

## Minireview Article

### **Ethnomedicinal, and phytopharmacological aspects of *Vernonia amygdalina* utilized as a traditional medicinal herb.**

#### **Abstract**

*Vernonia amygdalina* Delile, commonly known as bitter leaf, is a shrub in the Asteraceae family, widely seen in tropical regions of Africa. *Vernonia amygdalina* is found to be traditionally used in African medicine, various parts of this plant, especially the leaves, are utilized to treat ailments such as fever, diabetes, and gastrointestinal issues. Recent research has highlighted its broad range of bioactive compounds, including alkaloids, flavonoids, saponins, tannins, and terpenoids, which contribute to its medicinal properties. *Vernonia amygdalina* possesses enormous therapeutic potential. It has demonstrated several effects such as antimicrobial, anti-inflammatory, anticancer, antioxidant, and antidiabetic effects during research. Its antibacterial properties have been confirmed against pathogens like *Salmonella typhi* and *Streptococcus pyogenes*. Studies have shown that the polar (acetone, water, and ethanol) extracts from this plant can effectively reduce inflammation. *Vernonia amygdalina* has shown promise in inhibiting cancer cell proliferation, inducing apoptosis, and modulating the cell cycle, positioning it as a potential candidate for cancer therapy. Luteolin, a rich effective phenolic compound (found in *Vernonia Amygdalina*) significantly minimizes diabetics through the regulation of blood sugar. Furthermore, the plant exhibits hepatoprotective and nephroprotective effects, protecting liver and kidney damage from toxins. *Vernonia amygdalina* continues to be an important topic of traditional and modern medical research due to its rich phytochemical profile and several therapeutic properties. This article was written by the authors to bring together the recent progress in studying the therapeutic potential of *Vernonia amygdalina*.

## 1. INTRODUCTION:

*Vernonia amygdalina* Delile, belonging to the family Asteraceae, is a shrub or small tree. *Vernonia amygdalina* is commonly called “bitter leaf” in the English language because of its bitter taste. It is a member of the Asteraceae family and is a small shrub that grows in the tropical regions of Africa, with heights reaching 2-5m. The leaves are lanceolate to narrowly elliptic, usually about four times as long as wide, glabrous, or with sparse hairs. The leaves are widely used for fevers and also as a quinine-substitute in Nigeria and some other African countries. The young leaves are used in folk medicine as anthelmintic, antimalarial, laxative/purgative, enema, expectorant, worm expeller, and fertility inducer in subfertile women. The capitula form clusters up to 15 cm, creamy white, occasionally tinged with mauve. The small fruits have both small glands and hairs as well as a pappus of bristly hairs. *Vernonia amygdalina* has been shown to have antimalarial, antimicrobial, anti-inflammatory, anti-oxidant, antipyretic, antidiabetic [1, 2], antibacterial, and anticancer properties [3]. *Vernonia amygdalina* has been used in the treatment of emesis [4], nausea, diabetes, loss of appetite-induced anorexia, amoebic dysentery [5], and other gastrointestinal tract problems. *Vernonia amygdalina* is well known as a medicinal plant with several uses including for the treatment of diabetes, fever reduction, and recently for a non-pharmaceutical solution to persistent fever, headache, and joint pain associated with AIDS (an infusion of the plant is taken as needed). Indigenous to various ecological zones, bitter leaf thrives in diverse environments, adapting to habitats ranging from forest margins to grasslands [6].

## 2. METHODOLOGY

The literature search for the article was conducted using the following scientific databases: ResearchGate (<https://www.researchgate.net/>), National Library of Medicine (<https://www.nlm.nih.gov/>), African Journals Online (<https://www.ajol.info/index.php/ajol>), and Semantic Scholars (<https://www.semanticscholar.org/>). The search covered articles published between 2005 and 2024 and only articles written in the English language were included. For the ResearchGate search, only the articles in the first to third search result pages were considered. The search was tailored down to about 100 articles and then to 56 articles. Articles were included if they specifically discussed the medicinal and therapeutic properties of *Vernonia amygdalina*. Search terms such as “*Vernonia amygdalina*,” “bitter leaf,” “phytochemical properties,” and “therapeutic effects” were used. Boolean operators such as “AND” and “OR” were used to refine the search.

## 3. BOTANICAL CLASSIFICATION:

Kingdom: Plantae

Division: Angiosperms

Order: Asterales

Family: Asteraceae

Genus: *Vernonia*

Species: *V. amygdalina*

Botanical Name: *Vernonia amygdalina*

[7]



Figure 1: An image of *Vernonia amygdalina* (Bitter leaf)

#### 4. PHYTOCHEMICAL COMPOSITION:

Phytochemical analysis of *Vernonia amygdalina* revealed the presence of alkaloids, flavonoids, tannins, saponins, terpenoids, carbohydrates, cardiac glycosides, and anthraquinones [6, 8]. Phytochemicals such as steroids, coumarins, phenolic acids, lignans, xanthenes, edotides, and sesquiterpenes have been extracted and isolated from *Vernonia amygdalina* [5, 9].

*Note: See table 2 for details*

#### 5. DIETARY COMPOSITION:

The result of the proximate analysis of *Vernonia amygdalina* leaf samples analyzed by Garba and Oviosa, [10] showed that loss of moisture increases nutrient content and helps to prolong the quality of the vegetable because high moisture content promotes the growth of bacteria which can cause spoilage in the vegetable.

Table 1: Nutrient composition of *Vernonia amygdalina* (bitter leaf)

Nutrient	Concentration	Plant part	Reference
Moisture	Present	Leaves	[10]
	11.34±0.03 %	Leaves	[11]
Fiber	Present	Leaves	[10]
	15.48±0.07 %	Leaves	[11]
Lipids and Fats	Present	Leaves	[10]
	4.34±0.03%	Leaves	[11]
Protein	20.39±0.01 %	Leaves	[11]
Calcium	7.43–71.16 mg/100 g	Leaves	[10]
	11.50 mg/100 ml to 830.00 mg/100 ml	Leaves	[12]
Magnesium	40.29–43.04 mg/100 g	Leaves	[10]
	29.46 mg/100 ml to 677.0 mg/100 ml	Leaves	[12]
Potassium (K)	2.26 mg/100 ml to 2814.15 mg/100 ml	Leaves	[12]
Sodium (Na)	0.21 mg/100 ml to 370.0 mg/100ml	Leaves	[12]
Phosphorous (P)	5.00 mg/100ml to 600.00 mg/100 ml	Leaves	[12]
Iron (Fe)	Fresh leaves: 2.40 mg/100 g	Leaves	[10]

	Sun-dried: 3.12 mg/100 g		
	Oven-dried: 2.73 mg/100 g		
	Solar-dried: 2.81 mg/100 g		
	Air-dried: 2.95 mg/100 g		
	11.0 ± 0.0 mg	Leaves	[13]
<b>Copper</b>	Fresh leaves: 0.31 mg/100 g	Leaves	[10]
	Dried leaves: 0.24–0.29 mg/100 g		
<b>Vitamin A</b>	Present	Leaves	[14]
	345.50 ± 0.0 IU	Leaves	[13]
<b>Vitamin C</b>	Present	Leaves	[14]
	228.40 ± 0.0 mg	Leaves	[13]
	5.70 mg/100 ml to 815.00 mg/100 ml	Leaves	[12]
<b>Vitamin E</b>	Present	Leaves	[14]
	37.30 ± 0.01 mg	Leaves	[13]
<b>Vitamin B1</b>	Present	Leaves	[14]
	1.0 ± 0.00 mg	Leaves	[13]
<b>Vitamin B2</b>	Present	Leaves	[14]
	3.10 ± 0.00 mg	Leaves	[13]
<b>Niacin (B3)</b>	0.41 ± 0.0 mg	Leaves	[13]

Table 2: Phytochemicals in *Vernonia amygdalina*

Phytochemicals	Plant part	Presence	Properties	Reference
Sesquiterpene Lactones	N/A	+	Anticancer	[15]
Vernolide	Leaves	+	Anticancer and antiproliferative	[16]
Vernodaline	leaves	+	Treatment for monkeypox	[17]
Vernonioside V	leaf	+	Anti-inflammatory	[18]
Luteolin	leaves	+	Anti-diabetic, treatment for monkeypox	[17]
Cynaroside (Luteolin-7-O-glucoside)	leaves	+	Anti-oxidant	[19]
Tannins	leaves	+	Anti-oxidant, anti-cancer, anti-microbial	[20] [21] [22]
Alkaloids	leaves	+	Anti-parasitic, anti-microbial, anti-microbial	[24] [22]
Flavonoids	leaves	+	Anti-oxidant, anti-microbial	[20] [22]
Saponins	leaves	+	anti-microbial	[22]
Phenolic Compounds	leaves	+	Anti-oxidant, Anti-aging, anti-microbial	[20] [23] [22]
Steroids	leaves	+	Anti-inflammatory	[20]
Terpenoids	leaves	+	Anti-cancer, anti-parasitic, anti-microbial	[24]

## 6. TRADITIONAL USE:

*Vernonia amygdalina* is a perennial herb belonging to the Asteraceae family. Extracts of the plant have been used in various folk medicines as remedies against helminthic, protozoal, and bacterial infections with scientific support for these claims [5]. The leaves are useful for the

creation of herbal concoctions. The plant's activities are a result of diverse bioactive compounds found in different parts of the plant. These metabolites have specifically been efficacious against parasites, especially worms. The mechanisms of activities include paralysis of worms, interference with energy generation, and impairment with nutrient absorption, motility, and reproduction. The lack of considerable toxicity associated with the plant makes it a choice for further drug discovery [25].

## 7. ANTI-INFLAMMATORY EFFECT:

Inflammation is part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. It is a natural defense mechanism that helps to maintain homeostasis and promotes tissue repair. However, excessive inflammation can lead to cellular, tissue, or organ dysfunction, as well as contribute to the development of acute vascular events and diseases like Crohn's disease, psoriasis, obesity, diabetes, and cancer [26, 27, 28]. Pro-inflammatory molecules like tumor necrotic factor  $\alpha$  (TNF $\alpha$ ), certain interleukins, prostaglandins, and even pathogenic concentrations of nitric oxide are instrumental in raising inflammatory response. Many current anti-inflammatory drugs target these mediators at different levels, yet they lack specificity and their untoward effects restrict their long-term use [8]. Hence, there is a constant demand for better therapeutic alternatives.

Research work from Adedapo et al, [8] showed that the acetone extract of *Vernonia amygdalina* significantly reduced paw edema in histamine-induced rats. The mechanism believed to be responsible for this is that reports have shown that *vernonia amygdalina* possesses flavonoids, tannins, and saponins [29]. These phytochemicals are responsible for the anti-oxidative effect observed. Another research from Georgewill and Georgewill, [30] revealed that there was a 69.10% reduction of the inflammatory response following topical application to the right ear of the rat of the extract of the plant *V. Amygdalina*, this reduction indicated the anti-inflammatory property of *V. amygdalina*. This result is in line with the research of Du-Bois Asante et al, [31] which suggests that both EthYL and EthOL extracts of *Vernonia amygdalina* might act as peripheral analgesics, altering the local reaction caused by the release of inflammatory mediators.

Prananda et al, [32] research results indicate that *Vernonia amygdalina* may exert its protective effects by modulating the inflammatory response and mitigating the deleterious consequences of inflammation in doxorubicin-induced hepatic and renal damages.

## 8. ANTIBACTERIAL EFFECT:

Research from Matthew et al, [6] showed that the extracts of *Vernonia amygdalina* and *Cocos nucifera* water had significant antibacterial activity. Results of research from this study revealed that the mixture of *Vernonia amygdalina* and *Cocos nucifera* water showed a broad-spectrum antibacterial activity, with efficacy increasing with higher concentrations. *Salmonella typhi* strains were highly sensitive to the mixture, with zones of inhibition ranging from 9.5mm to 17mm at concentrations of 12.5mg/ml to 100 mg/ml. *Streptococcus pyogenes* strains were less sensitive, showing zones of inhibition from 9.0mm to 13mm at the same concentrations. The MIC (minimum inhibitory concentration) and MBC (minimum bactericidal concentration) tests revealed that the mixture had a good antibacterial effect on *Salmonella typhi*, with MIC and MBC values of 25 mg/ml and 100 mg/ml, respectively. For *Streptococcus pyogenes*, the MIC was 100 mg/ml, but the MBC was not applicable. Their

results suggest that the mixture was bacteriostatic at lower concentrations and bactericidal at higher concentrations, which supports the traditional use of large quantities of extracts in many African homes for treating infections.

#### 9. ANTICANCER PROPERTIES:

Research from Hasibuan et al, [33] indicated the presence of diterpene (ingenol-3-angelate), phenolics (chlorogenic acid and 4-methoxycinnamic acid), flavonoids (apigenin, luteolin, diosmetin, baicalin, rhoifolin, and scutellarin), and coumarins (7-hydroxycoumarin, 4-methylumbelliferone, and 4-methylumbelliferyl glucuronide) as active compounds in *Vernonia amygdalina*. Apigenin, a natural product belonging to the flavone class that is the aglycone of several naturally occurring glycosides can inhibit several types of cancer such as breast, liver, **pancreatic**, and lung [34]. It carries this function by triggering cell apoptosis, inducing autophagy, and modulating the cell cycle. Apigenin also decreases cancer cell motility and inhibits cancer cell migration and invasion [35]. **Coumarin can be found in *Vernonia amygdalina* and is a potential anticancer agent.** Coumarins such as imperatorin and esculetin inhibit the proliferation of cancer cells through cell cycle arrest [33, 36].

**In another study by Joseph et al, [37], the results of the research showed that the ethanol extract and *Vernonia amygdalina* silver nanoparticles inhibit MCF-7 cell proliferation with an average half-maximal inhibitory concentration (IC<sub>50</sub>) value of 67 µg/mL and 6.11 µg/mL, respectively, after 72 hours of treatment. The ethanol extract and *Vernonia amygdalina* silver nanoparticles also initiated G1 phase cell cycle arrest, induced apoptosis, and nuclear fragmentation in MCF-7 cells. Additional research from Nkono et al. (2022) [38] indicates that *Vernonia amygdalina* extract may activate tumor suppressor genes, such as the TP53 gene implicated in numerous cancers, in order to promote programmed cell death or slow its cycle. The p53 protein has been demonstrated to be involved in programmed cell death. Given that TP53 gene mutations are linked to both familial and sporadic forms of cancer.**

#### 10. ANTIDIABETIC PROPERTIES:

A study by Ejiofor et al, [39] isolated the phytochemicals present in the methanolic stem-bark extract of *Vernonia amygdalina*. Novel and new compounds were isolated using the column chromatographic technique. The structures of the isolates were elucidated, characterized, and identified based on their infra-red, mass, <sup>1</sup>H NMR, and <sup>13</sup>C NMR spectra; 11 $\alpha$ -Hydroxyurs-5,12-dien-28-oic acid-3 $\alpha$ ,25-olide (CMP1), 10-Geranyl-O- $\beta$ -D-xyloside (CMP2), Glucuronolactone (CMP3), 1-Heneicosanol O- $\beta$ -D-glucopyranoside (CMP4), and 6 $\beta$ ,10 $\beta$ ,14 $\beta$ -Trimethylheptadecan-15 $\alpha$ -olyl-15-O- $\beta$ -D-glucopyranosyl-1,5 $\beta$ -olide (CMP5) (*Vernonia*olide glucoside). The result obtained indicates that the isolated compound CMP5, found in *vernonia amygdalina*, caused a reduction in the blood glucose level to a near-normal in comparison with the standard treated group, but the mechanism that prompted or caused the utilization or removal of more glucose from the blood is unknown.

Nkono et al, [38] discussed that the leaves of *Vernonia amygdalina* contain biflavonoids such as luteolin, luteolin 7-O- $\beta$ -glucoside, and luteolin 7-O- $\beta$ -glucuronoside since it is known that flavonoids are involved in the regulation of blood sugar, it is probable that the hypoglycemic activity of *Vernonia amygdalina* as reported in this study, maybe a function of its rich flavonoid content. Also, *Vernonia amygdalina* can simultaneously suppress gluconeogenesis

and potentiate glucose oxidation via the pentose phosphate pathway in streptozotocin-induced diabetic rats. VA was able to reverse the loss in weight observed in the diabetic rats. Weight loss indicates the presence of diabetes, and a reversal of this confirms the efficiency of VA in the treatment of diabetics[40].

#### 11. IT'S HEPATOPROTECTIVE EFFECT

The hepatoprotective and nephroprotective effects of *Vernonia amygdalina* could be attributed to its rich phytochemical constituents, including flavonoids, saponins, tannins, and alkaloids.

Research from Tokofai et al, [41] showed that birds treated with CCl<sub>4</sub> + *Vernonia amygdalina* extracts (VALE) had lower levels of ALP(Alkaline Phosphatase) and tended to have lower serum AST(Aspartate Transaminase) levels, suggesting the hepatoprotective effect of the VALE extract against CCl<sub>4</sub>-induced liver damage. Also, SOD and CAT were better upregulated in birds treated with CCl<sub>4</sub> and supplemented with VALE. This suggests that improvement in these endogenous enzymes is among VALE's protective mechanisms of action. Similarly, Pranandaet al, [32]research result demonstrated that *Vernonia amygdalina* ethanol extract significantly ameliorated doxorubicin-induced histopathological alterations in both liver and kidney tissues.

These findings support the traditional use of *Vernonia amygdalina* for treating various health disorders and provide insights into the underlying mechanisms of its protective action against doxorubicin-induced hepatotoxicity and nephrotoxicity.

#### 12. HYPOLIPIDEMIC PROPERTIES:

The buildup of lipoproteins and triglycerides is implicated as risk factors in the progression of coronary heart disease [42]. *Vernonia amygdalina* (200 mg/kg) reduced hepatic triglyceride biosynthesis and favored cholesterol redistribution among the lipoprotein molecules. It also led to a significant elevation of plasma HDL-cholesterol, indicating its promising protective role against cardiovascular diseases[43]. These findings are consistent with the research results of Alozie et al, [42] which indicated that the ethanol and methanol extract of *Vernonia amygdalina* caused a significant reduction of total cholesterol concentration; while the ethanol, methanol toluene, and benzene extract resulted in a significant reduction of elevated LDL-cholesterol concentration. It also significantly restored altered HDL-cholesterol concentration.

#### 13. ETHNOPHARMACOLOGICAL PROPERTIES:

There are various traditional, industrial, medical, and culinary uses for *Vernonia amygdalina*. In traditional and herbal medicine, the plant is used as a tonic to cure fever(because it possesses crude saponin which has antipyretic and antinociceptive properties)[44], malaria, hemorrhoids, cough[45], and constipation(by the accumulation of fluid in the intestinal loop of the body, thereby increasing the bulk of the stools and stimulating the gastrointestinal motility)[46], and a host of other ailments. Sexually transmitted infections are treated with tonics made from this medicinal herb. (Omilani, [47] suggested that when the leaves of *Momordicacharantia* and *Vernonia amygdalina* are squeezed in water to extract juice, this extract can be used to treat gonorrhoea, vulvovaginitis, and syphilis. In general, the plant is grown to yield a sizable amount of edible vegetables. Additionally, the plant can be used in the brewing sector to produce beer in place of hops [48].

#### 14. ANTIDIARRHOEAL ACTIVITY

Research by MosisaGudeta et al, [49] in which castor oil was used to induce diarrhea in mice showed that the extract of *Vernonia amygdalina* leaves at all tested doses significantly delayed the onset of defecation, and reduced the number and weight of both wet and total fecal output. After the study, a reduction in the frequency of defecation, the weight of wet stools, and total stools were observed, indicating the efficacy of the extract of *Vernonia amygdalina* as an antidiarrheal agent. The crude extract of *Vernonia amygdalina* inhibited diarrhea significantly by extending its onset and reducing the frequency of defecation [50]. The aqueous extract of *Vernonia amygdalina* reduced diarrhea caused by microbial loading in piglets [51]. Studies from Dougnon et al, [52] showed that the ethanolic extract of *Vernonia amygdalina* was able to inhibit the ability of *Salmonella typhimurium* to cause diarrhea

#### 15. ANTIHELMINTHIC PROPERTIES:

Methanol extracts of *vernonia amygdalina* showed anthelmintic activities against earthworms. The normal mode of action of anthelmintic is to cause paralysis of the worm. Still, the methanol extract of *Vernonia amygdalina* was not only able to cause paralysis but also to kill the earthworm [53]. In a study by Ejiofor et al, [54] the compound CMP3 (glucuronolactone) extracted from *Vernonia amygdalina* caused paralysis and death of the helminth (*Eisenia foetida*). The ethanolic extracts of *Vernonia amygdalina* had anthelmintic efficacy on *Toxocara canis* in dogs [55]. *Vernonia amygdalina* showed anthelmintic and anticoccidial effects in rabbits fed with both leaves and stalk [56].

#### 16. TOXICITY:

The toxicity for *Vernonia amygdalina* indicated the presence of lead in fresh leaves (0.08 mg/100 g), sun-dried leaves (0.05 mg/100 g), oven-dried leaves (0.04 mg/100 g), and solar-dried leaves (0.04 mg/100 g) and air-dried (0.06 mg/100 g). This study showed the presence of lead to be very minute, and posing no danger, emphasizing the fact that moderate consumption of bitter leaves has no risk of lead toxicity [14].

#### CONCLUSION:

*Vernonia amygdalina*, or bitter leaf, is a potent medicinal plant with diverse therapeutic benefits. Its rich array of bioactive compounds contributes to its anti-inflammatory, antibacterial, anticancer, and antidiabetic effects. The plant also offers hepatoprotective and nephroprotective properties, supports cardiovascular health, and has a long history of traditional use. These findings highlight *Vernonia amygdalina's* potential as a complementary treatment and underscore the need for further research to explore its full clinical applications.

#### Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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