Minireview Article

A REVIEW ON MEDICINAL AND THERAPEUTIC PROPERTIESOF *VERNONIA AMYGDALINA* (bitter leaf)

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, antidiabetic, and antibacterialeffects during research. Its antibacterial properties have been confirmed against pathogens like *Salmonella typhi* and *Streptococcus pyogenes*. Studies have shown that 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. Due to the qualities demonstrated by *Vernonia amygdalina*, *Vernonia amygdalina* extract is currently being studied as a cotreatment, to be given in addition to the primary chemotherapeutic medication. Its anti-diabetic properties are also significant, with compounds such as luteolin aiding in blood sugar regulation. 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 abstract was written by the authors to bring together the recent progress in studying the therapeutic potential of *Vernonia amygdalina*, drawing from recent research available through scientific databases and journals.

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INTRODUCTION:

Vernonia amygdalina Delile (Khmer name: Bramat Khla Khmoum), belonging to the familyAsteraceae, 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 Africa, with heights reaching 2-5m. The leaves are lanceolate to narrowly elliptic, usually aboutfour 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 hairsas well as a pappus of bristly hairs. *Vernonia amygdalina* has antimalarial,antimicrobial, anti-inflammatory, anti-oxidant, antipyretic, anticancerous, and antidiabetic properties [1, 2].Many herbalists and naturopathic doctors recommend aqueous extracts for the treatment of emesis, nausea, diabetes, loss of appetite-induced abrosia, dysentery, and other gastrointestinal tract problems in their patients. *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 [3].

BOTANICAL CLASSIFICATION:

The plant is scientifically classified as belonging to the Kingdom Plantae. It is an angiosperm, of the order Asterales, of the family Asteraceae, genus *Vernonia*, and species *V. amygdalina*. The full binomial name is *Vernonia amygdalina* Del [4].

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

PHYTOCHEMICAL COMPOSITION:

Phytochemical analysis of *Vernonia amygdalina* revealed the presence of alkaloids, flavonoids, tannins, saponins,terpenoids, carbohydrates, cardiac glycosides, and anthraquinones[3, 5].Phytochemicals such as steroids, coumarins, phenolic acids, lignans, xanthones, edotides, and sesquiterpenes have been extracted and isolated from *Vernonia amygdalina* [4, 21].

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CLINICAL RESEARCH AND THERAPEUTIC BENEFITS

1. 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[6, 7, 8].Pro-inflammatory molecules like tumor necrotic factor α (TNFα), certain interleukins, prostaglandins, and even pathogenic concentrations of nitric oxide are instrumental in raising inflammatory response. Many current antiinflammatory drugs target these mediators at different levels, yet they lack specificity and their untoward effects restrict their long-term use [5]. Hence, there is a constant demand for better therapeutic alternatives.

- Research work from Adedapo et al, (2014) [5] showed that the acetone extract of *Vernonia amygdalina* at (100 and 200 mg/kg) and indomethacin (10 mg/kg) (standard drug) significantly (P< 0.05) reduced paw edema at 1, 2, and 3 hr in histamine-induced rats when compared to the control. The anti-inflammatory effect of 200mg acetone extract of *Vernonia amygdalina*is most pronounced after 3hr as indicated in the image below.

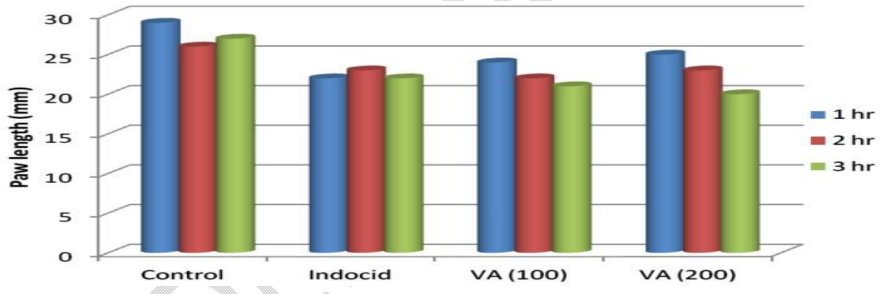

Figure 2. Anti-inflammatory activity of the acetone leaf extract of *Vernonia amygdalina* (VA) on histamine-induced edema in the right hind limb of rats.

Also, their research showed the effect of the acetone extract of *Vernonia amygdalina* (100 and 200 mg/kg) and indomethacin (standard drug) on the carrageenan-induced paw edema in rats and this indicated that both 100mg and 200mg of the extract reduced inflammation at 1hr, 2hr and 3hr compare to control. The effect of 200mg is more pronounced than 100mg at 1hr, 2hr, and 3hr. 200mg is the most pronounced at 3hr and this is more pronounced than the standard drug.

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Time (hr)	Control 3 ml/kg	Indomethacin 10 mg/kg	Extract (acetone) 100 mg/kg	200 mg/kg
0	21.8±1.1	24.6±1.7	25.2±2.3	23.4±1.1
1	23.8±0.8	23.2±1.3 (5.7)	22.0±1.1 (12.7)	22.2±0.4 (5.1)
2	23.8±0.8	21.8±0.8 (11.4)	22.6±1.6 (10.3)	21.4±1.7 (8.6)
3	23.4±0.9	22.0±0.7 (10.6)	22.0±1.2 (12.7)	20.8±2.3 (11.1)

Table 1. Anti-inflammatory activity of the acetone leaf extract of *Vernonia amygdalina* on carrageenan-induced edema in the right hind limb of rats (in mm). Percentage inhibitions of the carrageenan-induced inflammation (edema) are in parenthesis

- Another research from (Georgewill and Georgewill, 2009) [9] 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, which showed that extract of the plant V. amygdalina possesses anti-inflammatory property. This result is in line with the research of (Du-Bois Asante et al, 2019) [10]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, (2023) [11] 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.

2. Antibacterial effect:

Research from (Matthew et al, 2024) [3]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.

3. Anticancer properties:

Research from (Hasibuan et al, 2020) [12] indicated the presence ofditerpene (ingenol-3-angelate), phenolics (chlorogenic acid and 4-methoxycinnamic acid), flavonoids (apigenin, luteolin, diosmetin, baicalin, rhoifolin, and scutellarin), and coumarines (7-hydroxycoumarine, 4-methylumbelliferone, and 4-methylumbelliferyl glucuronide) as active compoundsin *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

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cancer such as breast, liver, prostate, and lungs[13]. 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 [14].Coumarin can be found in *Vernonia amygdalina*. Coumarin are potential anticancer agent, coumarines such as imperatorin and esculetin inhibit the proliferation of cancer cells through cell cycle arrest [12, 15]. Following this study, Joseph et al, (2021) [16]showed that the ethanol extract and *Vernonia amygdalina*silver nanoparticles inhibit MCF-7 cell proliferation with an average half-maximal inhibitory concentration (IC_{50}) value of 67µg/mL and 6.11µg/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.Given that TP53 gene mutations are linked to both familial and sporadic forms of cancer, additional research from Nkono et al. (2022) [17] 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.

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4. Antidiabetic properties:

A study by Ejiofor et al,carried out in 2020 [18] isolated the phytocompounds 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, 1H NMR, and 13C NMR spectra; 11α-Hydroxyurs-5,12-dien-28-oic acid-3α,25-olide (CMP1), 10-Geranilanyl-O-β-D-xyloside (CMP2), Glucuronolactone (CMP3), 1-Heneicosenol O-β-D-glucopyranoside (CMP4), and 6β,10β,14β-Trimethylheptadecan-15α-olyl-15-O-β-D-glucopyranosyl-1,5β-olide (CMP5) (Vernoniaolide 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, in 2022 [17] discussed that the leaves of *Vernonia amygdalina* contain biflavonoids such as luteolin, luteolin 7-0-B-glucoside, and luteolin 7-0-B-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.

5. HEPATOTOXICITY EFFECT

The hepatoprotective and nephroprotective effects of *Vernonia amygdalina* could be attributed to its rich phytochemical constituents, including flavonoids, saponins, tannins, and alkaloids [11].

Research from (Tokofai et al, 2021) [19] showed that birds treated with CCl_4 + *Vernonia amygdalina* extracts (VALE) had lower levels of ALP and tended to have lower serum AST levels, suggesting the hepatoprotective effect of the VALE extract against CCl_4-induced liver damage. Also, SOD and CAT were better upregulated in birds treated with CCl_4 and

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supplemented with VALE. This suggests that improvement in these endogenous enzymes is among VALE's protective mechanisms of action. Similarly, Prananda et al, (2023) [11] 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 [11].

6. HYPOLIPIDEMIC PROPERTIES:

(adaramoye et al, 2008) [20] Research results suggest that *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. These findings are consistent with the research results of (Alozie et al, 2022) [22] 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.The buildup of lipoproteins and triglycerides is implicated as risk factors in the progression of coronary heart disease

7. ETHNOPHARMACOLOGICAL PROPERTIES OF *VERNONIA AMYGDALINA*

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, constipation, and a host of other ailments. Sexually transmitted infections are treated with tonics made from this medicinal herb. 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. The Congolese make the most of Vernonia amygdalina's medicinal properties by treating hemorrhoids and coughs. In Ethiopia, the leaves are commonly used to treat malaria [23].

8. ANTIDIARRHOEAL ACTIVITY

Research by (MosisaGudeta et al, 2021) [24] in which castor oil was used to induce diarrheal 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. The highest doses in this study, at 400 mg/kg, significantly delayed the onset of diarrhea caused by castor oil when compared with the negative controls and the percentage of inhibition of defecation produced was closer to inhibition produced by the standard drug. A dose-dependent reduction in the percentage of weight of wet fecal output ($R2 = 0.996$, $p < 0.05$) and weight of total fecal output ($R2 = 0.964$, $p < 0.05$) was observed. After the study, a reduction in the frequency of defecation, the weight of wet stools, and total stools was observed, indicating the efficacy of the extract of *Vernonia amygdalina* as an antidiarrheal agent.

DIETARY COMPOSITION OF VERNONIA AMGYDALINA

The result of the proximate analysis of *Vernonia amygdalina* leaf samples analyzed by (Garba and Oviosa, 2019) [25] 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. In this study, there was the

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presence of fibre in Vernonia amygdalina. The study indicated the presence of lipids and fats, also calcium and potassiumwere present and the concentration of calcium ranged from 7.43 to 71.16 mg/100 g. The results obtained from magnesium ranged from 40.29 to 43.04 mg/100 g. Iron was present and the concentration values obtained for iron are fresh leaves (2.40 mg/100 g), sun-driedleaves (3.12 mg/100 g), oven-dried leaves (2.73 mg/100 g), solar-dried leaves (2.81 mg/100 g) and air-dried (2.95 mg/100 g). The concentration of copper found was low, at (0.31 mg/100 g) for fresh leaves and a range of 0.24–0.29 mg/100 g for dried leaves. It showed that *Vernonia amygdalina*leaf was a low source of dietary copper. The toxicity for *Vernonia amygdalina* indicated the presence of lead in freshleaves(0.08 mg/100 g), sun-driedleaves(0.05 mg/100 g), oven-driedleaves (0.04 mg/100 g), and solar-driedleaves(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 [26]. (Biru et al, 2022) [27] listed some of the isolated compounds found in vernonia amygdalina, which include, Vernolide, Vernodalol, Glucuronolactone, 6β,10β,14β-Trimethylheptadecan-15α-olyl-15-O-β-D-glucopyranosyl1,5β-olide, Vernodalinol, Vernonioside V, and Vernoamyoside A, B, C, and D. Other compounds include luteolin-7-O-gluc-glucopyranoside (cynaroside), Luteolin, isorhamnetin, 1-Heneicosenol O-β-D-glucopyranoside, 11α-Hydroxyurs-5,12-dien-28-oic acid-3α,25-olide, 10-Geranilanyl-O-β-D-xyloside, and Glucuronolactone. Moreover, the leaf contains vitamins like vitamin A, vitamin C (ascorbic acid), vitamin E, vitamin B1, vitamin B2, and niacin [26, 28, 29].

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TRADITIONAL USE OF VERNONIA AMYGDALINA

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 [4].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 [30].

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.

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