



Ethnomedicinal and Phytopharmacological Aspects of *Vernonia amygdalina* (Bitter Leaf) Utilized as a Traditional Medicinal Herb

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Author's contribution

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

Article Information

DOI: <https://doi.org/10.9734/ajrb/2024/v14i6326>

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/123640>

Minireview Article

Received: 01/08/2024

Accepted: 02/10/2024

Published: 14/10/2024

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Cite as: Oseghale, Ikalo David, Olabisi Promise Lawal, Daniel Osezuwa Ubebe, Vivian Chidera Orjiewulu, Aimuanmwosa Andrew Igunma, Omali Patricia Odey, Dorcas Temitope Ajibola, Divine Ibecheozor Chima, Nwigbo Kiakpugi Tuador, and Chinaemerem Precious Ani. 2024. "Ethnomedicinal and Phytopharmacological Aspects of *Vernonia Amygdalina* (Bitter Leaf) Utilized As a Traditional Medicinal Herb". *Asian Journal of Research in Biochemistry* 14 (6):41-57. <https://doi.org/10.9734/ajrb/2024/v14i6326>.

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. Research from multiple researchers has shown a wide range of phytochemical and bioactive compounds present in *Vernonia amygdalina*; examples are terpenoids, tannins, alkaloids, saponins, flavonoids, steroids, glycosides, etc., which have contributed to the medicinal properties of *Vernonia amygdalina*.

Vernonia amygdalina has shown its therapeutic and remedial potentials due to the presence of phytochemicals which exhibit effects such as anti-microbial, anti-inflammatory, anti-cancer, anti-oxidant, anti-diabetic, anti-hyperglycemic, anti-diarrheal, anti-helminthic, anti-pyretic, and anti-nociceptive effects. In this article, the authors highlight recent progress in using *Vernonia amygdalina* and its therapeutic effects.

Research, review, and case study articles were used to write this review. The articles were obtained from academic websites such as Research Gate, Google Scholar, the National Library of Medicine, African journals online, and Semantic journals, and some articles were obtained through a simple Google search. Articles that discussed the medicinal, ethanopharmacological, and therapeutic properties of *Vernonia amygdalina* were selected for the review. Search terms such as “*Vernonia amygdalina*,” “bitter leaf,” “phytochemical properties,” and “therapeutic effects” were used to search for relevant articles on the academic databases. Boolean operators such as “AND” and “OR” were used to refine the search further and ensure a comprehensive selection of articles.

Keywords: *Vernonia amygdalina*; phytochemicals; extracts; effects; bitter leaf.

1. INTRODUCTION

“*Vernonia amygdalina* Delile is a perennial shrub or small tree plant that belongs to the Asteraceae family. *Vernonia amygdalina* is commonly called “bitter leaf” in English 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. They have leaves that are lanceolate to narrowly elliptic and are glabrous or with sparse hairs. The leaves are usually about four times as long as wide. The leaves are widely used for fevers and as a quinine substitute in Nigeria and other African countries. In folk medicine, the young leaves are used as anthelmintic, antimalarial, laxative/purgative, enema, expectorant, worm expeller, and fertility inducer in subfertile women. *Vernonia amygdalina* has been shown to have antimalarial, antimicrobial, anti-inflammatory, anti-oxidant, antipyretic, antidiabetic, antibacterial, and anticancer properties” [1-3]. “*Vernonia amygdalina* has been used to treat emesis, nausea, diabetes, loss of appetite-induced abrosia, amoebic dysentery, and other gastrointestinal tract problems.” [4-5] *Vernonia amygdalina* is well known as a medicinal plant with several uses, including treating diabetes and fever and, recently, as a non-pharmaceutical solution to persistent fever, headache, and joint

pain. Indigenous to various ecological zones, *Vernonia amygdalina* 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 English were included. For the ResearchGate search, only the articles in the first to third search result pages were considered. The search was tailored to about 150 articles and further reduced to 86. 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: amygdalina Del
 Botanical Name: *Vernonia amygdalina*
 [7]

4. PHYTOCHEMICAL COMPOSITION

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



Fig. 1. *Vernonia amygdalina* (Bitter leaf) leaves sourced from Satellite Town, Lagos, Nigeria.

Table 1. Phytochemicals found in *Vernonia amygdalina* and their mechanism of action

| Phytochemicals and active compounds | Plant part | Presence | Properties | Reference | Mechanism of action of phytochemicals found in VA in disease treatment or control |
|---|------------|----------|--|-----------|--|
| Sesquiterpene Lactones (SLs) (examples: Vernolide, Vernodaline, Vernonioside V) | N/A | + | Anticancer, anti-inflammatory | [10] | SLs exhibit their anti-inflammatory activities through the inhibition of the production of cytokines, lipid mediators, and other related molecules, modulation of pro- and antioxidant contents, and regulation of intracellular signaling pathways [11] |
| Vernolide | Leaves | + | Anticancer and antiproliferative | [12] | Vernolide can exhibit its anti-cancer effects through the inhibition of STAT3 and NF-κB. It is also able to arrest the S phase of the cell cycle of cancer cell lines [14] |
| | flowers | + | Anti-bacteria | [13] | |
| Vernodaline | leaves | + | Treatment for monkeypox | [15] | Vernodaline inhibits cell proliferation, adhesion, and metastasis and induces apoptosis in cancer cells [17]. Vernodaline exhibits its antiproliferation and |
| | | | antibacterial, anticancer, antihelminthic, and antioxidant | [16] | |

| Phytochemicals and active compounds | Plant part | Presence | Properties | Reference | Mechanism of action of phytochemicals found in VA in disease treatment or control |
|-------------------------------------|------------|----------|---|----------------|---|
| | | | | | antimetastatic activities by targeting extracellular signal-regulated kinase 1 (ERK-1), extracellular signal-regulated kinase 2 (ERK-2), nuclear factor-κB (NF-κB), signal transducer and activator of transcription 3 (STAT3), matrix metalloproteinase 9 (MMP9), and matrix metalloproteinase 2 (MMP-2). It is also able to induce apoptosis through the enhancement of caspase 9 and caspase 3, while inhibition of Bcl-2 and Bcl-xL results in the release of cytochrome c into the cytosol [18] |
| Vernonioside V | leaf | + | Anti-inflammatory | [19] | N/A |
| Cynaroside (Luteolin-7-O-glucoside) | leaves | + | Anti-oxidant | [20] | |
| Tannins | leaves | + | Anti-oxidant, anti-cancer, anti-microbial | [21, 22] [23] | Plant tannins exhibit anti-inflammatory effects by inhibiting NO and prostaglandin-E2 (PGE2), regulating cytokine expression, reducing the production of inflammatory substances, and enhancing complexation with other molecules [24]. Tannins also exert anti-microbial by inhibiting extracellular microbial enzymes and oxidative phosphorylation, which directly affects microbial metabolism, depriving microorganisms of substrates needed for growth and increasing membrane permeability [24]. |
| Alkaloids | leaves | + | Anti-parasitic, anti-microbial anti-microbial Anti-inflammatory | [25] [23] [26] | Plant-derived alkaloids show anti-inflammatory activities, and they do this by suppressing a range of pro-inflammatory protein complexes implicated in inflammatory signaling pathways. This complex includes extracellular signal-regulated protein kinase 1/2 (ERK1/2), nuclear factor-κB, Akt, and signal transducer and activator of transcription 1 (STAT1) as well as |

| Phytochemicals and active compounds | Plant part | Presence | Properties | Reference | Mechanism of action of phytochemicals found in VA in disease treatment or control |
|---|------------|----------|-----------------------------|-----------|--|
| | | | | | inflammatory mediators, such as prostaglandin E2 (PEG2), nitric oxide (NO), cytokines, and chemokines [26] |
| Flavonoids (quercetin, rutin, kaempferol, daidzein, naringenin, hesperidin, anthocyanins (cranberry) apigenin, baicalein, luteolin, fisetin, epigallocatechin-3-gallate and oligonal) | leaves | + | Anti-oxidant | [21] | The anti-cancer effects of flavonoids are exerted by their ability to modulate ROS-scavenging enzyme activities, participate in arresting the cell cycle, induce apoptosis and autophagy, and suppress cancer cell proliferation and invasiveness [27] |
| | | | anti-microbial | [23] | |
| | | | Anti-cancer | [27] | |
| | | | Anti-inflammatory | [28] | |
| | | | | | The anti-inflammatory properties of flavonoids can be seen in their ability to interact with many molecules involved in inflammatory pathways and decrease the activity of cytokines, chemokines, and inflammatory enzymes [29]. Flavonoid that inhibits inflammation include quercetin, rutin, kaempferol, daidzein, naringenin, hesperidin, anthocyanins (cranberry), apigenin, baicalein, luteolin, fisetin, epigallocatechin-3-gallate and oligonal [30] |
| | | | | | Flavonoids can also stimulate the production of antioxidant enzymes such as superoxide dismutase (SOD) and catalase in the body; this process elicits their antioxidant effects [31] |
| Saponins | leaves | + | anti-microbial, anti-cancer | [23] | Saponins can treat and prevent cancer through several mechanisms, some of which include the induction of cell cycle arrest, promotion of apoptosis, induction of autophagy, anti-angiogenesis, inhibition of migration, and induction of tumor cell differentiation [32] |
| Phenolic Compounds | leaves | + | Anti-oxidant | [21,33] | The antioxidant functions of phenolic compounds are achieved through scavenging free radicals, regulating nuclear factor-like 2 (NRF2) /ARE signaling |
| | | | Anti-aging, anti-microbial | [23] | |

| Phytochemicals and active compounds | Plant part | Presence | Properties | Reference | Mechanism of action of phytochemicals found in VA in disease treatment or control |
|-------------------------------------|------------|----------|---|-----------|---|
| | | | | | pathways, and regulating enzymes such as Superoxide dismutase (SOD), Glutathione S-Transferases (GST), and glutathione (GSH) [34] |
| Steroids | leaves | + | Anti-inflammatory, anti-cancer | [21] | β -sitosterol (SIT), a plant-derived steroid, can carry out its anticancer effect by enhancing apoptosis, inducing cell cycle arrest, bidirectionally regulating oxidative stress, improving metabolic reprogramming, inhibiting invasion and metastasis, modulating immunity and inflammation, and combating drug resistance [35,36] In prostate cancer, β -sitosterol is able to suppress proliferation by initiating cell cycle arrest in the G2/M phase. In addition, it promotes prostaglandin secretion, raises ROS levels, and triggers apoptosis [37]. |
| Terpenoids | leaves | + | Anti-cancer, anti-parasitic, anti-microbial, anti-inflammatory, antioxidant | [25] | Geraniol (Terpenoid) was able to suppress the growth of MCF-7 breast cancer cells via the induction of cell cycle arrest in the G1 phase [38]. The anti-inflammatory and antioxidant properties of terpenoids are exhibited in their ability to reduce ROS and MDA (malondialdehyde) production and increase the activity of superoxide dismutase in radical scavenging [39] |
| Glycoside | leaves | + | Anti-oxidant, anti-inflammatory | [40] | Increases the activity of SOD in the blood [40]. |

5. NUTRIENT COMPOSITION

The result of the proximate analysis of *Vernonia amygdalina* leaf samples analyzed by Garba and Oviosa [41] 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 2 shows the nutrient composition of *Vernonia amygdalina*.

6. TRADITIONAL USE

“*Vernonia amygdalina* is a perennial herb or shrub belonging to the Asteraceae family. Plant extracts of *Vernonia amygdalina* 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 result from 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” [55].

Table 2. Nutrient composition of *Vernonia amygdalina* (bitter leaf)

| Nutrient | Concentration | Plant part | Reference | Role of nutrient in biological processes |
|------------------------|-------------------------------------|-------------------|------------------|---|
| Moisture | Present | Leaves | [41] | Lower or reduced moisture increases nutrient content and extends the quality of vegetables. |
| | 11.34±0.03 % | Leaves | [42] | |
| Fiber | Present | Leaves | [41] | Fibre helps cleanse the digestive tract by removing potential carcinogens from the body. It also prevents the absorption of excess cholesterol. |
| | 15.48±0.07 % | Leaves | [42] | |
| Lipids and Fats | Present | Leaves | [41] | Fats help insulate body organs against shock and keep body temperature stable. |
| | 4.34±0.03% | Leaves | [42] | |
| Protein | 20.39±0.01 % | Leaves | [42,43] | Protein improves lean body mass gain, skeletal muscle strength, and physical function in healthy subjects. |
| Calcium | 7.43–71.16 mg/100 g | Leaves | [41] | Calcium plays a role in bone and teeth development in children and pregnant and lactating women. |
| | 11.50 mg/100 ml to 830.00 mg/100 ml | Leaves | [44] | |
| Magnesium | 40.29–43.04 mg/100 g | Leaves | [41] | Magnesium helps in calcium metabolism in the bone |
| | 29.46 mg/100 ml to 677.0 mg/100 ml | Leaves | [44] | |
| Potassium (K) | 2.26 mg/100 ml to 2814.15 mg/100 ml | Leaves | [44] | It helps the nerves, muscles, and heart to function correctly. |
| Sodium (Na) | 0.21 mg/100 ml to 370.0 mg/100ml | Leaves | [44] | It is essential for maintaining normal cellular homeostasis |
| Phosphorous (P) | 5.00 mg/100ml to 600.00 mg/100 ml | Leaves | [44] | Phosphorus is a component of bones and cells. Phosphorous functions in energy processing, i.e., ATP (as phosphate) and various other functions |
| Iron (Fe) | Fresh leaves: 2.40 mg/100 g | Leaves | [41] | Required for the synthesis of myoglobin and hemoglobin, which are oxygen-transport proteins [45,46] |
| | 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 | | | |
| Copper | 11.0 ± 0.0 mg | Leaves | [47] | |
| | Fresh leaves: 0.31 mg/100 g | Leaves | [41] | Copper can be used in promoting incisional wound healing, killing cancer |

| Nutrient | Concentration | Plant part | Reference | Role of nutrient in biological processes |
|--------------------|--|------------|-----------|--|
| | Dried leaves: 0.24–0.29 mg/100 g | | | cells, Positron Emission Tomography (PET) imaging, radio immunological tracing, and radiotherapy of cancer [48] |
| Vitamin A | Present | Leaves | [49] | It has antioxidant properties [50] and promotes the support of the immune system [51]. |
| | 345.50 ± 0.0 IU | Leaves | [47] | |
| Vitamin C | Present | Leaves | [49] | Vitamin C is a potent antioxidant that helps with the transport and uptake of non-heme iron at the mucosa, the reduction of folic acid intermediates, and the synthesis of cortisol. |
| | 228.40 ± 0.0 mg | Leaves | [47] | |
| | 5.70 mg/100 ml to 815.00 mg/100 ml | Leaves | [44] | |
| Vitamin E | Present | Leaves | [49] | Vitamin E possesses antioxidant properties [52] and helps to maintain the immune system [53]. |
| | 37.30 ± 0.01 mg | Leaves | [47] | |
| Vitamin B1 | Present | Leaves | [49] | Vitamin B1 functions as a coenzyme (thiamine pyrophosphate), which is involved in carbohydrate metabolism [54] |
| | 1.0 ± 0.00 mg | Leaves | [47] | |
| Vitamin B2 | Present | Leaves | [49] | It helps to metabolize carbohydrates, fats, and proteins to glucose in the body. |
| | 3.10 ± 0.00 mg | Leaves | [47] | |
| Niacin (B3) | 0.41 ± 0.0 mg | Leaves | [47] | It helps the body make various sex and stress-related hormones in the adrenal glands and other body parts. |

7. 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), malaria, hemorrhoids, cough, 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), and a host of other ailments. Sexually transmitted infections are treated with tonics made from this medicinal herb” [56-58]. Omilani [59] suggested that “when the leaves of *Momordica charantia* and *Vernonia amygdalina* are squeezed in water to extract juice, this extract can be used to treat gonorrhoea, vulvovaginitis, and syphilis. Additionally, the plant can be used in the brewing sector to produce beer instead of hops” [60].

Table 3. Properties/uses of *Vernonia amygdalina*

| Properties | Phytochemical (s) involved | Type of extract | Reference |
|-------------------------------|---|------------------------------------|-----------|
| Anti-inflammatory | Flavonoid, tannin, saponin | Acetone extract | [8] |
| | Flavonoid, saponin | EthYL and EthOL extracts | [61] |
| | Nil | Water extract | [62] |
| | Trigonelline | Ethanol extract | [63] |
| Anti-bacterial/anti-microbial | Saponin, tannin, alkaloid | Coconut water extract | [6] |
| | Saponin, flavonoid, alkaloid | Water extract | [64] |
| | Flavonoids, terpenoids, saponin, alkaloid | Boiled water extract | [65] |
| | Flavonoid and tannin | Aqueous and hydroethanolic extract | [66] |
| Anti-cancer | Apigenin (flavonoid) | Ethanol extract | [67] |
| | Nil | Ethanol extract | [68] |

| Properties | Phytochemical (s) involved | Type of extract | Reference |
|-------------------------|---|------------------------------------|-----------|
| Anti-diabetic | Nil | Water-ethanol extract | [69] |
| | Vernoniaolide glucoside | Methanol extract | [70] |
| | flavonoid, alkaloid | Aqueous extract | [71] |
| | glycoside | Methanolic stem bark extract | [72] |
| Antihyperglycemic | Flavonoid, tannin, saponin | Benzene extract, ethanol extract | [73] |
| | flavonoids | Hydroalcoholic extract | [69] |
| Hepatoprotective effect | flavonoids, saponins, tannins, and alkaloids | Ethanol extract | [63] |
| | flavonoid, alkaloid, phenolics | Water extract | [74] |
| Hypolipidemic | Flavonoid, tannin, saponin | methanol extract, ethanol extract | [73] |
| Antidiarrheal | Flavonoid, tannin, saponin, alkaloid | 80% methanol | [75] |
| | Tannin, alkaloid | 80% methanol | [76] |
| | Flavonoids, terpenoids, saponin, alkaloid | Boiled water extract | [65] |
| | Flavonoid and tannin | Aqueous and hydroethanolic extract | [66] |
| Anti-helminthic | Glucuronolactone (lactone) | Methanolic stem bark extract | [72] |
| | Terpenoids, phenols, sesquiterpene lactones, | ethanolic extract | [77] |
| | Coumarins, triterpenes, flavonoids, sesquiterpene lactone | The animals ate the leaves | [78] |
| Anti-oxidant | flavonoids and vernosides | The animals ate the leaves | [78] |
| Anti-pyretic | Saponin, and flavonoids | Aqueous extract | [56] |
| Anti-nociceptive | Saponin | Aqueous extract | [56] |

8. ANTI-INFLAMMATORY EFFECT

Inflammation is part of the body's complex biological response to an irritant or harmful stimuli, such as damaged cells or pathogens. It is a natural defense mechanism that the body employs to help maintain homeostasis and promote tissue repair. However, excessive inflammation can result in cellular, tissue, or organ dysfunction. Inflammation also contributes to the development of acute vascular events and diseases like obesity, Crohn's disease, psoriasis, diabetes, and cancer [79,18,80]. Pro-inflammatory molecules like tumor necrotic factor α (TNF α), certain interleukins, prostaglandins, and even pathogenic nitric oxide concentrations raise inflammatory response. Many current anti-inflammatory drugs target these mediators of inflammation at different levels. Yet, their long-term use is sometimes restricted because of their lack of specificity and side effects [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" [81]. These phytochemicals were believed to be responsible for the anti-oxidative effect observed. Another research from Georgewill and Georgewill, [62] "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. [61], which suggested 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.

Lastly, a study from Prananda et al. [63] indicated that *Vernonia amygdalina* may exert its

protective effects by modulating the inflammatory response and mitigating the harmful consequences of inflammation in doxorubicin-induced hepatic and renal damages.”

9. 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 their study revealed that the mixture of *Vernonia amygdalina* and *Cocos nucifera* water showed a broad-spectrum antibacterial activity, with efficacy increasing with higher concentrations. Their results suggested 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. According to Prananda et al. [64], the water extracts of *vernonia amygdalina* showed anti-microbial effects against *Escherichia coli* and *Staphylococcus aureus* at 25mg/ml.

10. ANTICANCER EFFECT

Research from Hasibuan et al, [67] “indicated the presence of diterpene (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 compounds in *Vernonia amygdalina*. The presence of apigenin in *Vernonia amygdalina* contributes to its anti-cancer properties, as apigenin, a natural product belonging to the flavone class, possesses the ability to inhibit several types of cancer such as breast, liver, pancreatic, and lung” [82]. Apigenin carries this function by triggering cell apoptosis, inducing autophagy, and modulating the cell cycle. Apigenin can also decrease the motility of cancer cells and inhibit cancer cell migration and invasion [83]. Coumarin, a plant-derived secondary metabolite with anti-cancer properties, can also be found in *Vernonia amygdalina*. Coumarines such as imperatorin and esculetin inhibit the proliferation of cancer cells through cell cycle arrest [67, 84].

In another study by Joseph et al. [68], 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 (IC₅₀) 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, nuclear fragmentation in MCF-7 cells, and induced apoptosis. Additional research from Nkono et al. [69] indicated that *Vernonia amygdalina* extract may activate tumor suppressor genes, such as the TP53 gene implicated in numerous cancers, to promote programmed cell death or slow its cycle.

11. ANTI-DIABETIC EFFECT

Ejiofor et al. [70] carried out a study to isolate the phytochemicals in the methanolic stem-bark extract of *Vernonia amygdalina*. Novel and new compounds were isolated using the column chromatographic technique in this study. The result obtained from this study indicated that one of the isolated compounds - 6β,10β,14β-Trimethylheptadecan-15α-olyl-15-O-β-D-glucopyranosyl-1,5β-olide (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.

Another study by Nkono et al. [69] discussed that certain biflavonoids such as luteolin, luteolin 7-O-B-glucuronoside, and luteolin 7-O-B-glucoside were found in the leaves of *Vernonia amygdalina*. Since it is known that flavonoids are involved in regulating blood sugar, it is probable that the hypoglycemic activity of *Vernonia amygdalina*, which was reported in their study, may be a function of its rich flavonoid content. *Vernonia amygdalina* was also able to simultaneously suppress gluconeogenesis and potentiate glucose oxidation via the pentose phosphate pathway in streptozotocin-induced diabetic rats. It was able to reverse the loss in weight observed in diabetic rats. Since weight loss indicates the presence of diabetes, a reversal of this confirms the efficiency of VA in treating diabetics [71].

12. HEPATOPROTECTIVE EFFECT

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

Research from Tokofai et al. [74] showed that birds treated with CCl₄ + *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 CCl₄-induced liver damage. Also, SOD and CAT were better upregulated in birds treated with CCl₄ and supplemented with VALE. Their study suggested that improvement in endogenous enzymes is among VALE's protective mechanisms of action. Similarly, Prananda et al. [63] 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* to treat various health disorders.

13. HYPOLIPIDEMIC EFFECT

Research has shown that the buildup of lipoproteins and triglycerides is implicated as risk factors in the progression of coronary heart disease [73]. A study from Rawat and Reddy [85] showed that *Vernonia amygdalina* at 200 mg/kg reduced hepatic triglyceride biosynthesis and favored cholesterol redistribution among lipoprotein molecules. It also significantly elevated plasma HDL-cholesterol levels, indicating its protective role against cardiovascular diseases. These findings are consistent with the research results of Alozie et al. [73], which suggested 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 substantial decrease of elevated LDL-cholesterol concentration.

14. ANTI-DIARRHEAL EFFECT

Research by Mosisa Gudeta et al., [75] "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." "At the end of 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 [76]. "The aqueous extract of

Vernonia amygdalina reduced diarrhea caused by microbial loading in piglets" [51]. Studies from Dognon et al. [52] showed that the ethanolic extract of *Vernonia amygdalina* was able to inhibit the ability of *Salmonella typhimurium* to cause diarrhea

15. ANTI-HELMINTHIC EFFECT

Research results from Adaramoye et al. [86] revealed that the "methanol extracts of *vernonia amygdalina* showed anthelmintic activities against earthworms. In this study, the methanol extract of *Vernonia amygdalina* not only caused paralysis but also killed the earthworm". Also, in a study by Ejiofor et al., [70] "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" in a study by Degu et al. [77]. "*Vernonia amygdalina* showed antihelminthic and anticoccidial effects in rabbits fed with both leaves and stalk" [78]. "*Vernonia amygdalina* extracts were found to possess anthelmintic activity against *Ascaridia galli* due to the inhibition of embryonation of eggs and the reduction in fecal egg count" [72]

16. TOXICITY

In a study by Wang et al. [49], the result of the research indicated the presence of lead in *Vernonia amygdalina* but in a very minute quantity. This study emphasized that moderate consumption of bitter leaves has no lead toxicity risk and poses no danger to health.

17. CONCLUSION

Vernonia amygdalina, or bitter leaf, is a potent medicinal plant with diverse therapeutic benefits. Its rich bioactive compounds contribute 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 complete clinical applications.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

The author(s) hereby declare that generative AI technologies, such as Large Language Models,

etc., have been used during the writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology, as well as all input prompts provided to the generative AI technology.

Details of the AI usage are given below:

1. **AI Technology Used:**

- Name: ChatGPT
- Version: GPT-4
- Model: GPT-4 architecture
- Source: OpenAI

2. **Purpose of AI Use:**

- The AI was used to assist with editing the reference section of the manuscript.

3. **Input Prompts Provided:**

- Example prompts include:
 - "Generate a Vancouver-style reference for the article "Kaur, D., Kaur, N., & Chopra, A. (2019). A comprehensive review on phytochemistry and pharmacological activities of *Vernonia amygdalina*. *Journal of Pharmacognosy and Phytochemistry*, 8(3), 2629-2636"

4. **Human Supervision:**

- All content generated by the AI was thoroughly reviewed, revised, and validated by the authors to ensure accuracy, relevance, and adherence to the scope of the manuscript.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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