Minireview Article

Ethnomedicinal, and phytopharmacological aspects of *Vernoniaamygdalina*(Bitter leaf) utilized as a traditional medicinal herb

Abstract

Vernoniaamygdalina*Delile**, commonly known as bitter leaf, is a shrub in the Asteraceae family, widely seen in tropical regions of Africa.Vernoniaamygdalina***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.*Vernoniaamygdalina*possesses enormous therapeutic potential. It has demonstrated several effects such as antimicrobial, anti-inflammatory, anticancer, antioxidant, andantidiabeticeffects 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.*Vernoniaamygdalina* 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 VernoniaAmygdalina)significantlyminimizes diabetics through the regulation of blood sugar. Furthermore, the plant exhibits hepatoprotective and nephroprotective effects, protecting liver and kidney damage from toxins.*Vernoniaamygdalina* continues to be an important topic of traditional and modern medical research due to its rich phytochemical profile and several therapeutic properties. This articlewas written by the authors to bring together the recent progress in studying the therapeutic potential of *Vernoniaamygdalina*.

Keywords: *Vernoniaamygdalina,* phytochemicals, extracts, effects, bitter leaf

1. INTRODUCTION:

"*Vernoniaamygdalina*Delile, belonging to the familyAsteraceae, is a shrub or small tree.*Vernoniaamygdalina* 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 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. *Vernoniaamygdalina* has been shown to have antimalarial,antimicrobial, anti-inflammatory, anti-oxidant, antipyretic, antidiabetic, antibacterial, and anticancer properties" [1-3]."*Vernoniaamygdalina* has been used in the treatment of emesis, nausea, diabetes, loss of appetite-induced abrosia, amoebic dysentery, and other gastrointestinal tract problems". [4-5]*Vernoniaamygdalina* 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 150 articles and then to 86 articles. Articles were included if they specifically discussed the medicinal and therapeutic properties of *Vernoniaamygdalina*. Search terms such as "*Vernoniaamygdalina*," "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: *Vernoniaamygdalina*

[7]

Figure 1: *Vernoniaamygdalina* (Bitter leaf) leaves sourced from Satellite Town, Lagos, Nigeria.

4. PHYTOCHEMICAL COMPOSITION:

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

Table 1: Some phytochemicals found in *Vernoniaamygdalina* 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]	Vernodalineinhibits cell proliferation, adhesion, and metastasis and induces apoptosis in cancer cells [17]. Vernodaline exhibits its antiproliferation and 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 2 (MMP-2), and matrix metalloproteinase 9 (MMP9). 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 cytoc hrome c into the cytosol [80]
			antibacterial, anticancer, antihelminthic, and antioxidant	[16]	
Vernonioside V	leaf	+	Anti-inflammatory	[18]	N/A
Cynaroside (Luteolin-7-O-glucoside)	leaves	+	Anti-oxidant	[19]	
Tannins	leaves	+	Anti-oxidant,	[20] [21]	Plant tannins exhibit anti-inflammatory effects by inhibiting NO and prostaglandin-E2 (PGE2), regulating cytokine expression, reducing the production of inflammatory
			anti-cancer, anti-microbial	[22]	

					substances, and enhancing complexation with other molecules [23]. 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 [23].
Alkaloids	leaves	+	Anti-parasitic, anti-microbial	[24]	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 nuclear factor-kappa-light-chain-enhancer of activated B cells (NF-kB), extracellular signal-regulated protein kinase 1/2 (ERK1/2), Akt, and signal transducer and activator of transcription 1(STAT1) as well as inflammatory mediators, that is, prostaglandin E2 (PEG2), nitric oxide (NO), cytokines, and chemokines [26]
			anti-microbial	[22]	
			Anti-inflammatory	[26]	
Flavonoids (quercetin, rutin, kaempferol, daidzein,	leaves	+	Anti-oxidant	[20]	The anti-cancer effects of flavonoids are exerted by their ability to modulate
			anti-microbial	[22]	
			Anti-cancer	[27]	

naringenin, hesperidin, anthocyanins (cranberry) apigenin, baicalein, luteolin, fisetin, epigallocalechin-3-gallate and oligonal**)**			Anti-inflammatory	[28]	ROS-scavenging enzyme activities, participate in arresting the cell cycle, induce apoptosis, and autophagy, and suppress cancer cell proliferation and invasiveness [27] 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 also inflammatory enzymes [29]. Flavonoid that inhibits inflammation include quercetin, rutin, kaempferol, daidzein, naringenin, hesperidin, anthocyanins (cranberry) apigenin, baicalein, luteolin, fisetin, epigallocalechin-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 elicit their antioxidant effects [31]
Saponins	leaves	+	anti-microbial, anti-cancer	[22]	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 [33]
Phenolic	leaves	+	Anti-oxidant	[20] [32]	The antioxidant functions

Compounds			Anti-aging, anti-microbial	[22]	of phenolic compounds are achieved through scavenging free radicals, regulating nuclear factor-like 2 (NRF2) /ARE signaling pathways, and regulating enzymes such as Superoxide dismutase (SOD), Glutathione S-Transferases (GST), and, glutathione (GSH) [34]
Steroids	leaves	+	Anti-inflammatory, anti-cancer	[20]	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	[24]	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. DIETARY COMPOSITION:

The result of the proximate analysis of *Vernoniaamygdalina*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: Nutrient compositionof*Vernoniaamygdalina* (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 and hence prevent the absorption of excess cholesterol
	15.48±0.07 %	Leaves	[42]	
Lipids and Fats	Present	Leaves	[41]	Fats function to help insulate body organs against shock, and to 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 in the proper functioning of the nerves, muscles, and heart.
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/100mlto 600.00 mg/100 ml	Leaves	[44]	A component of bones, cells, in energy processing, in DNA & 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			
	11.0 ± 0.0 mg	Leaves	[47]	
Copper	Fresh leaves: 0.31 mg/100 g	Leaves	[41]	Copper can also be used in promoting incisional wound healing, killing cancer cells, Positron Emission Tomography (PET) imaging, radio immunological tracing, and radiotherapy of cancer [48]
	Dried leaves: 0.24–0.29 mg/100 g			
Vitamin A	Present	Leaves	[49]	Possess 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 parts of the body

6. TRADITIONAL USE:

"*Vernoniaamygdalina* is a perennial herb belonging to the Asteraceae family. Plant extracts of *Vernoniaamygdalina* 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].

7. ETHNOPHARMACOLOGICAL PROPERTIES:

"There are various traditional, industrial, medical, and culinary uses for *Vernoniaamygdalina*. 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 *Momordicacharantia* and*Vernoniaamygdalina*are squeezed in water to extract juice, this extract can be used to treat gonorrhea, 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"[60].

Table 3: Properties/uses of *Vernoniaamygdalina*

Property	**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]
	Nil	Water-ethanol extract	[69]
Anti-diabetic	Vernoniaolide glucoside	Methanol extract	[70]
	flavonoid, alkaloid	Aqueous extract	[71]
	glycoside	Methanolic stem bark extract	[72]
	Flavonoid, tannin, saponin	Benzene extract, ethanol extract	[73]
Antihyperglycemic	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	Leaves were eaten by the animals	[78]
Anti-oxidant	flavonoids and vernosides	Leaves were eaten by the animals	[78]
Anti-pyretic	Saponin, and flavonoids	Aqueous extract	[56]
Anti-nociceptive	Saponin	Aqueous extract	[56]

8. 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" [79,80,81]."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" [8]. Hence, there is a constant demand for better therapeutic alternatives.

Research work from Adedapo et al, [8] showed that "the acetone extract of *Vernoniaamygdalina* significantly reduced paw edema in histamine-induced rats. The mechanism believed to be responsible for this is that reportshave shown that *vernoniaamygdalina* possesses flavonoids, tannins, and saponins" [82]. These phytochemicals are 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 suggests that both EthYL and EthOL extracts of *Vernoniaamygdalina* might act as peripheral analgesics, altering the local reaction caused by the release of inflammatory mediators.

Prananda et al, [63]"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".

9. ANTIBACTERIAL EFFECT:

Research from Matthew et al, [6] showed that "the extracts of *Vernoniaamygdalina* and *Cocos nucifera* water had significant antibacterial activity.Results of research from this study revealed that the mixture of *Vernoniaamygdalina* and *Cocos nucifera* water showed a broad-spectrum antibacterial activity, with efficacy increasing with higher concentrations. 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. Water extracts of vernoniaamygdalina showed anti-microbial effects against *Escherichia coli* and *Staphylococcus aureus* at 25mg/ml" [64].

10. ANTICANCER EFFECT:

Research from Hasibuan et al, [67]"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 *Vernoniaamygdalina*.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" [83]. "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" [84]."Coumarin can be found in *Vernoniaamygdalina* and is a potential anticancer agent.Coumarines such as **imperatorin** and **esculetin** inhibit the proliferation of cancer cells through cell cycle arrest" [67, 85].

In another study by Joseph et al, [68], the results of the researchshowed that the ethanol extract and *Vernoniaamygdalina*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 *Vernoniaamygdalina* 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) [69]"indicates that Vernoniaamygdalina 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".

11. ANTI-DIABETIC EFFECT:

A study by Ejiofor et al, [70] isolated thephytocompounds present in the methanolic stem-bark extract of *Vernoniaamygdalina*. 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 vernoniaamygdalina, 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, [69] discussed that the leaves of *Vernoniaamygdalina* 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 *Vernoniaamygdalina* as reported in this study, maybe a function of its rich flavonoid content. Also, *Vernoniaamygdalina*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[71].

12. 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, [74] showed that birds treated with CCl_4 + *Vernoniaamygdalina* 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_4-induced liver damage. Also, SOD and CAT were better upregulated in birds treated with CCl_4 and supplemented with VALE. This suggests that improvement in these endogenous enzymes is among VALE's protective mechanisms of action. Similarly, Prananda et al, 's[63]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.

13. HYPOLIPIDEMIC EFFECT:

The buildup of lipoproteins and triglycerides is implicated as risk factors in the progression of coronary heart disease [73]. *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[86]. These findings are consistent with the research results of Alozie et al, [73] 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.

14. ANTI-DIARRHEAL EFFECT

Research by MosisaGudeta et al, [75]"in which castor oil was used to induce diarrheal in mice showed that the extract of*Vernoniaamygdalina*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 *Vernoniaamygdalina*as an antidiarrheal agent.The crude extract of *Vernoniaamygdalina*inhibiteddiarrhea significantly by extending its onset and reducing the frequency of defecation"[76]. "The aqueous extract of *Vernoniaamygdalina*reduced diarrhea caused by microbial loading in piglets" [51]. Studies fromDougnon et al, [52] showed that the ethanolic extract of *Vernoniaamygdalina* was able to inhibit the ability of *Salmonella typhimurium* to cause diarrhea

15. ANTI-HELMINTHIC EFFECT:

"Methanol extracts of vernoniaamygdalina showed anthelminthic activities againstearthworms. The normal mode of action of anthelmintic is to cause paralysis of the worm. Still, the methanol extract of *Vernoniaamygdalina* was not only able to cause paralysis but also to kill the earthworm" [25]. In a study by Ejiofor et al, [70]"the compound CMP3 (glucuronolactone) extracted from *Vernoniaamygdalina* caused paralysis and death of the helminth (*Eiseniafoetida*)"."The ethanolic extracts of *Vernoniaamygdalina*had anthelmintic efficacy on *Toxocaracanis* in dogs" [77]."*Vernoniaamygdalina* showed antihelminthic and anticoccidial effects in rabbits fed with both leaves and stalk" [78]."V*ernoniaamygdalina* extracts were found to possess anthelmintic activity against *Ascaridiagalli* due to the inhibition of embryonation of eggs and the reduction in faecal egg count" [72]

16. TOXICITY:

"The toxicity for *Vernoniaamygdalina* 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" [49].

CONCLUSION:

Vernoniaamygdalina, 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 *Vernoniaamygdalina's* potential as a complementary treatment and underscore the need for further research to explore its full clinical applications.

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Details of the AI usage are given below:

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2. **Purpose of AI Use**:

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

3. **Input Prompts Provided**:

- Example prompts include:
    - "List some examples of phytochemicals found in *Vernoniaamygdalina*."
    - "Generate a Vancouver-style reference for the article 'Gasaliyu et al., Effects of Vernoniaamygdalina methanol leaf extract and fractions on Ascaridiagalli'."

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.

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