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Review on Nutritional and Medicinal Values of *Vernonia amygdalina* and its Uses in Human and Veterinary Medicines

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Abstract: *Vernonia amygdalina*, a member of the *Asteraceae* family, is a small shrub that grows in the tropical Africa. Here we try to review the health and nutritional benefits of bitter leaf (*V. amygdalina*), a homely plant that grows almost everywhere especially in the tropical areas of Africa. It is a multi-purpose plant that has a number of potential uses both in human and Veterinary medicines. It is regarded as a wonderful gift from God to mankind because of its numerous medicinal values including cure for stomach ache, skin infections, diabetes, insomnia, tooth ache, acne, pneumonia, stoke, arthritis, fatigue, cough and bleeding. It is also established that the plant has anti-parasitic, anti-bacterial, anti-inflammatory and anti-helminthic properties. Bitter leaf detoxifies the whole system and it is useful in toning vital organs of the body especially liver and kidney. Nutritionally, bitter leaf is one of the leafy vegetables that have been used to alleviate the problems of micronutrients malnutrition as it is exceptionally rich in proteins, vitamins and mineral elements including iron, phosphorus, calcium, potassium, zinc, copper, folic acids and ascorbic acid. It is further maintained that bitter leaf can be put into use in soap making, ornaments, substituted for hop in beer brewing, restoration of stamina as well as contribution to carbon sequestration there by reducing environmental degradation.

Key words: Bitter Leaf · Health · Nutrition · *V. amygdalina* · Veterinary Medicine

INTRODUCTION

Traditional medicines occupy a central place among rural communities of developing countries for the provision of health care in the absence of an efficient public health care system [1]. The use of traditional remedies is common in sub-Saharan Africa and visits to traditional healers remain a mainstay of care for many people because of preference, affordability and limited access to hospitals and modern health practitioners [2, 3].

V. amygdalina (Del. composite of the family *Astaraceae*) commonly called bitter leaf and/or also referred to as iron weed is the most widely cultivated species of the genus *Vernonia* which has about 1,000 species of shrubs [4]. It was named after an English Botanist William Vernon. *V. amygdalina* is frequently found in gardens, adapt to a variety of climates unlike other plants that are native to certain areas and grown in many countries, in savannah zones and cultivated fields [5].

Although most popularly used for food, it has also, been traditionally used for its medicinal properties [6]. True to its name, bitter leaf is bitter to taste but surprisingly delicious in meals. Bitter leaf has anti-helminthic and antimalarial properties [7].

In Ethiopian highland, *V. amygdalina* has been classified by the farmer as a multipurpose fodder tree with high biomass yield, easy propagation, high adaptability and high compatibility with other crops which do not compete with them for soil nutrients or moisture but instead help to improve the soil fertility and growth of perennial crops [8, 9]. Regardless of these facts the plant is used for treatment of various ailments in human as well as animal health in different parts of the country.

The objective of this paper is to review the medicinal values of *V. amygdalina* in human and veterinary medicines.

Compound Isolated from *V. amygdalina*: Several investigators have isolated and characterized a number of chemical compounds with potent biological activities from the leaves of *V. amygdalina*. Some of the previously isolated constituents in *V. amygdalina* (Del.) include:

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sesquiterpene lactones [10-13] flavonoids like luteolin, luteolin 7-O-glucosides and luteolin 7-O-glucuronide, steroid glycosides and vernonioside A, B, A_1, A_2, A_3, B_2, B_3 and A_4 [14,15]. Edotides from the aqueous extract of the plant was also characterized [16-19]. Very recently, sesquiterpene lactones, epivernodalol and another elemanolide from the dichloromethane fraction are isolated and characterized from *V. amygdalina* [19].

Traditional Uses of *V. Amygdalina*: Bitter leaf is an abundant source of the poly-unsaturated fatty acids, linoleic and linolenic. These poly-unsaturated fatty acids have been found to be protective against cardiovascular disease [20-22]. It is very useful in the care of the liver and kidney and multi healer. It should be taken always for good health [6, 15]. It soothes inflamed joints and eradicates pains common with arthritis or rheumatism patients [23] and also used for improvement of contraction during labour, treatment of toothache, hypertension, whooping cough, gingivitis and sexually transmitted diseases [24].

Leaves of this plant are used in Nigeria as a green vegetable or as a spice in soup, especially in the popular bitter-leaf soup. Such preparation includes freshly harvested leaves which are macerated with either cold or hot water to reduce the bitterness of the leaves to a desirable level. The latter are then added with other condiments for the soup while the water extract may be taken as a tonic to prevent certain illnesses. The leaves can be taken as an appetizer and the water extract as a digestive tonic [25].

The leaves have also been used in Ethiopia as hops in preparing tela beer [26]. The leaves are widely used for fevers and are known as a quinine–substitute in Nigeria and some other African countries [27]. The young leaves are used in folk medicine as anti-helminthic, antimalarial, laxative/purgative, enema, expectorant, worm expeller and fertility inducer in sub-fertile women and female animals. Some wild chimpanzees in Tanzania had been observed to use this plant for the treatment of parasite related diseases [28, 29].

Biological Properties of *V. amygdalina*

Antioxidant Properties: The antioxidant and cytoprotective activities of boiled, cold and methanolic extracts of nine edible vegetables in Southwest Nigeria were evaluated in the 1, 1-diphenyl-2-picrylhydrazyl free radical assay and hemagglutination assay in bovine erythrocytes, respectively [30]. The antioxidant effects of an aqueous extract of *V. amygdalina* leaves against acetaminophen-induced hepatotoxicity and oxidative stress in mice also described. Pre-administration of *V. amygdalina* resulted in a dose-dependent reversal of acetaminophen-induced alterations of all the liver function parameters and suppressed acetaminophen-induced lipid peroxidation and oxidative stress [31].

The antioxidant mechanism of *V. amygdalina* has been justified recently [32] and it has been attributed to the presence of flavonoids, as reported by Igile *et al.* [12]. The advantage of this antioxidant property has been revealed in neurotoxic studies since it has been established that flavonoids can traverse the blood brain barrier [33].

Chemo Preventive Properties: The inhibitory activity of the chloroform extract of *V. amygdalina in vitro* against cells derived from human carcinoma of the nasopharynx carried in tissue culture [34]. Bioassay-guided fractionation of the extract yielded two compounds namely *vernodalin* (C19H20O7) and *vernomygdin* (C19H25O7), both of which had cytotoxic properties (14). The aqueous extract was a potent inhibitor of cultured human breast tumors cells (MCF-7) growth *in vitro*. This may imply tumour stabilization or preventive effects *in vivo.* Applying the reverse-phase chromatography method, fractions of *V. amygdalina* extract was found to inhibit DNA synthesis [10, 11,35,36].

Nutritional Values and Chemical Composition of *V. Amygdalina*: The leaves and young shoots are cooked as vegetables, rich in protein, vitamins and mineral elements. Bitter leaf is one of the leafy vegetables that have been used to alleviate the problem of micronutrients, malnutrition and it is very prominent in tropical Africa [37]. The leaves are relatively inexpensive and rich in several nutrients especially â-carotene and vitamin C which are essential for human health. It is also rich in minerals like iron, phosphorus, calcium and potassium [24,38].

Bitter leaf is also rich in carotene, proteins, ascorbic acid, iron, folic acid and dietary anemia factors [7]. Carotene normalizes the synthesis of female sex hormones, allowing women to stay young and healthy for long. In industrial countries, bitter leaf is used for their fortification of some common foods. The micronutrients in bitter leaf include: iron, magnesium, copper, sodium, zinc and potassium [39].

Table 1: Bioactive compound isolated from *V. amygdalina*

Compound	Class of compound
Vernodalol	Sesquiterpene lactones
Vernodalin	Sesquiterpene lactones
Vernomygdlin	Sesquiterpene lactones
Vernoniosides D and E	Steroid glucoside
Vernoniosides A_4, B_2, B_3	Steroid glucoside
Vernoniosides A_1,A_2, A_3,B_1	Steroid glucoside
Epivernodalol	Sesquiterpene lactones

Sources: [14- 21].

Table 2: Constituents of *V. amygdalina* (mg/100 dry matter)

Constituent	Value (g/mg)
Crude protein	25.10g
Ash	17.13g
Cellulose content	12.31g
Edible	100g
Fats	0.4g
Proteins	5.2g
Water	82.0g
Energy	218g
Carbohydrate	10.0g
Dietary fiber	1.5g
Calcium	145mg
Phosphorus	0.7mg
Iron	5.0mg
Zinc	85.0mg
Manganese	710.0mg
Ascorbic acid	5.1mg

Sources: [40].

Medicinal Values of *V. amygdalina*

Anti-Bacterial Activity: The antimicrobial activity of hot and cold ethanolic extract of *V. amygdalina* showed that the extracts possess antibacterial activity against *S. aureus, P. aeruginosa and E. coli. P. aeruginosa* found the most sensitive organisms to the hot ethanolic extract of *V. amygdalina* with the zone of inhibition of 13.00 mm and *S. aureus* show zone of inhibition of 6.00 mm at the same concentration (200 mg/ml) [41-43]. A similar plant species, *V. tenoreana*, contains saponins, flavonoids, tannins and anthraquinones was found to have very potent antibacterial as well as antifungal activities [44]. These phytochemical constituents are responsible for many antimicrobial activities of different plant species in human and animal health [45-46].

Aqueous extracts of *V. amygdalina* leaves was evaluated *in-vitro* for anti-microbial activity against *S. aureus* and *E. coli* [47]. The minimal inhibitory concentration of the aqueous extract was found to be 62.50 mg/ml, while the minimal bactericidal concentration of the aqueous extract was 250mg/ml.

Anti-Inflammatory and Anti-pyretic Activity: Inflammation is a common tissue phenomenon when tissue exposed to trauma or injury [48-50]. The preliminary phytochemical test on the leaves of *V. amygdalina* showed the presence of saponins, alkaloids, flavonoids, tannins, glycosides, carbohydrate and reducing sugar. Many plants containing alkaloids and flavonoids have been shown to have diuretic, antispasmodic, anti-inflammatory and analgesic action [51].

The anti-inflammatory activity of the extract of *V. amygdalina* which was comparable in magnitude to the activity of dexamethasone may be explained in part, to be a consequence of the presence of flavonoids, tannins, glycosides and trace elements such as zinc, copper and manganese [5]. The leaf and root extract of *V. amygdalina* possess antipyretic property. The antipyretic activity is strongly noticed with the leaf extract as compared to the root [52,53].

Brewer's yeast has been shown to induce pyrexia in laboratory animals, in similar manner to lipopolysaccharides. Such induction activates the arachidonic acid pathway and has been associated with elevated prostaglandin E2 (PGE2) level in the hypothalamus [54]. Antipyretic agents in the plant have been shown to antagonize the PGE2 elevation by inhibiting the activity of cyclo-oxygenase there by suppressing pyrexia [55].

Anti-Malarial Activity: Malaria is one of the most important tropical diseases and the greatest cause of hospitalization and death among children age 6 months to 5 years [56,57]. The alarming rate at which *plasmodium falciparum* has developed resistance to chloroquine and other synthetic anti-malarial drugs makes it necessary to search for the more effective anti malarial compounds [58]. Traditional medicinal plants are frequently used to treat or cure malaria [59,60]. Both aqueous and ethanolic extracts of the stem bark and leaves of *V. amygdellina* are reported to have been used as purgative, antimalarial [17, 19] and in the treatment of eczema [61]. The leaves, root and twig of the plant are used for treating malaria infection [16, 18-20, 62].

The presence of some bitter sesquiterpenes lactones compounds such as, *vernolide, vernodalin, hydroxy vernolides* and the steroid related constituents, *vernoniosid* B_1 and *vernonoid* B_1 in the bitter leaf are responsible for anti-plasmodia activity especially *P. falciparum* [15, 18,63]. These compounds found to be present in the leaves and the pith of young shoots of the plants which may be responsible for its bitter taste and significant bioactivity [27].

Anti-Cancer Activity: There has been growing interest in combination therapy for cancer as it induces a greater effect in the improvement of patients' survival. Since cancer is the result of the accumulation of numerous mutations, it is rational to combine two or more drug with different mechanisms of action to increase cell killing [64-66]. *V. amygdalina* Del (Composite) is an African medicinal plant well known for providing the anticancer agents like *vernodaline* and *vernolide*. *Vernodaline* and *vernolide* elicited anti tumor activities in leukemia cell. Recently reported that some peptide (Edotides) from the aqueous extract of *V. amygdalina* showed cell growth inhibitory effects in prostate cancer cell line (PC-3) [35].

V. amygdalina combines with a current chemotherapeutic alkylating agent, doxorubicin, to determine their synergistic effect in human breast cancer cells. Doxorubicin exerts its effects by intercalating base pairs between DNA, there by inhibiting both DNA and RNA synthesis. In addition, it mediates its main cytotoxic action through inhibiting the activity of topoisomerase II, which is an enzyme responsible for the uncoiling of DNA [67]. The anti-cancer effect of *V. amygdalina* was first show in human carcinoma of nasopharynx and later in leukemia cell p-388 and L-1210 using the chloroform extract of *V. amygdalina* and similar effects were also reported in valuable domestic animals [68].

Anti-Helminthic Activity: The anti-helminthic efficacy of the aqueous crude extract from *V. amygdalina* on *Toxocaracanis* (Ascarids) and *Ancylostoma caninum* (Hook worm) is well established. The anti-helminthic activity of the crude extracts could be attributed to secondary plant metabolites that could be present [69]. The ethanolic extract of this plant inhibited 55.4% larval migration at 2mg/ml and the dichloromethane extract showed 67.1% inhibition of migration at 3mg/ml while ethanol extracts inhibited egg hatching by 72.6% by the lowest concentration tested (0.15mg/ml). However, there was no activity on larval migration inhibition (LMI) with n-hexane extract at any concentration explored despite, both the ethanolic and dichloromethane extract inhibited egg hatching by >90% at higher concentration [70].

The anti-helminthic assay performed on adult earthworms (*Lumbricus terrestris*) due to its physiological resemblance with the intestinal roundworm parasite of human beings [71] also gave clue on the effect of the plant. From phytochemical screening all the extracts have alkaloids, tannins and glycosides which have been associated with anthelmintic activity [72].

Alkaloids in the aerial parts of *Cissampelos capensis* (*Menispermaceae*) and *Macleaya microcarpa* (Maxim) fade is known to be responsible for their anti-helminthic activity [48, 73]. Tannins are known to produce anti-helminthic activity by binding to glycoprotein on the cuticle of the parasite. They hinder energy production in helminthic parasites by uncoupling oxidative phosphorylation [74]. This effect is also true in most nematodes in human and veterinary medicines. Comparing anthelmintic activity of *V. amygdalina* and *Alstoniaboonei* to piperazine (A known GABA mimetic anthelmintic), the extracts may contain constituents that could probably have weak GABA-mimetic effect similar to piperazine citrate [74,75].

CONCLUSION

The nutritional and medicinal benefits of *V. amygdalina* assist in combating malnutrition, prevention of many diseases as well as contributing to the food security system of rural areas. Medicinal plants are in danger due to marketing and using of them for different activities. Thus, public enlightenment programmes should be encouraged on the importance of *V. amygdalina* due to its nutritional and health benefits. Research should be needed to determine the optimal doses and concentrations of the preparation and to identify the side effects of the remedies. Every citizen should give care and conserve the plant in its natural habitat.

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