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Ethnobotanical Significance and Traditional uses of *Vernonia Amygdalina* (Bitter Leaf): A Comprehensive Review

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ABSTRACT: *Vernonia amygdalina* Delile (Asteraceae), commonly known as bitter leaf, is a culturally and medically significant African ethnobotanical resource used widely as both food and medicine. Despite its ubiquity across West, Central, and East Africa, knowledge of its applications, phytochemistry, and pharmacology remains fragmented across disparate local surveys and laboratory studies. This review synthesizes ethnobotanical records, phytochemical profiles, pharmacological findings, and toxicological evidence to provide a comprehensive understanding of *V. amygdalina* and identify priority areas for future research. Ethnobotanical data reveal broad applications, including treatment of malaria, gastrointestinal disorders, helminth infections, diabetes, wounds, postpartum conditions, and use in cultural rituals. Preparation methods—such as leaf washing, crushing, decoction, infusion, and topical poultices—reflect both culinary and medicinal traditions. Key phytochemicals include sesquiterpene lactones (e.g., vernolide, vernodalol, vernodalin), flavonoids (e.g., luteolin and luteolin-7-O-glucoside), phenolic acids, saponins, tannins, and alkaloids. These constituents exhibit antimalarial, antimicrobial, antidiabetic, anticancer, hepatoprotective, anti-inflammatory, and antioxidant activities in experimental models. However, clinical validation remains limited to a single controlled malaria trial demonstrating partial symptomatic relief but inadequate parasite clearance. Toxicological studies indicate low acute toxicity at dietary

and traditional-use doses, though high-dose or prolonged exposure may elicit hepatic or renal stress, and isolated sesquiterpene lactones show cytotoxicity at micromolar concentrations. Safety concerns also arise from potential contamination of commercial dried leaf products. Conservation and sustainability challenges include overharvesting of wild stocks, habitat pressure, and variable phytochemical quality linked to environmental factors. Major knowledge gaps include region-specific ethnobotanical documentation, standardized dosing, mechanistic pharmacology, chronic toxicity, reproductive safety, and genetic diversity mapping. Future research should prioritize multi-center clinical trials, integrated omics approaches, cultivation and conservation programs, and value-chain improvement for safe commercialization. Overall, *V. amygdalina* represents a compelling example of “food-as-medicine,” offering nutraceutical, pharmacological, and socio-economic potential. Its sustainable development will require coordinated interdisciplinary approaches that respect traditional knowledge while applying modern scientific rigor.

INTRODUCTION

Vernonia amygdalina Delile (synonym sometimes reported as *Gymnanthemum amygdalinum*), commonly known as bitter leaf, is a perennial shrub of the Asteraceae family native to tropical Africa (Ogwu and Ikhajiagbe, 2024). The species grows widely across West, Central and East Africa and has been introduced to parts of Asia and South America (Degu et al., 2024). Its bitter taste is attributed to diverse secondary metabolites (sesquiterpene lactones, alkaloids, saponins, tannins) that also underlie many of its reported pharmacological activities (Degu et al., 2024; Danladi et al., 2018). Traditional knowledge systems use *V. amygdalina* leaves, stems, roots, and occasionally inflorescences as food, medicine, and in cultural practices; its roles range from everyday culinary uses (as a leafy vegetable in soups and stews) to remedies for malaria, gastrointestinal ailments, diabetes, wounds, and fertility problems (Degu et al., 2024; Ogwu and Ikhajiagbe, 2024). The plant’s prominence in both folk medicine and as a dietary vegetable makes it an interesting subject for integrative ethnobotanical review and translational research.

Although numerous regional ethnobotanical surveys and laboratory studies exist, the knowledge is dispersed across short reports, local journals, and laboratory papers; comprehensive synthesis that explicitly cross-references traditional uses with phytochemical and pharmacological evidence is valuable for guiding clinical translational work and conservation efforts. This review therefore aims to: (1) collate and critically evaluate ethnobotanical records of *V. amygdalina* across Africa, (2) summarize methods of preparation and cultural contexts of use, (3) review phytochemical constituents and relevant pharmacology, (4) assess toxicology and clinical data, and (5) identify knowledge gaps and research priorities for safe, ethical, and sustainable development of *V. amygdalina*-based interventions.

BOTANICAL DESCRIPTION AND DISTRIBUTION

Taxonomy and nomenclature

Vernonia amygdalina Delile is in the family Asteraceae (Compositae). The species is commonly referred to as “bitter leaf” in English, “onugbu” among the Igbo (Nigeria), and by various local names across African language groups; some taxonomic treatments have used the genus *Gymnanthemum* for related taxa, and regional floras may record synonyms — careful taxonomic verification is needed when comparing studies. The vernacular multiplicity underscores the need to verify voucher specimens when linking ethnobotanical claims to plant chemistry.

Morphology

Mature *V. amygdalina* grows as a shrub or small tree (height reported up to ~7 m in some sources) with rough grey-brown bark. Leaves are oblong-lanceolate, typically 10–15 cm long and 4–5 cm wide, often with a distinct venation pattern; flowers are small, creamy white, borne in dense terminal and axillary inflorescences (Degu et al., 2024). Many phytochemical studies derive material from the fresh or air-dried leaves; morphological identification and deposition of voucher specimens in herbaria are inconsistently reported in older studies, limiting direct comparability.

Ecology and distribution

Native to tropical Africa, *V. amygdalina* thrives in humid forest margins, riverine zones, woodlands and cultivated fallows, and tolerates elevations up to ~2,800 m and annual precipitation between roughly 750–2,000 mm (Degu et al., 2024). It is widely cultivated or tolerated in home gardens and agroforestry systems across Nigeria, Ghana, Uganda, Ethiopia, Kenya, Tanzania, and parts of Yemen and Brazil (Degu et al., 2024; Ogwu and Ikhajiagbe, 2024). The plant's adaptability to various soils and climates contributes both to its accessibility as a folk remedy and to pressures from overharvesting in some locales if wild populations are collected unsustainably.

METHODOLOGY

A systematic literature approach was used to collate ethnobotanical, phytochemical and pharmacological information on *V. amygdalina*. Databases searched included PubMed/MEDLINE, Web of Science, Scopus, ScienceDirect, Google Scholar, and publisher platforms (Frontiers, Springer, Wiley) through March 2024. Search terms used alone and in Boolean combinations included: “*Vernonia amygdalina*,” “bitter leaf,” “ethnobotany,” “traditional uses,” “phytochemistry,” “pharmacology,” “clinical trial,” and country or region names (e.g., Nigeria, Uganda, Ghana). Inclusion criteria prioritized peer-reviewed articles, open-access reviews, clinical trials, and high-quality ethnobotanical surveys; relevant grey literature and reputable book chapters were considered when primary data were sparse. Non-English sources were examined when an English abstract provided sufficient data; older reports (pre-1990) were retained only if frequently cited by modern reviews. Data extraction templates recorded geographic origin, plant part used, preparation method, ethnomedical indication, active compound(s) identified (if any), experimental evidence (in vitro, in vivo, clinical), and safety/toxicity notes. Where possible, voucher specimen information and botanical verification were captured. The review synthesis emphasizes studies with clear methodology and reproducible extraction/assay procedures.

Ethnobotanical uses (by region)

This section compiles traditional uses, preparation methods, and cultural contexts reported across Africa. Uses are organized by region (West Africa, Central Africa, East Africa, and other reported areas) and by major therapeutic domains (infectious disease—malaria/parasites, gastrointestinal, metabolic—diabetes, reproductive health, hematological uses, topical/wound care, and veterinary uses). The regional subsections highlight both consensus uses and notable local variations.

WEST AFRICA (NIGERIA, GHANA, CAMEROON, SIERRA LEONE)

Culinary and everyday uses

In West Africa, *V. amygdalina* leaves are widely employed as a cooked leafy vegetable. In southeastern Nigeria the leaves (locally called “onugbu”) are washed—often repeatedly or blanched—to reduce bitterness and incorporated into soups (e.g., ofe-onugbu) and stews as both a flavoring and nutritive green (Degu et al., 2024; Ogwu and Ikhajiagbe, 2024). Preparation methods vary: some households crush and rinse leaves multiple times, some briefly boil before addition to soups, and others ferment or combine with other herbs. The dietary role contributes to micronutrient intake (protein, vitamins, and minerals) in local diets (Degu et al., 2024).

Malaria and febrile illnesses

Across Nigeria and neighboring countries, decoctions or infusions of fresh leaf juice are used as an antimalarial remedy and for febrile illnesses. Several ethnobotanical surveys document community reliance on leaf infusions where formal health resources are limited (Degu et al., 2024; Sha’a et al., 2021; Challand and Willcox, 2009). Notably, ethnomedical usage informed clinical testing of an infusion for uncomplicated malaria in Uganda, where an infusion produced an adequate clinical response in some patients but incomplete parasitological clearance and high recrudescence—suggesting partial clinical benefit but need for standardization and optimization (Challand and Willcox, 2009).

Gastrointestinal, parasitic and febrile complaints

Traditional claims for the treatment of diarrhea, intestinal worms, dyspepsia and stomach upset are common in West African ethnomedicine. Preparations include decoctions administered orally or leaf juice taken as a tonic; other uses include postpartum treatments for retained placenta or uterine cleansing in some cultural contexts (Degu et al., 2024; Damtie, 2023;

Enebeli-Ekwutoziam et al., 2021). Ethnobotanical reports also record use as an anthelmintic and for treating schistosomiasis symptoms, though formal clinical validation for these indications in humans is lacking.

Topical and wound uses

Crushed leaves or leaf extracts are traditionally applied to wounds, sores, and skin infections, often combined with poultices or in conjunction with honey or other plant preparations. Antimicrobial claims are frequent in folk reports and have motivated multiple *in vitro* antibacterial and antifungal assays (Ugbogu et al., 2021).

Cultural and ritual roles

Beyond clinical uses, *V. amygdalina* plays roles in cultural rituals and daily life: as chewing sticks (dental hygiene), for postpartum practices, and sometimes for beauty or fertility rituals in particular ethnic groups; for example, some Hausa women attribute changes in sexual attractiveness to the plant (ethnographic notes in region surveys). These culturally embedded meanings can affect harvesting, gendered patterns of use, and transmission of knowledge.

The widespread antimalarial use documented ethnographically has motivated considerable laboratory work. Extracts and isolated compounds (sesquiterpene lactones such as vernodalol and vernolide) show activity against several *Plasmodium* life stages *in vitro* and *in vivo* models and demonstrate transmission-blocking properties in mosquito assays, which helps rationalize some traditional antimalarial uses; however, cytotoxicity in mammalian cell lines at higher concentrations is also reported, indicating narrow therapeutic windows for some fractions and a pressing need for safety profiling (Babylon et al., 2025; Degu et al., 2024; Bihonegn et al., 2019; Omoregie et al., 2010).

CENTRAL AFRICA (CAMEROON, DEMOCRATIC REPUBLIC OF CONGO, GABON, EQUATORIAL GUINEA)

Culinary uses

In Cameroon and parts of Gabon, *V. amygdalina* leaves are cooked as a staple vegetable in stews and porridges, often paired with groundnuts, palm oil, or smoked fish. In Bamileké cuisine, bitter leaf stews (ndolé) are a celebrated dish, prepared by prolonged washing or boiling of the leaves to achieve a characteristic balance of mild bitterness and nutty flavor (Degu et al., 2024).

Malaria and febrile conditions

Ethnobotanical surveys in Cameroon and DRC record decoctions of leaves and stems as febrifuges and antimalarial remedies. Some communities combine *V. amygdalina* with other antimalarial plants (e.g., *Azadirachta indica*, *Cymbopogon citratus*) for synergistic effect (Ugbogu et al., 2021).

Gastrointestinal and hepatic disorders

In rural Gabonese and Congolese communities, leaf infusions are taken for stomachaches, dysentery, and jaundice. These uses parallel hepatoprotective and antimicrobial activities demonstrated in experimental models, though direct clinical corroboration in humans is sparse (Degu et al., 2024).

Veterinary and ethnoveterinary uses

Farmers in Cameroon and Gabon report using leaf decoctions for deworming goats and poultry, treating ectoparasites, and improving livestock appetite. This aligns with reports from West Africa where leaf juice is given to horses to increase stamina (“Chusar Doki” among Hausa herders) (Japhet and Godgift, 2021; Ugbogu et al., 2021).

EAST AFRICA (UGANDA, KENYA, TANZANIA, ETHIOPIA)

Food uses and fermentation traditions

In parts of Uganda and Kenya, *V. amygdalina* is less commonly a staple vegetable but is incorporated into mixed greens and occasionally boiled as a famine food. In Ethiopia, leaves and twigs are used as a flavoring and bittering agent in the traditional beer “tela” and sometimes as a hops substitute (Degu et al., 2024). In Sidama communities, the plant also has ritual significance in seasonal celebrations.

Antimalarial and anti-parasitic uses

Ugandan herbalists prepare cold water infusions or decoctions of freshly crushed leaves for malaria, sometimes sweetened to increase patient compliance (Challand & Willcox, 2009). In Ethiopia and Tanzania, decoctions are used not only for malaria but also for helminthiasis and amoebic dysentery (Ugbogu et al., 2021).

Oral hygiene and dental health

In Uganda, stems are chewed as “chewing sticks” for cleaning teeth, similar to *Salvadora persica*. This use is supported by in vitro studies showing inhibition of oral pathogens by *V. amygdalina* extracts (Ugbogu et al., 2021).

Cultural beliefs and non-medicinal uses

In southern Ethiopia, smoke from burning *V. amygdalina* twigs is used as a fumigant in households, believed to repel insects and purify the air. Stems and branches may also be used as light fuelwood in rural households (Degu et al., 2024). The ethnobotanical uses of *V. amygdalina* in West Africa, Central Africa and East Africa is presented in Table 1.

Table 1. Ethnobotanical Uses of *Vernonia amygdalina* Across Regions

Region	Plant Part Used	Preparation Method	Traditional Indications	Key References
West Africa (Nigeria, Ghana)	Leaves, stems	Leaf washing, decoction, infusion, juice	Malaria, GI disorders, helminths, postpartum care, food	Degu 2024; Ugbogu 2021
Central Africa (Cameroon, DRC)	Leaves, stems	Decoctions, mixed herbal remedies	Malaria, dysentery, jaundice, veterinary uses	Ugbogu 2021
East Africa (Uganda, Ethiopia, Kenya)	Leaves, twigs	Infusions, chewing sticks, fumigation	Malaria, oral hygiene, helminths, cultural rituals	Challand & Willcox 2009; Degu 2024

Preparation methods and cultural context

Leaf preparation and bitterness reduction

A central feature of *V. amygdalina* preparation is the reduction of its intense bitterness, which is attributed to sesquiterpene lactones (e.g., vernolide, vernodalol). Common methods include:

- **Washing and squeezing:** fresh leaves are crushed and repeatedly rinsed in water.
- **Blanching:** briefly boiling leaves before final cooking.
- **Fermentation:** in some areas, leaves are slightly fermented before cooking, reportedly to mellow flavor and enhance digestibility.
- **Combination cooking:** mixing with fatty ingredients (palm oil, groundnuts) or aromatic herbs to balance bitterness.

These methods are not purely culinary; some are thought to influence medicinal potency. For example, cold infusions without washing are preferred for malaria treatment, to retain full bitterness and perceived “strength” (Ugbogu et al., 2021).

Dosage forms in traditional medicine

Reported dosage forms include:

- **Fresh leaf juice** (crushed leaves squeezed in water, taken orally).
- **Decoction** (boiled leaves and/or stems, taken warm or cooled).
- **Infusion** (leaves soaked in cold or warm water, often overnight).

- **Poultice** (crushed leaves applied to skin).
- **Chewing sticks** (fresh stems).

Volume and duration vary widely; some healers prescribe “a cup twice daily for three days” for malaria, while others recommend continued use for up to two weeks. Such variability complicates standardization for clinical research (Challand and Willcox, 2009).

Cultural-symbolic dimensions

In some ethnic groups, bitterness is associated with cleansing, purification, or moral strength, and the act of consuming bitter plants like *V. amygdalina* may carry symbolic weight. Postpartum women in certain Nigerian communities consume bitter leaf soup as part of “restoration” diets; in Ethiopia, its use in beer is partly symbolic of resilience and endurance.

Phytochemistry and Pharmacological Correlates

Overview of phytochemical composition

Phytochemical screening and targeted isolation studies of *Vernonia amygdalina* have revealed a complex mixture of bioactive secondary metabolites, including:

- **Sesquiterpene lactones (STLs)** — e.g., vernolide, vernodalin, vernodalol, vernoamyside B, vernolepin.
- **Flavonoids** — e.g., luteolin, luteolin-7-O- β -glucoside, isorhamnetin, apigenin.
- **Phenolic acids** — e.g., caffeic acid, chlorogenic acid.
- **Saponins** — triterpenoid saponins, steroidal saponins.
- **Alkaloids** — unspecified in many studies but reported as part of crude leaf extracts.
- **Other constituents** — tannins, glycosides, coumarins, and essential oils in trace amounts.

The relative abundance of these classes can vary with extraction method, plant part, developmental stage, and geographic origin (Degu et al., 2024; Ugbogu et al., 2021).

Sesquiterpene lactones

Vernolide and vernodalol

Vernolide and vernodalol are STLs widely cited as contributors to the plant’s bitter taste and multiple bioactivities.

- **Antiplasmodial activity:** In vitro and in vivo models show activity against *Plasmodium falciparum* and *P. berghei*, with IC₅₀ values in the low micromolar range (Wahyuni et al., 2023). Vernodalol also exhibits transmission-blocking effects against mosquito-stage parasites.
- **Anticancer potential:** Vernodalin and vernodalol demonstrate cytotoxicity toward certain human cancer cell lines (e.g., breast, colon, prostate), often through apoptosis induction and cell cycle arrest; however, they also show cytotoxicity toward normal cells at higher doses (Degu et al., 2024).
- **Antimicrobial effects:** Some STL fractions inhibit *Staphylococcus aureus* and *Candida albicans* in vitro (Samuel et al., 2025; Teia et al., 2021; Ugbogu et al., 2021).

Vernolepin

Vernolepin is a STL with notable platelet anti-aggregant activity and DNA polymerase inhibition, reported in older pharmacological studies and hypothesized to contribute to anti-thrombotic effects (Ugbogu et al., 2021; Laekeman et al., 1985).

FLAVONOIDS

Luteolin and derivatives

Luteolin and its glycosides (notably luteolin-7-O- β -glucoside) are consistently detected in polar extracts.

- **Antioxidant:** Potent radical scavenging activity in DPPH, ABTS, and FRAP assays.
- **Anti-inflammatory:** Inhibition of pro-inflammatory cytokines (TNF- α , IL-6) and modulation of NF- κ B signaling in cell models.
- **Antidiabetic:** Enhancement of insulin sensitivity and glucose uptake in rodent models (Degu et al., 2024).

Isorhamnetin

Isorhamnetin has demonstrated antimicrobial and antioxidant activities in both crude extract and isolated form, and may synergize with STLs for broad pharmacological effects (Degu et al., 2024).

Saponins and tannins

Saponins in *V. amygdalina* extracts may contribute to hypoglycemic and cholesterol-lowering effects observed in animal models, as well as membrane-permeabilizing actions relevant to antimicrobial effects. Tannins, meanwhile, can precipitate proteins and exhibit antimicrobial properties, though their role in therapeutic activity is less well-characterized for this species (Tran et al., 2024; Talwar et al., 2024; Ugbogu et al., 2021; Wang et al., 2018).

Phenolic acids

Caffeic and chlorogenic acids are present in methanolic extracts and contribute to antioxidant activity; chlorogenic acid in particular may play a role in hepatoprotective effects via modulation of oxidative stress and inflammatory pathways (Tura et al., 2024; Degu et al., 2024; Wang et al., 2018; Santana-Gálvez et al., 2017). The phytochemicals identified in *V. amygdalina* is summarized in Table 2.

Table 2. Major Phytochemicals Identified in *V. amygdalina*

Phytochemical Class	Representative Compounds	Reported Activities
Sesquiterpene lactones	Vernolide, Vernodalol, Vernodalol, Vernolepin	Antimalarial, anticancer, antimicrobial
Flavonoids	Luteolin, Luteolin-7-O-glucoside, Isorhamnetin	Antioxidant, anti-inflammatory, antidiabetic
Phenolic acids	Chlorogenic acid, Caffeic acid	Antioxidant, hepatoprotective
Saponins	Various triterpenoid saponins	Hypoglycemic, antimicrobial, cholesterol-lowering
Tannins	—	Astringent, antimicrobial

LINKING PHYTOCHEMISTRY TO PHARMACOLOGICAL ACTIVITY

Antimalarial

Multiple compounds — notably STLs (vernolide, vernodalol) — have demonstrated in vitro activity against *Plasmodium* species, with some evidence for gametocytocidal and transmission-blocking effects (Abay et al., 2015). These laboratory results align with widespread ethnomedicinal use for malaria, but clinical translation is still limited to one controlled trial (Challand & Willcox, 2009), which reported partial symptomatic benefit without consistent parasite clearance.

Antimicrobial

Crude extracts and fractions show antibacterial effects against Gram-positive and Gram-negative bacteria (e.g., *S. aureus*, *E. coli*, *Pseudomonas aeruginosa*), and antifungal activity against *Candida* spp. The activities are generally moderate compared to

standard antibiotics, but they support ethnobotanical claims for wound and infection treatment (Raji et al., 2025; Akintunde et al., 2025; Musyoki, 2024; Ugbogu et al., 2021).

Anticancer

In vitro studies indicate cytotoxic activity against breast, colon, cervical, and prostate cancer cell lines. Mechanistic studies suggest induction of apoptosis via mitochondrial pathways, cell cycle arrest at G2/M phase, and modulation of pro-apoptotic and anti-apoptotic gene expression. These effects are mainly attributed to STLs and certain flavonoids (Satria et al., 2024; Degu et al., 2024; Hasibuan et al., 2024; Yedjou et al., 2022; Fachrunisa et al., 2019; Wong et al., 2013).

Antidiabetic and metabolic

Aqueous and methanolic extracts reduce fasting blood glucose, improve lipid profiles, and enhance antioxidant enzyme activities in diabetic rat models. Mechanisms may involve stimulation of insulin secretion, increased glucose uptake in peripheral tissues, and reduced hepatic gluconeogenesis (Adekemi et al., 2024; Anosike et al., 2024; Asante and Wiafe, 2023; Jayaweera et al., 2022; Ugbogu et al., 2021; Akah et al., 2008).

Hepatoprotective

Extracts mitigate chemically induced liver injury (e.g., carbon tetrachloride, paracetamol) in rodents, likely through antioxidant effects, membrane stabilization, and modulation of hepatic enzyme activities (Degu et al., 2024; Ogunmoyole et al., 2022; Raimi et al., 2021; Adegbeye et al., 2017).

Anti-inflammatory and analgesic

Both aqueous and ethanol extracts reduce carrageenan-induced paw edema and acetic acid-induced writhing in mice, suggesting prostaglandin pathway modulation.

The various pharmacological activities of *V. amygdalina* is presented in Table 3.

Table 3. Summary of Pharmacological Activities

Activity	Evidence Type	Key Findings	Active Constituents
Antimalarial	In vitro, in vivo, clinical	Moderate suppression; partial symptom relief in trial	STLs (vernolide, vernodalol)
Antimicrobial	In vitro	Effective against <i>S. aureus</i> , <i>E. coli</i> , <i>Candida</i>	STLs, flavonoids, tannins
Antidiabetic	Animal models	↓ fasting glucose, ↑ insulin sensitivity	Flavonoids, saponins
Hepatoprotective	Animal models	↓ ALT/AST, oxidative protection	Chlorogenic acid, flavonoids
Anticancer	In vitro	Cytotoxicity, pro-apoptotic pathways	STLs, flavonoids

TOXICOLOGICAL AND SAFETY ISSUES

Ethnomedical perceptions of safety

In most traditional settings across West, Central, and East Africa, *Vernonia amygdalina* is generally perceived as safe when used in the amounts typical for food or short-term medicinal use. As a vegetable, it is consumed in large quantities over a lifetime in some communities without obvious toxicity, which has contributed to its “food-as-medicine” profile (Ugbogu et al., 2021). However, traditional healers sometimes caution against prolonged intake of high-concentration decoctions, particularly for pregnant women, citing risks of uterine contractions or miscarriage — a belief echoed in certain ethnographic surveys (Muoka et al., 2025; Degu et al., 2024; Isa et al., 2014; Achema et al., 2012).

Acute toxicity studies in animals

Several rodent studies have assessed acute toxicity using leaf extracts:

- **Aqueous extract:** LD₅₀ values in mice and rats are generally above 2,000 mg/kg body weight, suggesting low acute toxicity (Abebe and Gebru, 2015).
- **Crude aqueous extract:** Higher doses (>5,000 mg/kg) have been tolerated without mortality, though transient behavioral changes (reduced activity, mild diarrhea) have been observed (Azubuike et al., 2022). Histological examination at sub-lethal doses often shows no major organ pathology, though mild reversible hepatic changes have been reported in some studies.

Cytotoxicity of isolated compounds

Sesquiterpene lactones such as vernodalol and vernolide display cytotoxic effects in vitro on both cancerous and normal cell lines at micromolar concentrations (Mahapatra et al., 2025). While this is valuable for anticancer potential, it raises concerns for narrow therapeutic windows if concentrated fractions are used in humans. In ethnomedicine, the whole-plant preparations are typically less concentrated, possibly mitigating this risk.

Clinical trial safety data

The only published controlled human trial (Uganda, uncomplicated malaria) used an infusion of fresh leaves prepared in boiled water, administered twice daily for 7 days (Challand & Willcox, 2009). Reported safety outcomes included:

- No serious adverse events in the treatment group.
- Mild transient gastrointestinal upset in a small proportion of participants.
- No significant changes in hematological or liver function parameters at follow-up.

This suggests good tolerability for short-term use at doses comparable to traditional medicine preparations. However, the trial did not evaluate long-term safety or use in special populations (e.g., pregnant women, children under 5).

Heavy metals and contaminants

One emerging concern — particularly for commercially sold dried leaves in urban and export markets — is contamination with heavy metals (lead, cadmium, mercury) and microbial pathogens due to unhygienic drying or storage conditions. While peer-reviewed data on *V. amygdalina* specifically are scarce, similar leafy herbs in the same markets have shown contamination levels especially from data from Port Harcourt, Nigeria exceeding WHO limits, underscoring the need for monitoring and quality control in both domestic and international trade (Onwuli et al., 2025).

Overall, *V. amygdalina* appears safe at dietary and short-term medicinal doses, with low acute toxicity in animals and good tolerability in the only published clinical trial. Potential safety issues include:

1. Dose-dependent hepatic and renal effects with prolonged high-dose use.
2. Cytotoxicity of concentrated sesquiterpene lactone fractions.
3. Possible uterotonic effects — caution in pregnancy.
4. Risk of contamination in market-sold products.

Future research should focus on standardized safety assessments, including reproductive toxicity studies, drug–herb interaction evaluations, and surveillance of contaminants in traded material.

CONSERVATION, SUSTAINABILITY, AND COMMERCIAL POTENTIAL

Current cultivation and harvesting practices

Vernonia amygdalina is cultivated and harvested both for subsistence and commercial purposes across sub-Saharan Africa. In rural settings, it is frequently grown in home gardens, intercropped with staples such as cassava (*Manihot esculenta*) and maize

(*Zea mays*), or maintained along field boundaries as a perennial shrub (Ugbogu et al., 2021). The plant's tolerance to varied soil types and its drought resistance make it a reliable household vegetable crop.

Harvesting is usually done by pruning young leaves or tender shoots, which stimulates regrowth. However, in regions where *V. amygdalina* is harvested from wild stands—especially in parts of Central Africa—there is evidence of overharvesting during the dry season when demand is high and cultivated supply is low (Degu et al., 2024).

THREATS TO SUSTAINABILITY

Habitat loss

Although *V. amygdalina* is not listed as threatened on the IUCN Red List, agricultural expansion, urbanization, and infrastructure development can fragment habitats and reduce wild populations. While cultivated stocks buffer supply, wild accessions may possess valuable genetic diversity for resilience and medicinal potency.

Overexploitation for medicinal markets

The growing popularity of herbal teas, capsules, and exported dried leaves in African diaspora markets has increased commercial demand. Without regulated harvesting, this can lead to local depletion of wild plants, particularly in areas where they are not systematically cultivated (Ugbogu et al., 2021).

Climate change impacts

Projected shifts in rainfall patterns in West and Central Africa may influence *V. amygdalina*'s phenology, phytochemical profile, and disease susceptibility. This may indirectly affect both yield and medicinal quality (Degu et al., 2024).

Conservation strategies

Community-based cultivation programs

Encouraging smallholder farmers to domesticate *V. amygdalina* in home gardens and on farms can reduce pressure on wild stands. Integration into agroforestry systems may improve biodiversity and soil health while ensuring year-round supply (Ugbogu et al., 2021).

Germplasm conservation

Botanical gardens and agricultural research institutes in Nigeria, Ghana, and Kenya have initiated ex situ conservation through seed banking and vegetative propagation trials. These programs aim to safeguard genetic diversity for breeding programs and climate adaptation (Degu et al., 2024).

Sustainable harvesting guidelines

Establishing locally adapted harvesting protocols—such as limiting leaf removal to <50% of canopy biomass at any one time—can help maintain plant vigor and long-term productivity. Training for harvesters is essential to ensure adoption.

COMMERCIAL AND INDUSTRIAL POTENTIAL

Nutraceuticals and herbal supplements

The documented antioxidant, antimalarial, and antidiabetic properties of *V. amygdalina* have spurred interest in commercial herbal products, including teas, tinctures, powdered capsules, and functional food ingredients. Diaspora demand in Europe and North America has created niche export markets, though regulatory compliance and quality control remain critical barriers (Ugbogu et al., 2021).

Agro-industrial uses

Beyond medicinal and culinary roles, *V. amygdalina* has potential in natural pesticide formulations due to its sesquiterpene lactones' insecticidal activity. Pilot studies in Nigeria have shown efficacy against storage pests such as *Sitophilus zeamais* in maize (Degu et al., 2024).

Economic empowerment potential

Cultivation and trade of *V. amygdalina* products can provide income opportunities for women and smallholder farmers, especially when linked to cooperatives or fair-trade initiatives. Development agencies in Uganda and Cameroon have integrated bitter leaf into livelihood diversification programs with promising socio-economic outcomes (Ugbogu et al., 2021).

Challenges in commercialization

1. **Standardization** — Variations in phytochemical content across regions and seasons complicate product standardization.
2. **Quality control** — Microbial and heavy metal contamination in dried leaf products is a persistent problem.
3. **Regulatory compliance** — Export markets often require stringent documentation for herbal supplements, which small-scale producers may find difficult to obtain.
4. **Intellectual property and benefit sharing** — Ensuring that local communities receive equitable benefits from commercialization is a continuing ethical challenge.

Outlook

With strategic investment in cultivation, quality assurance, and equitable market access, *V. amygdalina* could become a flagship African leafy vegetable in global nutraceutical and functional food markets. However, sustainability hinges on balancing commercial expansion with conservation and fair benefit sharing.

Gaps in Knowledge and Recommendations for Future Research

Gaps in ethnobotanical documentation

While *Vernonia amygdalina* is widely known and studied in West and Central Africa, there are substantial documentation gaps in certain regions:

- **Underrepresentation of Eastern and Southern Africa** — Detailed ethnobotanical records from Tanzania, Malawi, and Mozambique are sparse compared to Nigeria and Cameroon.
- **Loss of indigenous knowledge** — Urbanization and shifting diets have reduced intergenerational transfer of preparation and medicinal-use knowledge, leading to possible erosion of unique local applications.
- **Cultural-context analysis** — Few studies integrate symbolic, ritual, and socio-cultural aspects of *V. amygdalina* into the ethnopharmacological narrative.

Pharmacological research gaps

Limited clinical validation

The majority of biomedical evidence for *V. amygdalina* comes from *in vitro* and animal studies. Only one controlled human trial (Challand & Willcox, 2009) has been published, focusing on malaria. No randomized controlled trials have addressed:

- Diabetes management.
- Hypertension and cardiovascular protection.
- Cancer-related supportive therapy.
- Antimicrobial efficacy in human infections.

Mechanistic studies

While bioactive compounds such as vernodalinal, vernolide, and luteolin have been identified, the precise mechanisms of action for many claimed activities (e.g., immunomodulatory, hepatoprotective) remain speculative. Integration of metabolomics, transcriptomics, and proteomics in future work could clarify molecular pathways.

Dose–response relationships

Traditional use does not follow standardized dosing, making translational research challenging. Most pharmacological studies test arbitrary doses without correlating them to realistic human intake levels. This hampers the development of dosage guidelines for safe and effective use.

Safety and toxicology research needs

1. **Reproductive toxicity studies** — Ethnobotanical reports warn against use during pregnancy, but there is no controlled animal or human study confirming teratogenic or uterotonic risks.
2. **Drug–herb interactions** — Given its use alongside antimalarial and antidiabetic pharmaceuticals, potential pharmacokinetic and pharmacodynamic interactions should be evaluated.
3. **Chronic exposure effects** — There is a lack of multi-year studies on habitual dietary intake of *V. amygdalina*, particularly at medicinal doses.

Conservation and sustainability research gaps

- **Wild genetic diversity mapping** — There is no comprehensive phylogeographic study documenting genetic variation across its native range, which would be critical for breeding and climate resilience.
- **Impact of climate change** — Longitudinal studies linking environmental factors to phytochemical composition are absent.
- **Sustainable yield studies** — Empirical data on optimal harvesting intensity and frequency for both wild and cultivated populations are limited.

Recommendations for future research

1. **Ethnographic deep-dives** — Conduct region-specific, participatory ethnobotanical surveys to document unique preparation methods, cultural contexts, and rare uses before they disappear.
2. **Multi-center clinical trials** — Design randomized controlled trials for major health claims (malaria, diabetes, hypertension), with standardized extracts and rigorous placebo controls.
3. **Integrated omics approaches** — Apply modern analytical platforms to uncover mechanistic insights and link specific phytochemicals to observed bioactivities.
4. **Safety standardization** — Develop WHO-aligned monographs including pharmacopoeial standards, dosing ranges, and toxicology profiles.
5. **Value-chain research** — Investigate post-harvest handling, storage, and processing methods to minimize contamination and preserve bioactive compounds.
6. **Conservation genomics** — Map and preserve wild genetic resources, incorporating them into breeding programs for high-yield and high-bioactivity cultivars.

Bridging the gap between traditional knowledge and modern scientific validation is both a challenge and an opportunity. *V. amygdalina*'s extensive ethnobotanical footprint and promising pharmacological profile make it a candidate for integration into evidence-based phytotherapy and functional foods. However, realizing this potential will require coordinated interdisciplinary research, fair benefit-sharing with indigenous communities, and sustainable resource management.

CONCLUSION

Vernonia amygdalina Delile occupies a unique position at the intersection of food, medicine, and culture in sub-Saharan Africa. Its dual role as a nutritious leafy vegetable and a widely used medicinal plant underscores the principle of “food as medicine” long embedded in African traditional knowledge systems. Ethnobotanical surveys reveal its application in the management of a broad spectrum of ailments, from malaria and gastrointestinal disorders to diabetes and hypertension, supported in part by pharmacological studies demonstrating antioxidant, anti-inflammatory, antimalarial, and antidiabetic effects.

Despite this rich heritage and emerging scientific support, substantial gaps remain in clinical validation, safety standardization, and mechanistic elucidation. Only limited human trials have been conducted, and the translation of in vitro and animal data to human health outcomes remains incomplete. Addressing these gaps through well-designed, multi-center randomized controlled trials, integrated omics research, and standardized extract development is essential to establish *V. amygdalina* as an evidence-based therapeutic agent.

From a sustainability perspective, *V. amygdalina* is generally resilient and adaptable, yet increased commercial demand—both domestically and internationally—poses risks of overexploitation in wild populations, particularly where cultivation is limited. Community-based cultivation programs, germplasm conservation, and sustainable harvesting protocols can safeguard this resource while enabling equitable market participation for local producers.

The plant's potential for commercialization in nutraceuticals, functional foods, and natural pesticides offers significant opportunities for rural economic empowerment. However, these must be pursued in a framework that respects intellectual property rights, ensures benefit-sharing with indigenous communities, and maintains environmental integrity.

In conclusion, *V. amygdalina* represents more than just a bitter leaf; it is a nexus of tradition, nutrition, medicine, and sustainable livelihoods. Realizing its full potential will require a concerted, interdisciplinary effort—linking ethnobotany, pharmacology, agronomy, and socio-economics—grounded in both scientific rigor and cultural respect. In doing so, this iconic African plant could emerge as a model for how traditional botanical knowledge can inform and enrich modern health care and sustainable development.

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