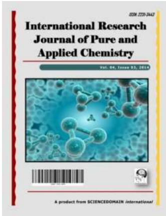

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A Review on the Biological Activity and the Triterpenoids from the Genus *Vernonia* (Asteraceae Family)

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Medicinal plants have always played a key part in health care. In fact, plants represent an enormous pool of new, undiscovered, and bioactive molecules. Therefore, ethnopharmacological and ethnobotanical studies are essential to discover new substances for the treatment of diseases. The *Vernonia* genus has about one thousand species and members of the genus are widely used as food and medicine. The plant-derived triterpenoids are commonly used for medicinal purposes in many countries, because they possess various pharmacological properties. A large number of triterpenoids are known to exhibit cytotoxicity against a variety of tumor cells as well as anticancer efficacy in preclinical animal models. Therefore this review presents an overview of *Vernonia* species with their biological potential, ethnomedicinal uses and the triterpenoids isolated from this genus. This will help to identify the state of ethnopharmacological knowledge in regard to this genus and to propose future research priorities.

Keywords: Vernonieae; biological activity; phytochemistry; triterpenoids.

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1. INTRODUCTION

Vernonia is one of the largest genera of flowering plants in the Asteraceae family, which includes more than 1500 species distributed widely in the tropical and sub-tropical region of Africa, Asia and America. Ethnomedicinally, species of the genus vernonia are used in the treatment of infectious and parasitic diseases. The infectious diseases range from those affecting the skin to those of the stomach (gastrointestinal infections). Other major applications include treatment of bacterial infections, gynaecological diseases and complications, respiratory diseases, diabetes, urinary tract infections and venereal diseases. Parasitic diseases include malaria, worm infection, amoebiasis and schistomiasis. Some species are also used as antivenom against snakebites and insect bites.

2. METHODOLOGY

The current review was achieved using an designed search of the scientific data published about antimicrobial activity, focusing on the antibacterial and antifungal activities of the species of the genus *Vernonia*. The searches were carried out using various databases, including PubMed (http://www.ncbi.nlm.nih.gov/pubmed), Science Direct (http://www.sciencedirect.com/), Scopus (http://www.scopus.com/), Scielo (http://www.scielo.org/), GoogleScholar (http://www.scholar.google.com/) and scifinder 2009.

2.1 Biological Activity of the Genus *Vernonia*

Among the diverse biological activities, antibacterial studies are the most reported in the genus *vernonia*. Antibacterial activity was found to be common to all species in all extracts followed by analgesic, antipyretic, anti-inflammatory and antiparasitic activity. Antibacterial compounds are mainly lipophilic and will partition from an aqueous phase into bacterial membrane structures, causing expansion of the membranes, increased fluidity, disordering of the membrane structure and inhibition of membrane embedded enzymes [1] Antifungal activity is also reported in five of the *Vernonia* species, while antiviral is not commonly reported in the *Vernonia* with only one report in the ethanol extract of the fruit of *V. amagdalina*.

Of the *Vernonia* species, *V. amygdalina* appears to be the most widely used. The leaves are the most commonly used plant part and is prepared as a decoction. In some cases a decoction of the whole plant is prepared. The method of preparation depends on the application, for example, a mixture of the root and leaf decoction is drunk to treat gastrointestinal diseases and as an antipyretic and the leaves soaked in alcohol is drunk to treat diabetes mellitus. The traditional medicinal applications of members of the genus are illustrated in Table 1.

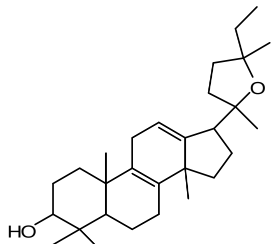
In rural areas where access to healthcare is not readily available, people rely on these extracts for common pain relief, inflammation and fever. Four of the nineteen species have also been reported to have antiparasitic activity, either antiplasmodial, antileishmanial, antischistomatic, anti-amoebic or antihelmintic. These are mainly reported for the polar extracts such as the aqueous and methanol extracts with few reports being in the chloroform or hexane extract.

Beside the antibacterial, antiparasitic and conditions associated with pain, inflammation and fever, extracts of these plants have also shown other activities such as antidiabetic, antioxidant, anticancer, antiulcer, immuno-modulatory, pesticidal and insecticidal activity.

The most extensively studied plant among all the *Vernonia* species is *V. amygdalina*, reported to possess several pharmacological activities such as antidiabetic, antibacterial, antimalarial, antifungal, antioxidant, liver protection and cytotoxic effects (Table 2). The biological activities of *Vernonia* species that have been studied and documented are listed in Table 2.

2.2 A Phytochemical Review of the Triterpenoids from *Vernonia* Species

The isolation of tritepenoids from this genus is recorded to have begun as early as 1979, where the tetracyclic triterpenoid, fasciculatol was isolated from *V. fasciculata*. This remains to be the only tetracyclic triterpenoid isolated from *Vernonia* and all other phytochemical studies have reported pentacyclic triterpenoids.



Fasciculatol

In this review, We focus on triterpenoids from *Vernonia* species. Seven classes of triterpenoids have been isolated and reported in this genus, of which five are closely related and possess five six-membered rings in their basic skeleton (oleanane, ursane, taraxarene, friedelane and friedoursane), the other two classes being lupane (four six membered rings and a five-membered ring) and a tetracyclic triterpenoid.

Table 1. Species of *Vernonia* used in traditional medicine

Plant species	Plant part	Traditional use	References
V. ambigua	Whole plant	Antimalarial	[2]
V. amygdalina	leaves	antimalarial, antidiabetic, antipyretic, gastrointestinal diseases, appetite stimulant, dermatological infections, antihelmintic, respiratory tract infections, gynaecological diseases and complications, infertility, antibacterial, antifungal and antivenom (snake bite)	[3] [4] [5] [6]
	stems	anti-HIV, antiviral and anti-amoebic	[5]
	leaves and fruits	antimalarial, antihelmintic, antibacterial and antiviral	[5] [7]
	roots	venereal diseases and gynaecological complications	[5] [8]
V. antihelmintica	seeds	antihelmintic, respiratory diseases, gastrointestinal diseases and complications, diuretic, anti-inflammatory, kidney protection and anti-ulcer	[9]
V. auriculifera	Leaves and roots	Antipyretic, antivenom, eye infections	[10]
V. branchycalyx	roots	gastrointestinal complication	[11]
V. cinerea	leaves and roots	antihelmintic, astringent, conjuctivitis, dermatological diseases, diuretic, antipyretic, gastrointestinal diseases, gynaecological diseases, respiratory diseases, antidote and urinary tract diseases	[12] [13] [14] [15]
V. colorata	leaves	dermatological infections, respiratory diseases, antidiabetic, gastrointestinal diseases, antipyretic, antiviral (hepatitis) and venereal diseases	[16] [17] [18]
V. condensata	leaves	analgesic, anti-ulcer, anti-diarrhoea, gastrointestinal diseases, liver protection and antivenom (snakebites)	[19] [20]
V. conferta	bark	anti-diarrhoea (bloody)	[21]
V. cumingiana	ns	antirheumatic arthritis, antiviral, bone	[22]

Plant species	Plant part	Traditional use	References
		and muscular injury, respiratory diseases, antimalarial, and dental diseases	[23]
V. ferruginea	ns	anti-inflammatory remedies	[24]
V. galamensis	leaves	antidiabetic (mellitus) and gastrointestinal diseases	[25]
V. guineensis	ns	antidote to poison, aphrodisiac, jaundice, anti malarial and prostatitis	[26]
V. jugalis	bark	anti-diarrhoea (bloody)	[21]
V. kotschyana	roots	abdominal pains, respiratory diseases including TB, antibacterial, dermatological infections, gastrointestinal disorder, analgesic, antiparasitic, antiprotozoa and anti-ulcers	[27] [28]
V. mapirensis	ns	anti-inflammatory	[29]
V. nigritiana	root	diuretic, gastrointestinal infections, emetic, antipyretic and antihelmintic	[21]
V. nudicaulis	whole plant	venereal diseases	[21]
V. pachyclada	ns	dermatological injury	[30]
V. paltula	whole plant	antimalarial, antirheumatic and gastrointestinal infections	[31]
	leaves	antiamoebic, antihelmintic, antiviral, respiratory tract infection, gastrointestinal infections and dermatitis	[32]
	roots	gastrointestinal infections, respiratory tract infection and colic	[32]
	flowers	eye problem, antipyretic and antirheumatic	[32] [33]
	seeds	antihelmintic, gastrointestinal disorder, urinary tract infection and dermatological infection	[32]
V. polytricholepis	ns	antipyretic and respiratory infections	[21]
V. potamophila	leaves	anticancer and skin infection	[34]
V. saligna	ns	respiratory tract infections and gynaecological complications	[35]
V. scorpioides	leaves	dermatological infection (diabetic lesions) and anti-ulcer	[36] [37]
V. trichoclada	ns	anti-inflammatory	[30]
V. tweediana	ns	respiratory tract diseases	[38]
V. urticifolia	laeves	Dermatological infection, antimalarial, respiratory infection, antihelmintic, alimentary infection.	[39] [40]

Key: ns-not specified

Table 2. Biological activities of extracts from *Vernonia*

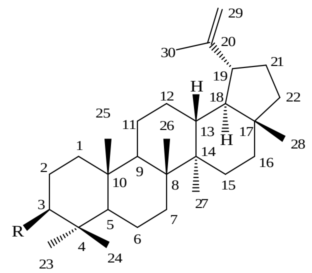
Plant species	Biological activity	Extract	Reference (s)
V. ambigua	antibacterial	ethanol[a] and chloroform[a]	[21]
	antiparasitic (antiplasmodial) and antioxidant	water[wp]	[2]
V. amagdalina	antibacterial	water[r] and ethanolic[l]	[41]
	bactericidal (oral bacterial)	cold water[s, b, p]	[42]
	antifungal	water[sb,r] and methanol[sb,r]	[43]
	antiviral	ethanol[fr]	[44]
	antiparasitic (antiamoebic)	methanol[l] and water[l]	[45]
	(antileishamanial)	chloroform[l] and ethanol[l]	[46]
	(antischistomiasis)	petroleum ether[l] and ethanolic[l]	[47]
	(antihelmintic)	water [l,s,r]	[47]
	(antiplasmodial)	ethanolic[l,r]	[48]
	analgesic and antipyretic	water[l] and ethanol[r]	[49]
	anti-inflammatory	water[l]	[50]
	antioxidant	ethanol[r] and methanol[ns]	[5]
	cytotoxic	cold water[wp]	[44]
	anticancer	cold water[l]	[51]
	antidiabetic	water[wp] and isopropanol[wp]	[7] [52]
	liver protective	methanol[l] and water[l]	[53]
	pesticidal and insecticidal	methanol[l]	[54]
V. antihelmintica	antibacterial	water[ns]-ethanolic[ns]	[55]
	anti-arthritic	ethanolic[sd]	[9]
	anti-inflammatory	water[ns]-ethanolic[ns]	[55]
	antidiabetic and antihyperglycemic	EtOAc:isopropanol (1:1)[sd]	[56]
V. auriculifera	Antibacterial and antiviral	Cold water	[10]
V. blumeoides	antibacterial	ethanol[a] and chloroform[a]	[21]
V. branchycalyx	antiparasitic (antileishmanial) (antiplasmodial)	$CHCl_3$:EtOAc(1:1) [l]	[11]
	(antimalarial)	water[l]	[11]
V. brasiliana	(antiplasmodial)	hexane[l]	[57]
V. cinerea	antibacterial	benzene[l]	[58] [59]
	antifungal	methanol[a]	[59]

Plant species	Biological activity	Extract	Reference (s)
	antioxidant	methanol[a]	[59] [60]
	anti-inflammatory	alcoholic[fl]	[59]
	antipyretic	methanol[wp]	[58]
	analgesic and antipyretic	chloroform[l], methanol[l] and ether[l]	[61]
	immunomodulatory	methanolic[ns]	[62]
V. colorota	antibacterial, antiparasitic (antiplasmodial), antidiabetic and anti-inflammatory	$CHCl_3$-MeOH (9:1)[l]	[16] [63]
	antidiabetic	aqueous[l]	[18]
V. condensata	analgesic, antigastritis, antiulcer and antinociceptive	acetone-EtOH-EtOAc[l]	[19] [28] [64]
V. glabra	antifungal	ns	[65]
V. hymenolepis	tumor inhibitory activity	alcoholic[l]	[66]
V. karaguensis	antibacterial and antileukaemic	Ns	[53] [67]
V. kotchyana	antibacterial, analgesic, antigastritis and antiulcer	aqueous/*n*-butanol[r] extract and acidic[r]	[19] [28] [68]
V. oocephala	Antibacterial	ethanol/chloroform[a]	[21]
V. paltula	antibacterial, antifungal, anti-inflammatory and antipyretic	ethanolic[wp, fl, fr, t, l]	[31]
V. polyanthes	Antiulcerogenic	methanolic[a] and chloroform[a]	[69]
V. pogosperma	Antibacterial	Ns	[70]
V. scorpioides	cytotoxic effects (anti-tumor)	dichloromethane[l]	[36]
	bactericidal and fungicidal	chloroform[l] and hexane[l]	[37] [71]
V. thomsoniana	antibacterial and antileukaemic	Ns	[53] [67]

Key: superscripts, a = aerial parts, fr = fruits, fl = flowers l = leaves, ns = not specified, r = roots, s = stems, sb = stem bark, sd = seeds, wp = whole plant

2.3 Lupane Triterpenoids

The lupane triterpenoids are characterised by four six-membered rings with a fifth five-membered ring to which an isopropyl group is attached. Five lupane triterpenoids have been isolated from *Vernonia* species, all with the same basic skeleton. All *Vernonia* species except for *V. cinerea*, *V. fasciculata* and *V. saligna* were found to contain lupeol (**1**). *V. cinerea* and *V. saligna* although not containing lupeol did contain derivatives of lupeol, lupenyl acetate (**2**) in *V. cinerea* and lupeol palmitate (**3**), a glycoside (**4**) and an acetate (**5**) in *V. saligna*.



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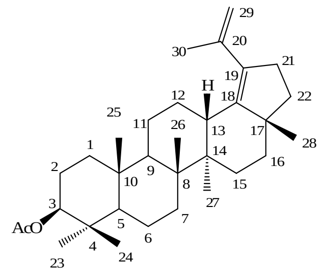

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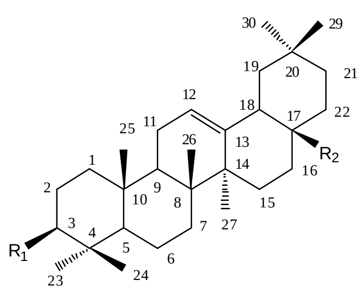
		R
1.	Lupeol	OH
2.	lupenyl acetate	OAc
3.	lupenyl palmitate	$OCO(CH_2)_{14}CH_3$
4.	lupenyl-20(29)en-3β-O-D-glucoside	O-Glu
5.	18,19-dehydrolupenyl acetate	OAc

2.4 Oleanane Triterpenoids

Another widely distributed triterpenoid in *Vernonia* is the oleanane triterpenoid, β-amyrin (**6**), being found in all *Vernonia* species except *V. arkansana*, *V. chunii*, *V. fasciculata* and *V. potamophilia,* however *V. chunii* did contain oleanolic acid (**10**). *V. mollissima* and *V. patula* contained β-amyrin acetate (**7**), while *V. saligna* and *V. patula* contained β-amyrin palmitate (**8**) and β-amyrin benzoate (**9**) respectively. The oleanane triterpenoids are characterised by five six-membered rings with a double bond at Δ^{12} and two methyl groups situated on the same carbon at position 20.



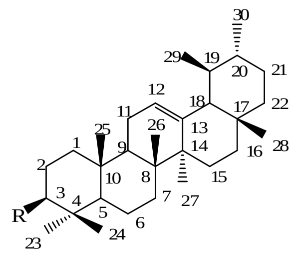
		R_1	R_2
6	α-amyrin	OH	CH_3
7	β-amyrin acetate	OAc	CH_3
8	α-amyrin palmitate	$OCO(CH_2)_{14}CH_3$	CH_3
9	α-amyrin benzoate	OCOPh	CH_3
10	oleanolic acid	OH	COOH

2.5 Taraxarane and Ursane Triterpenoids

The difference between the oleanane triterpenoids, the taraxarane and ursane triterpenoids lies in the position of the methyl groups on ring E. In the oleananes there are two methyl groups at C-20 whereas in the taraxaranes and the ursanes, a methyl group migrates from the oleanyl cation, resulting in the methyl groups being on adjacent carbon atoms, C-19 and C-20. The ursane, α-amyrin (**11**) is the third most common triterpenoid apart from lupeol (**1**) and β-amyrin (**6**), being found in ten of the sixteen *Vernonia* species studied phytochemically. The three compounds, lupeol (**1**), β-amyrin (**6**) and α-amyrin (**11**) form a suite of compounds found in nine of the sixteen species of *Vernonia* and may be used as a chemotaxonomic marker for the genus.

In addition, α-amyrin acetate (**12**) is found in *V. patula* and together with α-amyrin (**11**) in *V. saligna*. Taraxasterol (**14**) is found together with α-amyrin (**11**) in *V. incana* and *V. cognata*, while *V. chalybaea* contains α-amyrin (**11**), pseudotaraxasteryl acetate (**13**) and taraxasteryl acetate (**15**) and *V. cinerea* contains α-amyrin (**11**), α-amyrin acetate (**12**), 24-hydroxytaraxa-14-ene (**16**), 3β-acetoxyurs-13(18)-ene (**17**) and 3β-acetoxyurs-19-ene (**18**).

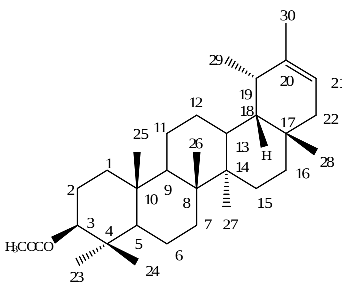
Between the taraxaranes and the ursanes, there is a difference in the position of the double bond, which is brought about by the way in which the taraxasteryl cation is quenched by the loss of the hydrogen with concomitant hydrogen migrations. In α-amyrin (**11**) and the rest of the ursanes, the H-12 proton is lost and the double bond is formed at Δ^{12}. Acetylation of **11** leads to formation of α-amyrin acetate (**12**).



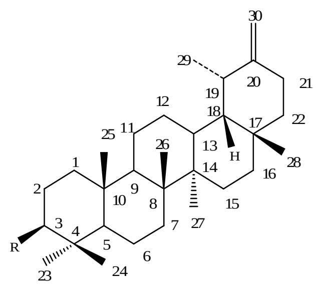
α–amyrin R = OH (11)
α–amyrin acetate R= OAc (12)

In the taraxaranes, the proton at either C-21 or C-30 is lost, leading to a double bond at either Δ^{20} (**13**) or at 20(30) leading to taraxasterol (**14**) with acetylation of **14** resulting in **15**.

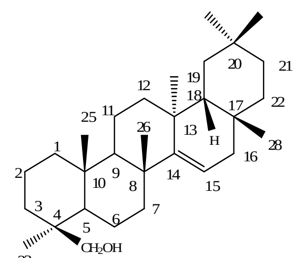
It is highly likely that the compound classified as a taraxarene (**16**) does not belong in this class and should be grouped with other compounds with a double bond at Δ^{14} resulting from the loss of a proton at C-15 in the oleanyl cation with hydride migrations quenching the cation.



pseudotaraxasteryl acetate **(13)**

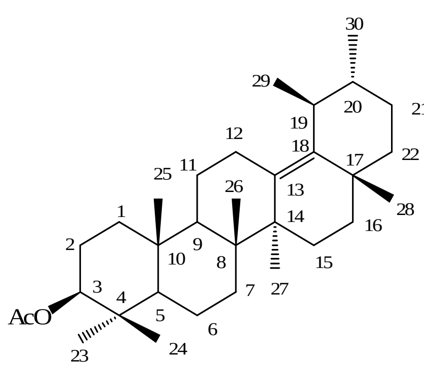


R= OH, taraxasterol **(14)**
R = OAc, taraxasteryl acetate **(15)**

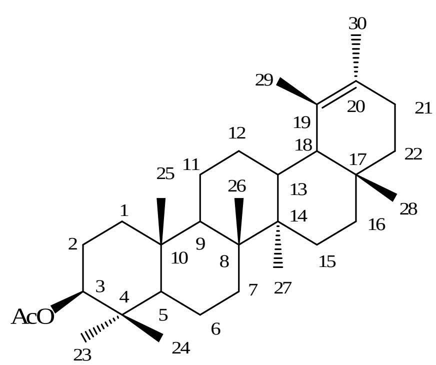


24-hydroxytaraxer-14-ene **(16)**

Compounds **17** and **18** have double bonds in positions different to the ursanes or the taraxaranes, **17** has a double bond between C-13 and C-18 and **18** has a double bond at Δ^{19} and is more likely to be associated with the taraxaranes as the loss of the proton occurs adjacent to the C-20 cation, just as that in **13**.



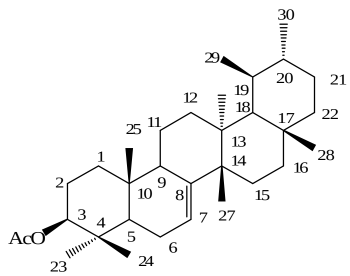
3β -acetoxyurs-13(18)-ene (17)



3β-acetoxyurs-19-ene (18)

2.6 Friedoursane Triterpenoids

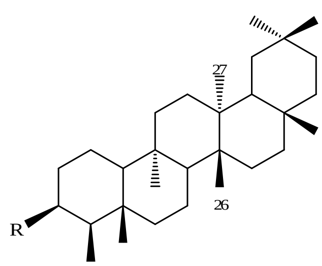
Unlike the cases where the double bond at Δ^{14} and 13(18) were not given their own classification, those with a double bond at the Δ^{7} position are classified as friedoursane triterpenoids as in bauerenyl acetate (**19**) isolated from *V. patula*. They come about by loss of a proton at C-7 with methyl and hydrogen shifts quenching the cation in the taraxasteryl cation.



bauerenyl acetate (19)

2.7 The Friedelane Triterpernoids

The Friedelane triterpenoids, 3β-friedelanol (**20**) and friedelin (**21**) are found in *V. patula* while friedelin (**20**) alone is found in *V. chalybaea* and *V. saligna*. The friedelane triterpenoids are characterised by methyl groups at C-4, C-5, C-9 and C-13, in addition to those at C-14, C-17 and C-20, which differ to the oleanane triterpenoids which have two methyl groups at C-4 and a methyl group at C-10 instead of C-9 and a proton at C-13 instead of the methyl group. This difference arises from the origin of the methyl migration being from the methyl group at C-4 resulting in a series of methyl and hydrogen migrations to quench the oleanyl cation. Friedelin (**21**) is brought about by the action of an oxidoreductase oxidising the 3β-hydroxyl group of 3β-friedelanol (**20**) to a ketone [72].



R = OH, 3β-friedelanol (20)
R = O, Friedlin (21)
R = $OCOCH_3$ Friedlin acetate (22)

The review revealed that lupeol (**1**), α-amyrin (**6**) and α-amyrin (**11**) were common to several species. *V. paltula* had the highest number of triterpenoids followed by *V. saligna* and *V. chalybaea*. *V. fasciculata* and *V. potamophilia* each had only one triterpenoid from the tetracyclic and lupane class respectively.

V. arkansana: The plant *V. arkansana* is known as Arkansas ironweed two triterpenoids have been isolated from its roots the belonging to the lupane class; lupeol **(1)** and lupenyl acetate **(2)** [73].

V. brasiliana: Two triterpenoids have been isolated from the leaves of *V. brasiliana* namely; lupeol (**1**) and β-amyrin (**6**) [57].

V. chamaedrys: From the flowers and the stem bark three triterpenoids have been isolated; β-amyrin (**6**) and α-amyrin (**11**) form a suite of compounds found in nine of the sixteen species of *Vernonia* and may be used as a chemotaxonomic marker for the [74].

V. chalybaea: The aerial parts of *V. chalybaea* afforded seven triterpenoids of different classes;lupeol, lupenyl acetate, β-amyrin (**6**) and α-amyrin (**11**), pseudotaraxasteryl acetate, taraxasteryl acetate and friedlin [75].

V. chunii: Lupeol (**1**) and Oleanolic acid (**10**) were isolated from *V. chunii* [76].

V. cinerea: The root bark of *V. cinerea* offered lupenyl acetate (**2**), β-amyrin (**6**) and α-amyrin (**11**), α-amyrin acetate (**12**), 24-hydroxytaraxa-14-ene (**16**), 3β-acetoxyurs-13(18)-ene (**17**) and 3β-acetoxyurs-19-ene (**18**) [15,77,78].

V. cognate: The fruits and the leaves four triterpenoids were isolated; Lupeol (**1**), β-amyrin (**6**) and α-amyrin (**11)** and taraxasterol **(14)** [79].

V. fasciculate: Fasciculatol is the only reported tetracyclic triterpenoid from *Vernonia* being isolated in *V. fasciculata* and is formed by the oxidation and then cyclisation of the side chain of euphol /tirucallol. Reduction at position 12 leads to the formation of a double bond with the concomitant loss of the methyl group at position 13 [80].

V. incana: The flowers and the leaves offered four triterpenoids; Lupeol, β-amyrin (**6**) and α-amyrin (**11)** and taraxasterol **(14)** [79].

V. mollissima: The aerial parts of *V. mollissima* Lupeol (**1**), β-amyrin (**6**), β-amyrin acetate (**7**) and α-amyrin (**11**) [81].

V. nitidula: The leaves and flowers yielded; Lupeol (**1**), β-amyrin (**6**), β-amyrin acetate (**7**) and α-amyrin (**11)** [79].

V. patula: lupeol, lupenyl acetate (**2**) in *V. cinerea* and lupeol palmitate (**3**), β-amyrin (**6**), β-amyrin acetate (**7**), β-amyrin benzoate (**9**), α-amyrin axcetate (**12**), bauerenyl acetate (**19**), 3β−friedelanol (**20**) and friedelin (**21**). They were isolated from the whole plant, [82,83].

V. potamophilia: The leaves of *V. potamophilia* yielded lupeol (**1**) [34].

V. saligna: The whole plant yielded lupeol palmitate (**3**), a glycoside (**4**) and an acetate (**5**) α-amyrin (**6**), α-amyrin palmitate (**8**), α-amyrin (**11),** α-amyrin axcetate (**12**), friedelin (**21**) [84].

V. squamulosa: The aerial parts of the plant *V. squamulosa* gave Lupeol (**1**), β-amyrin (**6**) and α−amyrin (**11)** [81].

V. tweediana: The aerial parts of the plant *V. tweediana* gave Lupeol (**1**), β-amyrin (**6**) and α-amyrin (**11)** [38].

V. auriculifera: The phytochemical investigation of *V. auriculifera* led to the isolation of seven triterpenoids. Extracts from the leaves were found to contain one lupane-type triterpenoid (lupenyl acetate **2**), one ursane-type triterpenoid (α-amyrin **11**), two oleanane-type triterpenoids (β-amyrin **6** and β-amyrin acetate **7**). The stem bark afforded friedlin/friedelanone (**21**) and friedelin acetate (**22**) belonging to the friedelane class. From the roots, oleanolic acid (**10**), the parent oleanane type triterpene, was isolated [85].

3. CONCLUSION

This review shows that the genus *Vernonia* is rich in species with extensive ethnomedicinal use, especially in Africa, and extracts obtained by various preparation methods are used, especially from the leaves, bark and roots. There are extensive studies of *V. amygdalina* and *V. scorpioides* pointing to their use in folk medicine and confirmed by their biological properties, and confirms that the genus is of immense value based on the studies of biology and chemistry of natural products.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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