodriguez B. Two new diterpenoids from *Plectranthus* species. *Phytochemistry Letters*. 2010;**3**:221-225. DOI: 10.1016/j.phytol.2010.08.002
- [82] Wellsow J, Grayer RJ, Veitch NC, Kokubun T, Lelli R, Kite GC, Simmonds MSJ. Insect-antifeedant and antibacterial activity of diterpenoids from species of *Plectranthus*. *Phytochemistry*. 2006;**67**:1818-1825. DOI: 10.1016/j.phytochem.2006.02.018
- [83] Alder AC, Ruedi P, Eugster CH. Glandular pigments from tropical labiates: Parviflorones from *Plectranthus strigosus* Benth. *Helvetica Chimica Acta*. 1984;**67**:1531-1534. DOI: 10.1002/hlca.19840670617
- [84] Gaspar-Marques C, Simoes MF, Valdeira ML, Rodriguez B. Terpenoids and phenolics from *Plectranthus strigosus*, bioactivity screening. *Natural Product Research*. 2008;**22**:167-177. DOI: 10.1080/14786410701654560
- [85] Kamatou GPP, Van Vuuren SF, Van Heerden FR, Seaman T, Viljoen AM. Antibacterial and antimycobacterial activities of South African *Salvia* species and isolated compounds from *S. chamelaeagnea*. *South African Journal of Botany*. 2007;**73**:552-557
- [86] Mukherjee KS, Mukhopadhyay B, Brahmachar G. A new triterpene from *Salvia coccinea*. *Journal of the Indian Chemical Society*. 2004;**81**:82-83
- [87] Savona G, Bruno M, Paternostro M, Marco JL, Rodriguez B. Salviacoccin, a neoclerodane diterpenoid from *Salvia coccinea*. *Phytochemistry*. 1982;**21**:2563-2566
- [88] Mukherjee KS, Ghosh PK. Further studies on *Salvia coccinea* Linn. *Journal of the Indian Chemical Society*. 1978;**55**:850
- [89] Hawas UW, Gamal-Eldee AM, El-Toumy SAA, Meyer JJM, Hussein AA. Inhibition of the initiation stage of carcinogenesis by *Salvia disermas* constituents. *Zeitschrift fuer Naturforschung, C: Journal of Biosciences*. 2009;**64**:831-839. DOI: 10.1515/znc-2009-11-1213
- [90] Kamatou GPP, van Zyl L, David H, van Heerden FR, Lourens ACU, Viljoen AM. Antimalarial and anticancer activities of selected South African *Salvia* species and isolated compounds from *S. radula*. *South African Journal of Botany*. 2008;**74**:238-243. DOI: 10.1016/j.sajb.2007.08.001
- [91] Nieto M, Gallardo VO, Rossomando PC, Tonn CE. 8-Hydroxysalviarin and 7,8-didehydro-rhyacophilin, two new diterpenes from *Salvia reflexa*. *Journal of Natural Products*. 1996;**59**:880-882
- [92] Mokoka TA, Peter XK, Fouche G, Moodley N, Adams M, Hamburger M, Kaiser M, Brun R, Maharaj V, Koorbanally N. Antileishmanial activity of 12-methoxycarnosic acid from *Salvia repens* Burch. ex Benth (Lamiaceae). *South African Journal of Botany*. 2014;**90**:93-95

- [93] Saleh MRI, Nazmi SN. Phytochemical study of *Salvia verbenaca* L. herb. Egyptian Journal of Pharmaceutical Sciences. 1982;**20**:411-415
- [94] Sabri NN, Abou-Donia AA, Assad AM, Ghaz NM, El-Lakany AM, Tempesta MS, Sanson DR. Abietane diterpene quinones from roots of *Salvia verbenaca* and *S. lanigera*. Planta Medica. 1989;**55**:582
- [95] Ahmed B, Al-Howiriny TA, Al-Rehaily AJ, Mossa JS. Verbenacine and salvinine: two new diterpenes from *Salvia verbenaca*. Zeitschrift fuer Naturforschung, C: Journal of Biosciences. 2004;**59**:9-14
- [96] Michael TD, English RB, Rivett DEA. Synrotolide, an α -pyrone from *Syncolostemon rotundifolius*. Phytochemistry. 1987;**26**:1497-1499
- [97] Van Puyvelde L, Nyirankuliza S, Panebianco R, Boily Y, Geizer I, Sebikali B, De Kimpe N, Schamp N. Active principles of *Tetradenia riparia*. I. Antimicrobial activity of 8(14),15-sandaracopimaradiene-7 α ,18-diol. Journal of Ethnopharmacology. 1986;**17**:269-275
- [98] Van Puyvelde L, De Kimpe N, Borremans F, Zhang W, Schamp N. 8(14),15-Sandaracopimaradiene-2 α ,18-diol, a minor constituent of the Rwandese medicinal plant *Tetradenia riparia*. Phytochemistry. 1987;**26**:493-495
- [99] Gazim ZC, Rodrigues F, Amorin ACL, de Rezende CM, Sokovic M, Tesevic V, Vuckovic I, Krstic G, Cortez LER, Colauto NB, et al. New natural diterpene-type abietane from *Tetradenia riparia* essential oil with cytotoxic and antioxidant activities. Molecules. 2014;**19**:514-524. DOI: 10.3390/molecules19010514
- [100] Fernandez ACAM, Rosa MF, Fernandez CMM, Bortolucci WC, Melo UZ, Siqueira VLD, Cortez DAG, Goncalves JE, Linde GA, Gazim ZC. Antimicrobial and antioxidant activities of the extract and fractions of *Tetradenia riparia* (hochst.) codd (lamiaceae) leaves. Brazil. Current Microbiology. 2017;**74**:1453-1460. DOI: 10.1007/s00284-017-1340-9
- [101] Van Puyvelde L, Lefebvre R, Mugabo P, De Kimpe N, Schamp N. Active principles of *Tetradenia riparia*; II. Antispasmodic activity of 8(14),15-sandaracopimaradiene-7 α ,18-diol. Planta Medica. 1987;**53**:156-158
- [102] Hakizamungu E, Van Puyvelde L, Wery M, De Kimpe N, Schamp N. Active principles of *Tetradenia riparia* III. Anti-trichomonas activity of 8(14),15-sandaracopimaradiene-7 α ,18-diol. Phytotherapy Research. 1988;**2**:207-208
- [103] Van Puyvelde L, De Kimpe N, Ayobangira FX, Costa J, Nshimyumukiza P, Boily Y, Hakizamungu E, Schamp N. Wheat rootlet growth inhibition test of Rwandese medicinal plants: Active principles of *Tetradenia riparia* and *Diplolophium africanum*. Journal of Ethnopharmacology. 1988;**24**:233-246
- [104] Van Puyvelde L, Ntawukiliyayo JD, Portaels F, Hakizamungu E. In vitro inhibition of mycobacteria by Rwandese medicinal plants. Phytotherapy Research. 1994;**8**:65-69

- [105] Hanson JR, Rivett DEA, Ley SV, Williams DJ. The x-ray structure and absolute configuration of insect antifeedant clerodane diterpenoids from *Teucrium africanum*. Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry. 1982;**4**:1005-1008
- [106] Nyiligira E, Viljoen AM, Van Heerden FR, Van Zyl RL, Van Vuuren SF, Steenkamp PA. Phytochemistry and *in vitro* pharmacological activities of South African *Vitex* (Verbenaceae) species. Journal of Ethnopharmacology. 2008;**119**:680-685