UNDER PEER REVIEW

Review paper

A Review on the Biological activity and the triterpenoids from the Genus *Vernonia* (Asteraceae Family).

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 posses 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.

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.

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

UNDER PEER REVIEW

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/), Google Scholar (http://www.scholar.google.com/) and scifinder 2009.

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 (Sikkema *et al*., 1995). 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.

Table 1 Species of *Vernonia* used in traditional medicine

Plant species	Plant part	Traditional use	References
V. ambigua	Whole plant	Antimalarial	Builders *et al*., 2011
V. amygdalina	leaves	antimalarial, antidiabetic, antipyretic, gastrointestinal diseases, appetite stimulant, dermatological infections, anthelmintic, respiratory tract infections, gynaecological diseases and complications, infertility, antibacterial, antifungal and antivenom (snake bite)	Akah and Okafor 1992; Akah and Ekekwe 1995; Yeap *et al*., 2010; Huffman *et al*., 1993
	stems	anti-HIV, antiviral and anti-amoebic	Yeap *et al*., 2010

UNDER PEER REVIEW

	leaves and fruits	antimalarial, anthelmintic, antibacterial and antiviral	Yeap *et al*., 2010; Erasto *et al*., 2006
	roots	venereal diseases and gynaecological complications	Yeap *et al*., 2010; Geissler *et al*., 2002
V. anthelmintica	seeds	anthelmintic, respiratory diseases, gastrointestinal diseases and complications, diuretic, anti-inflammatory, kidney protection and anti-ulcer	Otari *et al*., 2010
V. auriculifera	Leaves and roots	Antipyretic, antivenom, eye infections	Muthaura et al., 2007
V. branchycalyx	roots	gastrointestinal complication	Oketch-Rabah *et al*., 1997
V. cinerea	leaves and roots	anthelmintic, astringent, conjuctivitis, dermatological diseases, diuretic, antipyretic, gastrointestinal diseases, gynaecological diseases, respiratory diseases, antidote and urinary tract diseases	Deborah *et al*., 1992; Khare, 2007; Marita *et al.,* 1999; Misra *et al*., 1993
V. colorata	leaves	dermatological infections, respiratory diseases, antidiabetic, gastrointestinal diseases, antipyretic, antiviral (hepatitis) and venereal diseases	Cioffi *et al*., 2004; Rabe *et al*., 2002; Sy *et al*., 2004
V. condensata	leaves	analgesic, anti-ulcer, anti-diarrhoea, gastrointestinal diseases, liver protection and antivenom (snakebites)	Frutuoso *et al*., 1994; Pereira *et al*., 1994
V. conferta	bark	anti-diarrhoea (bloody)	Aliyu *et al*., 2011
V. cumingiana	ns	antirheumatic arthritis, antiviral, bone and muscular injury, respiratory diseases, antimalarial, and dental diseases	Lin *et al*., 1985; Zhonghuabencao, 1999
V. ferruginea	ns	anti-inflammatory remedies	Malafronte *et al*., 2009
V. galamensis	leaves	antidiabetic (mellitus) and gastrointestinal diseases	Chhabra *et al*., 1989
V. guineensis	ns	antidote to poison, aphrodisiac, jaundice, anti malarial and prostatitis	Tchinda *et al*., 2002
V. jugalis	bark	anti-diarrhoea (bloody)	Aliyu *et al*., 2011
V. kotschyana	roots	abdominal pains, respiratory diseases including TB, antibacterial, dermatological infections, gastrointestinal disorder, analgesic, antiparasitic, antiprotozoa and anti-ulcers	Sanogo *et al*., 1998; Nergard *et al*., 2004
V. mapirensis	ns	anti-inflammatory	Morales-Escobar *et al*., 2007
V. nigritiana	root	diuretic, gastrointestinal infections, emetic, antipyretic and anthelmintic	Aliyu *et al*., 2011
V. nudicaulis	whole plant	venereal diseases	Aliyu *et al*., 2011

UNDER PEER REVIEW

V. pachyclada	ns	dermatological injury	Williams *et al*., 2005
V. paltula	whole plant	antimalarial, antirheumatic and gastrointestinal infections	Chiu and Chang, 1987
	leaves	antiamoebic, anthelmintic, antiviral, respiratory tract infection, gastrointestinal infections and dermatitis	Gani, 1998
	roots	gastrointestinal infections, respiratory tract infection and colic	Gani, 1998
	flowers	eye problem, antipyretic and antirheumatic	Mollik *et al*., 2010 Gani, 1998
	seeds	anthelmintic, gastrointestinal disorder, urinary tract infection and dermatological infection	Gani, 1998
V. polytricholepis	ns	antipyretic and respiratory infections	Aliyu *et al*., 2011
V. potamophila	leaves	anticancer and skin infection	Babady-bila *et al.,* 2003
V. saligna	ns	respiratory tract infections and gynaecological complications	Huang *et al*., 2003
V. scorpioides	leaves	dermatological infection (diabetic lesions) and anti-ulcer	Pagno *et al*., 2006; Buskuhl *et al*., 2010
V. trichoclada	ns	anti-inflammatory	Morales-Escobar *et al*., 2007
V. tweediana	ns	respiratory tract diseases	Zanon *et al*., 2008
V. urticifolia	laeves	Dermatological infection, antimalarial, respiratory infection, antihelmintic, alimentary infection.	Anoka *et al*., 2008; Misra *et al*., 1984

Key: ns-not specified

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, immunomodulatory, pesticidal and insecticidal activity.

UNDER PEER REVIEW

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.

Table 2: Biological activities of extracts from *Vernonia*

Plant species	Biological activity	Extract	Reference (s)
V. ambigua	antibacterial	ethanol[a] and chloroform[a]	Aliyu *et al*., 2011
	antiparasitic (antiplasmodial) and antioxidant	water[wp]	Builders *et al*.,2011
V. amagdalina	antibacterial	water[r] and ethanolic[l]	Ogbulie *et al*., 2007
	bactericidal (oral bacterial)	cold water[s, b, p]	Rotimi and Mosadomi, 1987
	antifungal	water[sb,r] and methanol[sb,r]	Nduagu *et al*., 2008
	antiviral	ethanol[fr]	Vlietinck *et al*., 1995
	antiparasitic (antiamoebic)	methanol[l] and water[l]	Moundipa *et al*., 2005
	(antileishamanial)	chloroform[l] and ethanol[l]	Carvalho and Ferreira 2001
	(antischistomiasis)	petroleum ether[l] and ethanolic[l]	Adedapo *et al*., 2007
	(anthelmintic)	water [l,s,r]	Adedapo *et al*., 2007
	(antiplasmodial)	ethanolic[l,r]	Abosi and Raseroka, 2003
	analgesic and antipyretic	water[l] and ethanol[r]	Tekobo *et al*., 2002
	anti-inflammatory	water[l]	Iroanya *et al*., 2010
	antioxidant	ethanol[r] and methanol[ns]	Yeap *et al*., 2010
	cytotoxic	cold water[wp]	Vlietinck *et al*., 1995
	anticancer	cold water[l]	Izevbigie *et al*., 2003
	antidiabetic	water[wp] and isopropanol[wp]	Erasto *et al*., 2006 Taiwo *et al*., 2009
	liver protective	methanol[l] and water[l]	Adesanoye and Farombi, 2009
	pesticidal and insecticidal	methanol[l]	Ohigashi *et al.,* 1991
V. anthelmintica	antibacterial	water[ns]-ethanolic[ns]	Parekh and Chanda 2008
	anti-arthritic	ethanolic[sd]	Otari *et al*., 2010

UNDER PEER REVIEW

	anti-inflammatory	water[ns]-ethanolic[ns]	Parekh and Chanda 2008
	antidiabetic and antihyperglycemic	EtOAc:isopropanol (1:1)[sd]	Fatima *et al.,* 2010
V. auriculifera	Antibacterial and antiviaral	Cold water	Muthaura et al., 2007
V. blumeoides	antibacterial	ethanol[a] and chloroform[a]	Aliyu *et al*., 2011
V. branchycalyx	antiparasitic (antileishmanial) (antiplasmodial)	$CHCl_3$:EtOAc(1:1) [l]	Oketch-Rabah *et al*., 1998
	(antimalarial)	water[l]	Oketch-Rabah *et al*., 1997
V. brasiliana	(antiplasmodial)	hexane[l]	Alves *et al*., 1997
V. cinerea	antibacterial	benzene[l]	Gupta *et al*., 2003a; Latha *et al*., 2009
	antifungal	methanol[a]	Latha *et al*., 2009
	antioxidant	methanol[a]	Kumar *et al*., 2009; Latha *et al*., 2009
	anti-inflammatory	alcoholic[fl]	Latha *et al*., 1998
	antipyretic	methanol[wp]	Gupta *et al*., 2003b
	analgesic and antipyretic	chloroform[l], methanol[l] and ether[l]	Mazumder *et al*., 2003
	immunomodulatory	methanolic[ns]	Pratheeshkumar and Kuttan, 2010
V. colorota	antibacterial, antiparasitic (antiplasmodial), antidiabetic and anti-inflammatory	$CHCl_3$-MeOH (9:1)[l]	Chukwujekwu *et al*., 2009; Cioffi *et al*., 2004
	antidiabetic	aqueous[l]	Sy *et al*., 2004
V. condensata	analgesic, antigastritis, antiulcer and antinociceptive	acetone-EtOH-EtOAc[l]	Frutuoso *et al.,* 1994; Sanogo *et al*., 1996; Risso *et al*., 2010
V. glabra	antifungal	ns	Gundidza, 1986
V. hymenolepis	tumor inhibitory activity	alcoholic[l]	Kupchan *et al*., 1969
V. karaguensis	antibacterial and antileukaemic	Ns	Mungarulire,1993; Taiwo *et al*., 1999
V. kotchyana	antibacterial, analgesic, antigastritis and antiulcer	aqueous/*n*-butanol[r] extract and acidic[r]	Frutuoso *et al*., 1994; Germano *et al*., 1996; Sanogo *et al*., 1996, 1998
V. oocephala	antibacterial	ethanol/chloroform[a]	Aliyu *et al*., 2011

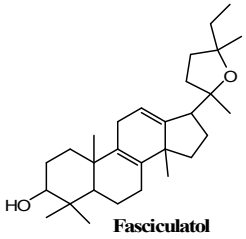
UNDER PEER REVIEW

V. paltula	antibacterial, antifungal, anti-inflammatory and antipyretic	ethanolic[wp, fl, fr, t, l]	Chiu and Chang 1987
V. polyanthes	antiulcerogenic	methanolic[a] and chloroform[a]	Barbastefano *et al.,* 2007
V. pogosperma	antibacterial	Ns	Tripathi *et al.,* 1981
V. scorpioides	cytotoxic effects (anti-tumor)	dichloromethane[l]	Pagno *et al*., 2006
	bactericidal and fungicidal	chloroform[l] and hexane[l]	Buskuhl *et al*., 2010; Freire *et al*., 1996
V. thomsoniana	antibacterial and antileukaemic	Ns	Mungarulire, 1993; Taiwo *et al.,* 1999

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

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.



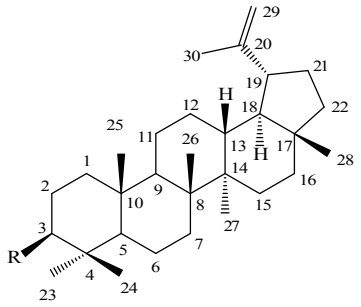
Fasciculatol

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 posses 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.

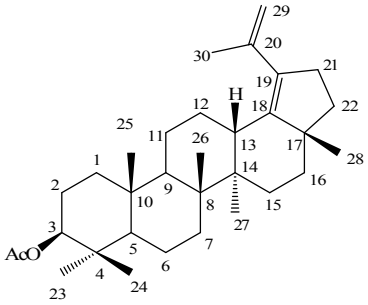
UNDER PEER REVIEW

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*.



1-4



5

		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

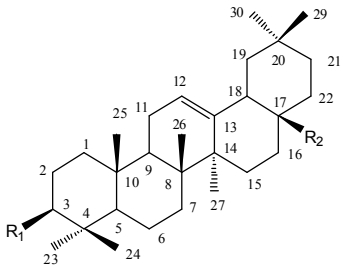
Oleanane triterpenoids

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

UNDER PEER REVIEW

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



Taraxarane and Ursane triterpenoids

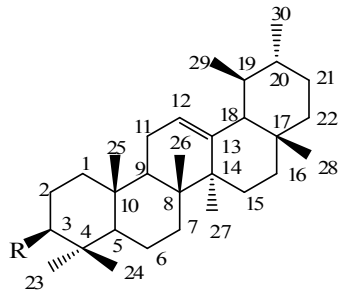
The difference between the oleanane triterpenoids, the taraxarane and ursane triterpenoids lies in the position of the methyl groups on ring E. In the oleananes there are two methyl groups at C-20 whereas in the taraxaranes and the ursanes, a methyl group migrates from the oleanyl cation, resulting in 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

UNDER PEER REVIEW

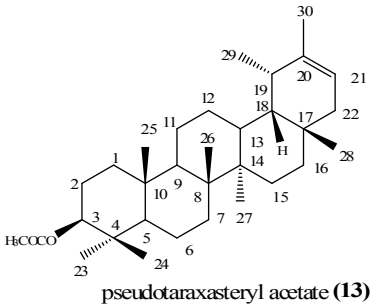
the ursanes, the H-12 proton is lost and the double bond is formed at Δ^{12}. Acetylation of **11** leads to formation of α-amyrin acetate (**12**).



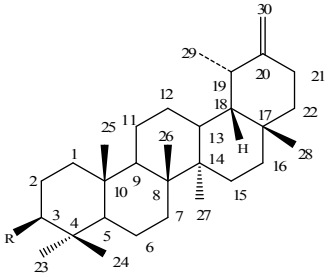
α–amyrin R = OH (11)
α–amyrin acetate R= OAc (12)

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**.

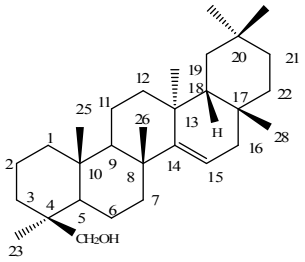
It is highly likely that the compound classified as a taraxarene (**16**) does not belong in this class and should be grouped with other compounds with a double bond at Δ^{14} resulting from the loss of a proton at C-15 in the oleanyl cation with hydride migrations quenching the cation.



pseudotaraxasteryl acetate **(13)**



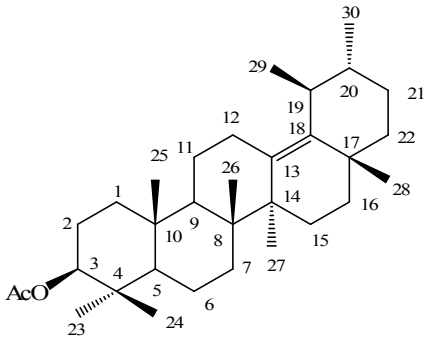
R=OH, taraxasterol **(14)**
R = OAc, taraxasteryl acetate **(15)**



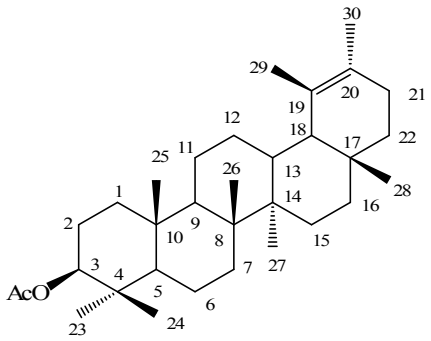
24-hydroxytaraxer-14-ene **(16)**

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**.

UNDER PEER REVIEW



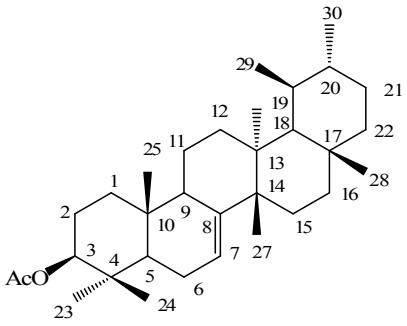
3β -acetoxyurs-13(18)-ene (17)



3β-acetoxyurs-19-ene (18)

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.



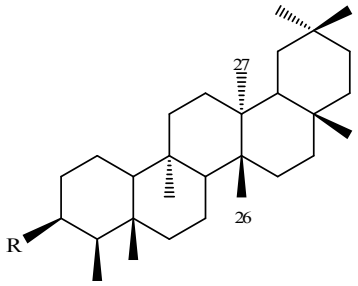
bauerenyl acetate (19)

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

UNDER PEER REVIEW

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 (Corsino *et al*., 2000).



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)** Bohlmann *et al.,* 1981.

V. brasiliana

Two triterpenoids have been isolated from the leaves of *V. brasiliana* namely; lupeol (**1**) and β-amyrin (**6**) Alves *et al*., 1997

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 genus Catalán *et al*., 1988.

UNDER PEER REVIEW

V. chalybaea

The aerial parts of *V. chalybaea* offorded seven triterpenoids of different classes;lupeol, lupenyl acetate, β-amyrin (**6**) and α-amyrin (**11**), pseudotaraxasteryl acetate, taraxasteryl acetate and friedlin (da Costa *et al*., 2008).

V. chunii

Lupeol (**1**) and Oleanolic acid (**10**) were isolate from *V. chunii* (Yuan *et al*., 2008).

V. cinerea

The root bark of *V. cinerea* afforded 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**) (Misra *et al*., 1984a, 1984b, 1993).

V. cognata

The fruits and the leaves four triterpenoids were isolated; Lupeol (**1**), β-amyrin (**6**) and α-amyrin (**11**) and taraxasterol **(14)** (Bardon *et al*., 1988).

V. fasciculata

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 (Narain,1979).

V. incana

The flowers and the leaves afforded four triterpenoids; Lupeol, β-amyrin (**6**) and α-amyrin (**11**) and taraxasterol **(14)** (Bardon *et al*., 1988).

V. mollissima

The aerial parts of *V. mollissima* Lupeol (**1**), β-amyrin (**6**), β-amyrin acetate (**7**) and α-amyrin (**11**) (Catalán and Iglesias, 1986).

V. nitidula

The leaves and flowers yielded; Lupeol (**1**), β-amyrin (**6**), β-amyrin acetate (**7**) and α-amyrin (**11**) (Bardon *et al*., 1988a).

UNDER PEER REVIEW

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 isolated from the whole plant, (Liang and Min, 2003; Liang *et al*., 2010).

V. potamophilia

The leaves of *V. potamophilia* yielded lupeol (**1**) (Babady-Bila *et al*., 2003).

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**) Huang and Liu, 2004.

V. squamulosa

The aerial parts of the plant *V. squamulosa* gave Lupeol (**1**), β-amyrin (**6**) and α–amyrin (**11)** (Catalán and Iglesias, 1986).

V. tweediana

The aerial parts of the plant *V. tweediana* gave Lupeol (**1**), β-amyrin (**6**) and α-amyrin (**11)** **(**Zanon *et al*., 2008).

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 (Kiplimo *et al*., 2011).

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,

UNDER PEER REVIEW

and confirms the genus importance in studies of the biology and chemistry of natural products.

References

Abosi, A. O., Raseroka, B. H. **2003**. *In vivo* antimalarial activity of *Vernonia amygdalina*. *Brit. J. Biomed. Sci*., 60, 89-91.

Adedapo, A. A., Otesile, T., Soetan, K. O. **2007**. Assessment of the anthelmintic efficacy of an aqueous crude extract of *Vernonia amygdalina*. *Pharm. Biol*., 45, 564-568.

Adesanoye, O. A., Farombi, E. O. **2009**. Hepatoprotective effects of *Vernonia amygdalina* (Asteraceae) in rats treated with carbon tetrachloride. *Exp. Toxicol. Pathol*., 62, 197-206

Akah, P. A., Ekekwe, R. K. **1995**. Ethnopharmacology of some of the Asteraceae family used in Nigerian traditional medicine. *Fitoterapia*, 66, 352-355.

Akah, P. A., Okafor, C. L. **1992**. Blood sugar lowering effect of *Vernonia amygdalina* (Del.) in an experimental rabbit model. *Phytother. Res*., 6, 171-173.

Aliyu, A. B., Musa, A. M., Abdullahi, M. S., Ibrahim, H., Oyewale, O. A. **2011**. Phytochemical screening and antibacterial activities of *Vernonia ambigua, Vernonia blumeoides, Vernonia oocephala* (Asteraceae). *Acta Pol. Pharm. Drug Res.*, 68, 67-73.

Alves, T. M., Nagem, T. J., De Carvalho, L. H., Krettli, A. U., Zani, C. L. **1997**. Antiplasmodial triterpene from *Vernonia brasiliana*. *Planta Med.*, 63, 554-555.

Babady-Bila, Kilonda, A., Mihigo, S., Lohohola, O., Tshibey, T. S. Compernolle, F., Toppet, S., Hoornaert, G. J. **2003**. Potamopholide, a new sesquiterpene lactone from *Vernonia potamophila*. *Eur. J. Org. Chem*., 123-127.

Barbastefano, V., Cola, M., Luiz-Ferreira, A., Farias-Silva, E., Hiruma-Lima, C. A., Rinaldo, D., Vilegas, W., Souza-Brito, A. R. **2007**. *Vernonia polyanthes* as a new source of antiulcer drugs. *Fitoterapia*, 78, 545-551.

UNDER PEER REVIEW

Bardón, A., Catalán, C. A. N., Gutiérrez, A. B., Herz, W. **1988a**. Glaucolides and other constituents from *Vernonia nitidula. Phytochemistry*, 27, 2691-2694.

Bohlmann, F. Sigh, P., Borthakur, N., Jakupovic, J. **1981**. Three bourbonenolides and other sesquiterpene lactones from two *Vernonia* species. *Phytochemistry*, 20, 2379-2381.

Builders, M. I., Wannang, N. N., Ajoku, G. A., Builders, P. F., Orisadipe, A., Aguiyi, J. C. **2011**. Evaluation of the antimalarial potential of *Vernonia ambigua* Kotschy and Peyr (Asteraceae). *Int. J. Pharm.*, 7, 238-247.

Buskuhl, H., de Oliveira, L. F., Blind, Z. L., de Freitas, R. A., Barison, A.,Campos, F. R., Corilo, Y. E., Eberlin, M. N., Caramori, F. G., Biavatti, M. W. **2010**. Sesquiterpene lactones from *Vernonia scorpioides* and their *in vitro* cytotoxicity. *Phytochemistry*, 71, 1539-1544.

Catalán, C. A. N., de Iglesias, D. I. A. **1986**. Sesquiterpene lactones and other constituents of *Vernonia mollissima* and *Vernonia squamulosa*. *J. Nat. Prod*., 49, 351-353.

Catalán, C. A. N., De Iglesias, D. I. A., Kavka, J., Sosa, V. E., Herz, W. **1988**. Glaucolides and related sesquiterpene lactones from *Vernonia chamaedrys*. *Phytochemistry*, 27, 197-202.

Chhabra, S. C., Mahunnah, R. L. A., Mshiu, E. N. **1989**. Plants used in traditional medicine in Eastern Tanzania. II angiosperms (Capparidaceae-Ebenaceae). *J. Ethnopharmacol.*, 25, 339 - 359.

Chiu, N. Y., Chang, K. H. **1987**. The Illustrated Medicinal plants of Taiwan. 1, 230. Southern materials centre, inc., Taipei, Taiwan.

Chukwujekwu, J. C., Lategan, C. A., Smith, P. J. **2009**. Antiplasmodial and cytotoxic activity of isolated sesquiterpene lactones from the acetone extract of *Vernonia colorata*. *S. Afr. J. Bot.*, 75, 176-179.

Cioffi, G., Sanogo, R., Diallo, D., Romussi, G., De Tommasi, N. **2004**. New compounds from an extract of *Vernonia colorata* leaves with anti-inflammatory activity. *J. Nat. Prod.*, 67, 389-394.

UNDER PEER REVIEW

Corsino, J., De Carvalho, P. R. F., Kato, M. J., Latorre, L. R., Oliveira, O. M. M. F., Araújo, R. A., Bolzani, V. S., França, C. S., Pereira, A. M. S., Furlan, M. **2000**. Biosynthesis of friedelane and quinonemethide triterpenoids is compartmentalized in *Maytenus aquifolium* and *Salacia campestris*. *Phytochemistry*, 55, 741-748

Da Costa, J. F., Bandeira, N. P., Rose, M., Albuquerque, J. R. **2008**. Chemical constituents of *Vernonia chalybacea*. Mart. *Quim. Nova.*, 31, 1691-1695.

Deborah, A., Lachman-white, Charles, D. A., Ulric, O. T. **1992**. A guide to medicinal plants of coastal Guyana. Commonwealth secretariat publications, London, 294.

Erasto, P., Grierson, D. S., Afolayan, A. J. **2006**. Bioactive sesquiterpene lactones from the leaves of *Vernonia amygdalina*. *J. Ethnopharmacol.*, 106, 117-120.

Fatima, S. S., Rajasekhar, M. D., Kumar, K. V., Kumar, M. T., Babu, K. R., Rao, C. A. **2010**. Antidiabetic and antihyperglylipidemic activity of ethyl acetate: isopropanol (1:1) fraction of *Vernonia anthelmintica* seeds in streptozotocin induced diabetic rats. *Food Chem. Toxicol*., 48, 495-501.

Freire, M. F. I., Abreu, H. S., Cruz, L. C. H., Freire, R. B. **1996**. Inhibition of fungal growth by extracts of *Vernonia scorpioides* (Lam.) Pers. *Microbiology*, *27*, 1-6.

Frutuoso, V. S., Gurjao, M. R., Cordeiro, R. S., Martins M. A. **1994**. Analgesic and anti-ulcerogenic effects of a polar extract from leaves of *Vernonia condensata. Planta Med*., 60, 21-25.

Geissler, P. W., Harris, S. A., Prince, R. J., Olsen, A., Odhiambo, R. A., Oketch-Rabah, H., Madiega, P. A., Andersen, A., Molgaard, P. **2002**. Medicinal plants used by Luo mothers and children in Bondo District, Kenya. *J. Ethnopharmacol*., 83, 39-54.

Germano, M. P., De Pascuale, R., Iauk, L., Galati, E. M., Keita, A., Sanogo, R., **1996**. Antiulcer activity of *Vernonia kotschyana* Sch. Bip. *Phytomedicine*, 2, 229-233.

UNDER PEER REVIEW

Gundidza, M. **1986**. Screening of extracts from Zimbabwean higher plants II: antifungal properties. *Fitoterapia*, 57, 111-114.

Gupta, M., Mazumder, U. K., Manikandan, L., Haldar, P. K., Bhattacharya, S., Kandar, C. C. **2003a**. Antibacterial activity of *Vernonia cinerea*. *Fitoterapia*, 74, 148-150.

Gupta, M., Mazumder, U. K., Manikandan, L., Bhattacharya, S., Haldar, P. K., Roy, S. **2003b**. Evaluation of Antipyretic Potential of *Vernonia cinerea* extract in rats. *Phytother. Res*., 17, 804-806.

Huang, Y. Ding, Z. H., Liu, J. K. **2003**. A New Highly Oxygenated Flavone from *Vernonia saligna. Z. Naturforsch*., 58c, 347-350.

Huang, Y., Liu, J. K. **2004**. Triterpenoids from *Vernonia saligna. Chinese J. Appl. Environ. Biol*.,10, 51-52.

Huffman, M. A., Gotoh, S., Izutsu, D., Koshimizu, K., Kalunde, M. S. **1993**. Further observations on the use of the medicinal plant *Vernonia amygdalina* (Del.), by a wild chimpanzee, its possible effect on parasite load, and its Phytochemistry. *Afr. Stud. Monogr*., 14, 227-240.

Iroanya, O., Okpuzor, J., Mbagwu, H. **2010**. Anti-nociceptive and antiphlogistic actions of a polyherbal decoction. *Int. J. Pharmacol*., 6, 31- 36.

Izevbigie, E. B., Bryant, J. L., Walker, A. **2003**. Edible *Vernonia amygdalina* leaf extract inhibits extracellular signal-regulated kinases and human breast cancer cell growth. *J. Nutr*., 133, 3860.

Khare, C. C. **2007**. Indian medicinal plants, An illustrated Dictonary Springer Verlag Berlin, pp. 699-700.

Kiplimo J. J., Koorbanally N. A. and Chenia H. (**2011**) Triterpenoids from *Vernonia auriculifera* Hiern exhibit antimicrobial activity. *African Journal of Pharmacy and Pharmacology* Vol. 5(8). pp. 1150-1156.

UNDER PEER REVIEW

316 Kumar, P. P., Kuttan, G. **2009**. *Vernonia cinerea* L., scavenges free radicals and regulates nitric
317 oxide and proinflammatory cytokines profile in carrageen, an induced paw edema model.
318 *Immunopharmacol. Immunotoxicol*., 31, 94-102.

319 Kupchan, S. M., Hemingway, R. J., Werner, D., Karim, A. **1969**. Tumor inhibitors. XLVI.
320 Vernolepin, a sesquiterpene dilactone inhibitor from *Vernonia hymenolepsis* A. Rich. *J. Org.*
321 *Chem.*, 34, 3903-3908.

322 Latha, Y. L., Darah, I., Sasidharan, S., Jain, K. **2009**. Antimicrobial activity of *Emilia*
323 *sonchifolia* D C., *Tridax procumbens* L. and *Vernonia cinerea* L. of the Asteraceae Family:
324 potential as food preservatives. *Mal. J. Nutr.*, 15, 223-231.

325 Liang, Q. L., Min, Z. D. **2003**. Studies on the Constituents from the Herb of *Vernonia patula.*
326 *Zhongguo Zhongyao Zazhi,* 28, 235-237

327 Liang, Q. L., Jiang, J. H., Min, Z. D. **2010**. A Germacrane Sesquiterpenoid from *Vernonia*
328 *paltula. Chinese J. Nat. Med*., 8, 104-106.

329 Lin, R., Chen, Y. L., Shi, Z. **1985**. In flora of China (Zhongguo Zhiwu zhi) Science press:
330 Beijing, 74, 21.

331 Malafronte, N., Pesca, M., Sabina, B., Angela, E., Luis, M. T. N. **2009**. New flavonoid
332 glycosides from *Vernonia ferruginea*. *Nat. Prod. Comm.*, 4, 1639-1642.

333 Marita, I. G., Keith, M., Colin, M. **1999**. Piggin upland Rice weeds of South and Southeast
334 Asia, International Rice Research Institute, Manila, 26-27.

335 Mazumder, U. K., Gupta, M., Manikandan, L., Bhattacharya, S., Haldar, P. K., Roy, S. **2003**.
336 Evaluation of anti-inflammatory activity of *Vernonia cinerea* Less. Extract on rats.
337 *Phytomedicine*, 10, 185-188.

338 Misra, T. N., Sigh, R. S., Upadhyay, J., Srivastava, R. **1984a**. Chemical constituents of
339 *Vernonia cinerea*, Part 1. Isolation and spectral studies of triterpenes. *J. Nat. Prod*., 47, 368-
340 372.

UNDER PEER REVIEW

Misra, T. N., Sigh, R. S., Upadhyay, J., Srivastava, R. **1984b**. Chemical constituents of *Vernonia cinerea*, Isolation and structure elucidation of a new pentacyclic triterpenoid. *J. Nat. Prod*., 47, 865-867.

Misra, T. N., Sigh, R. S., Srivastava, R., Pandey, H. S., Prasad, C., Singh, S. **1993**. A new triterpenoid from *Vernonia cinerea*, *Planta Med*., 59, 458-460.

Mollik, Md. A. H., Hossan, Md. S., Paul, A. K., Taufiq-Ur-Rahman, M., Jahan, R., Rahmatullah, M. **2010**. A Comparative analysis of medicinal plants used by Folk Medicinal healers in three Districts of Bangladesh and inquiry as to mode of selection of medicinal plants. *Ethnobot. Res. Appl*., 8, 195-218.

Moundipa, P. F., Flore, K. G. M., Bilong, C. F. B., Bruchhaus, I. **2005**. *In vitro* amoebicidal activity of some medicinal plants of the Bamun region (Cameroon). *Afr. J. Trad. Compl. Alt. Med*., 2, 113-121.

Mungarulire, J., Franz, C. H., Seitz, R. Y., Verlet, N. **1993**. Some developments in the search for cytotoxic constituents from Rwandese medicinal plants. *Acta hort*., 333, 211-216.

Morales-Escobar, L., Braca, A., Pizza, C., Tommasi, N. **2007**. New phenolic derivatives from *Vernonia mapirensis* Gleason. *ARKIVOC* (Gainesville, FL, United States), 7, 349-358.

Narain, N. K. **1979**. Fasciculatol, new tetracyclic triterpenoid ether from *Vernonia fasciculata* michx. *Can. J. Pharm. Sci*., 14, 33-35.

Nergard, C. S., Diallo, D., Michaelsen, T. E., Malterud, K. E., Kiyohara, H., Matsumoto, T., Yamada, H., Paulsen, B. S. **2004**. Isolation, partial characterisation and immunomodulating activities of polysaccharides from *Vernonia kotschyana* Sch. Bip. Ex Walp. *J. Ethnopharmacol*., 91, 141-152.

Nduagu, C., Ekefan, E. J., Nwankiti, A. O. **2008**. Effect of some crude plant extracts on growth of *Colletotrichum capsici* (Synd.) Butler and Bisby, causal agent of pepper anthracnose. *J. Appl. Biosci*., 6, 184-190.

UNDER PEER REVIEW

366 Ogbulie, J. N., Ogueke, C. C., Nwanebu, F. C. **2007**. Antibacterial properties of *Uvaria*
367 *chamae*, *Congronema latifolium*, *Garcinia kola*, *Vernonia amygdalina* and *Aframomium*
368 *melegueta*. *Afr. J. Biotechnol*., 6, 1549-1553.

369 Ohigashi, H., Takagaki, T., Koshimizu, K., Watanabe, K., Kaji, M., Hoshino, J., Nishida, T.,
370 Huffman, M. A., Takasaki, H., Jato, J., Muanza, D. N. **1991**. Biological activities of plant
371 extracts from tropical Africa. *Afr. Stud. Monogr.*, 12, 201-210.

372 Oketch-Rabah, H. A., Lemmich, E., Dossaji, S. F., Theander, T. G., Olsen, C. E., Cornett, C.,
373 Arsalan, K., Christensen, B. S. **1997**. Two new antiprotozoal 5-methylcoumarins from
374 *Vernonia brachycalyx. J. Nat. Prod.*, 60, 458-461.

375 Oketch-Rabah, H. A., Brøgger, C. S., Frydenvang, K., Dossaji, S. F., Theander, T. G., Cornett,
376 C., Watkins, W. M., Kharazmi, A., Lemmich, E. **1998**. Antiprotozoal properties of 16,17-
377 dihydrobrachycalyxolide from *Vernonia brachycalyx*. *Planta Med*., 64, 559-562.

378 Otari, K. V., Shete, R. V., Upasani, C. D., Adak, V. S., Bagade, M. Y., Harpalani, A. **2010**.
379 Evaluation of anti-inflammatory and anti-arthritic activities of the ethanolic extract of *Vernonia*
380 *anthelmintica* seeds, *J. Cell Tissue Res*., 10, 2269-2280.

381 Pagno, T., Blind, L. Z., da Saúde, C. C., Biavatti, W., Kreuger, M. R. O. **2006**. Cytotoxic
382 activity of the dichloromethane fraction from *Vernonia scorpioides* (Lam.) Pers. (Asteraceae)
383 against Ehrlich's tumor cells in mice. *Braz. J. Med. Biol. Res.*, 39, 1483-1491.

384 Parekh, J., Chanda, S. V. **2008**. Antibacterial activity of aqueous and alcoholic extracts of 34
385 Indian Medicinal Plants against some *Staphylococcus* species. *Turk J. Biol*., 32, 63-71.

386 Pereira, N. A., Pereira, B. M. R., Nascimento, M. C., Parente, J. P., Mors, W. B. **1994**. Folk
387 medicine as snake venomantidotes: protection against jararaca venom by isolated constituents,
388 *Planta Med.*, 60, 99.

UNDER PEER REVIEW

389 Pratheeshkumar, P., Kuttan, G. **2010**. Modulating of immune response by *Vernonia cinerea* L.
390 inhibits the proinflammatory cytokines profile, iNOS, and COX-2 expression in LPS-stimulated
391 macrophages. *Immunopharmacol. immunotoxicol*., 6, 1-11.

392 Rabe, T., Mullholland, D., van Staden, J. **2002**. Isolation and identification of antibacterial
393 compounds from *Vernonia colorata* leaves. *J. Ethnopharmacol.,* 80, 91-94.

394 Risso, W. E., Scarminio, I. S., Moreira, E. G. **2010**. Antinociceptive and acute toxicity
395 evaluation of *Vernonia condensata* Baker leaves extracted with different solvents and their
396 mixtures. *Indian J. Exp. Biol*., 48, 811-816.

397 Rotimi, V. O., Mosadomi, H. A., **1987**. The effect of crude extracts of nine African chewing
398 sticks on oral anaerobes. *J. Med. Microbiol.*, 23, 55-60.

399 Sanogo, R., Germano, M. P., de Tommasi, N., Pizza, C., Aquino, R. **1998.** Vernoniosides and
400 an androstane glycoside from *Vernonia kotschyana. Phytochemistry*, 47, 73-78.

401 Sanogo, R., de Pasquale, R., Germano, M. P. **1996**. *Vernonia kotschyana* Sch. Bip.:
402 Tolerability and Gastroprotective Activity. *Phytother. Res*., 10, 169-171.

403 Sikkema, J., De Bont, J. A. M., Poolman, B. **1995**. Mechanisms of membrane toxicity of
404 hydrocarbons. *Microbiol. Rev*., 59, 201-222.

405 Sy, G. Y., Nongonierma, R. B., Sarrr, M., Cisse, A., Faye, B. **2004**. Antidiabetic activity of the
406 leaves of *Vernonia colorata* (Wilid) Drake (Composes) in alloxan-induced diabetic rats. *Dakar*
407 *Med*., 49, 36-39.

408 Taiwo, O., Xu, H. X., Lee, S. F. **1999**. Antibacterial activities of extracts from Nigerian
409 chewing sticks. *Phytotherapy Res*., 13, 675-679.

410 Taiwo, I. A., Odeigah, P. G. C., Ogunkanmi, L. A. **2009**. The glycaemic effects of *Vernonia*
411 *amygdalina* and *Vernonia tenoreana* with tolbutamide in rats and the implications for the
412 treatment of diabetes mellitus. *J. Sci. Res. Dev*., 11, 122-130.

UNDER PEER REVIEW

Tekobo, A. M., Onabanjo, A. O., Amole, O. O., Emeka, P. M., **2002**. Analgesic and antipyretic effects of the aqueous extract of *Vernonia amygdalina. West Afri. J. Pharm*., 16, 68-74.

Tripathi, R. N., Tripathi, R. K. R., Pandey, D. K. **1981**. Assay of antiviral activity in the crude leaf sap of some plants. *Envir. India*, 4, 86-87.

Tchinda, A. T., Tsopmo, A., Tane, P., Ayafor, J. F., Connolly, J. D., Sterner, O. **2002**. Vernoguinosterol and Vernoguinoside, a trypanocidal stigmastane derivative from *Vernonia guineensis* (Asteraceae), *Phytochemistry*, 59, 371-374.

Vlietinck, A. J., Hoof, L. V., Totte, J., Lasure, A., Berghe, D. V. **1995**. Screening of hundred Rwandese medicinal plants for antimicrobial and antiviral properties. *J. Ethnopharmacol*., 46, 31-47.

Williams, R. B., Norris, A., Slebodnick, C., Merola, J., Miller, J. S., Andriantsiferana, R., Rasamison, V. E., Kingston, D. G. I. **2005**. Cytotoxic sesquiterpene lacones from *Vernonia pachyclada* from the Madagascar rainforest. *J. Nat. Prod*., 68, 1371-1374.

Yeap, S. K., Ho, W. Y., Beh, B. K., Liang, W. S., Ky, H., Yousr, A. H. N., Alitheen, N. B. **2010**. *Vernonia amygdalina*, an ethnoveterinary and ethnomedical used green vegetable with multiple bioactivities. *J. Med. Plant Res.*, 4, 2787-2812.

Yuan, K., Jian, A., Cai, X. I. **2008**. A new triterpene from *Vernonia chunii*. *Chinese Tradit. Herb. Drugs*, 39, 2, 168-169.

Zanon, R. B., Pereira, F. D., Boschetti, K. T., dos Santos, M., Athayde, L. M. **2008**. Fitoconstituintes isolados da fracão em dichlorometano das folhas de *Vernonia tweediana* Baker. Revista Brasileira de Farmacognosia *Brazilian J. pharmacog*., 18, 226-229.

Zhonghuabencao Editorial board, Zhonghuabencao, Shanghai Scientific and Technological Press, Shanghai, **1999**, Vol. 7, pp. 1001.