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Article · July 2017

DOI: 10.1016/j.bjbas.2017.07.007

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Review Article

Vernonia amygdalina: A folkloric herb with anthelminthic properties

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ARTICLE INFO

Article history:
Received 21 April 2017
Received in revised form 12 June 2017
Accepted 19 July 2017
Available online xxxx

Keywords:
Vernonia amygdalina
Folkloric medicine
Helminth infection
Bioactive compounds

ABSTRACT

Vernonia amygdalina, a widely grown shrub plant in Africa is consumed as vegetable and has high medicinal value. It has gained wide application in the treatment and management of various diseases. The leaves are useful components for herbal medicine constitution. The plant's activities is a result of diverse bioactive compounds isolated from the different parts of the plant. These metabolites have specifically been efficacious against parasites especially worms. The mechanisms of activities include paralysis of worm, 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. Effort should be made towards standardizing the extract(s) of *V. amygdalina* for use in alternative medicine for treatment of helminth-related diseases.

Contents

1. Introduction

Vernonia amygdalina Del (Asteraceae) is a small shrub with dark green leaves and rough barks growing predominantly in tropical Africa but has been domesticated in many parts of West Africa (Igile et al., 1994). It is a perennial plant with height between 1 m and 6 m (Nwosu et al., 2013). *V. amygdalina* Del is soft wooded and is a multipurpose and rapid regenerating shrub. Its bitter taste has made it to be fondly called "bitter leaf" and it is also referred to by several local names in different languages of different regions (Table 1). Anti-nutritional phytochemicals within the plants are responsible for its bitter taste (Bonsi et al., 1995). The leaves are consumed as green leafy vegetable. Its richness in minerals and vitamins has made it an important human diet (Sobukola et al., 2007). It has a wide folkloric uses against diverse tropical diseases. More importantly it has gained wide application in the treatment of amoebic dysentery (Moundipa et al., 2000), gastrointestinal disorders (Akah and Ekekwe, 1995), antimicrobial and antiparasitic activities (Akinpelu, 1999; Hladik et al., 2005). Some of the

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http://dx.doi.org/10.1016/j.bjbas.2017.07.007
2314-8535/

Please cite this article in press as: Oyeyemi, I.T., et al. *Vernonia amygdalina*: A folkloric herb with anthelminthic properties. Beni-Suef Univ. J. Basic Appl. Sci. (2017), http://dx.doi.org/10.1016/j.bjbas.2017.07.007

Table 1
Local names for *Vernonia amygdalina* in some African countries.

Country	Local name	References
Nigeria	Ewuro, Onugbu, Oriwo, Etidot, Ityuna, Chusar doki, Fatefata	Farombi and Owoeye (2011)
Uganda	Omubirizi, Mululuza	Njan et al. (2008) and Kigbua et al. (2016)
Ethiopia	Ebichaa	Yineger and Yewhalaw (2007)
Tanzania	Omubilizi	Moshi et al. (2010)
Ghana	Awonwono	Komlaga et al. (2015)
Guinea	Bantara bururé, Dakuna, Kossa fina	Burkill (1985)
Sierra Leone	Nje nyani, An-gbèntho	Burkill (1985)
Togo	Aluma, Gbondutsi	Agbodeka et al. (2016)
Cameroon	Ndoleh, Ying	Simbo (2010)
Rwanda	Umubilizi	Mukazayire et al. (2011)

identified bioactive compounds of *V. amygdalina* responsible for its ethnobotanical uses include alkaloids, saponins, terpenes, lignans, flavonoids, phenolic acids, steroids, anthraquinone, coumarins, sesquiterpenes, xanthones and edotides (Izevbigie, 2003; Cimanga et al., 2004; Muraina et al., 2010).

Helminth infections have become serious concerns in Africa affecting humans' wellbeing and causing high economic loss. Several broad-spectrum anthelminthic drugs commercially available have been widely adopted to improve livestock production and reduce disease morbidity in man. Helminths resistance to many of these available drugs are becoming a threat in some countries (Kumsa and Wosene, 2006; Devi et al., 2009) due to poor dosing and therapeutic strategies (Waller, 1993, 1997). The eco-friendly nature of plants has necessitated the search for anthelminthic drugs from them and *V. amygdalina* could be a probable source owning to its numerous folkloric uses. We have chosen to review studies on the anthelmintic properties of the plant so as to broaden our knowledge in this respect and laden us with information on best practice which could be useful for future anthelminthic chemotherapy development.

2. *Vernonia amygdalina* – distribution and cultivation

V. amygdalina is found in nature closed to rivers and lakes, in forests margins, woodland and grassland up to 2800 m altitude, in areas with mean annual rainfall 750–2000 mm. The plant can tolerate drought although humid environment is more suitable for its growth (Ndaeyo, 2007). It can thrive on all types of soil but grows better on humus-rich soils, these probably underscores its ability to thrive on a range of ecological zones.

In Nigeria, it is a commonly cultivated homestead vegetable and fodder tree (Ndaeyo, 2007) and is a common ingredient in the preparation of various delicacies following boiling or soaking in several changes of water to remove the bitter taste (Abosi and Reseroka, 2003; Onabanjo and Oguntona, 2003). In Ethiopian highland, it is regarded as a multipurpose fodder tree. It yields high biomass, it is easily propagated, highly adaptable and compatible with other crops because it does not compete with other plants for nutrients or moisture but instead improves soil fertility and growth of perennial crops (Mekoya et al., 2008). *V. amygdalina* is seedless under favourable conditions and propagation is by cuttings (Arene, 1972).

3. Folkloric uses of *Vernonia amygdalina*

Vernonia is often grown as culinary herb in soup and as food vegetable (Nwosu et al., 2013). It has so many folkloric uses (Table 2). The leaves serve as appetizer and extract from the leaves are taken to aid digestion in Nigeria. It is consumed by Hausa female of the Northern Nigeria with the belief that it enhances sexual attractiveness (Nwosu et al., 2013). In beer brewing, the leaf extract has been shown to serve as alternative to hops (Babalola and Okoh, 1996).

V. amygdalina has been widely used for the traditional treatment and/or management of various diseases in humans and animals in Africa (Tables 2 and 3). The leaves are effective against fevers and are common substitute for quinine in many African countries including Nigeria (Masaba, 2000). The plant is a potent malaria regimen in different regions of Africa (Madureira et al., 2002; Njan et al., 2008; Ene and Atawodi, 2012; Tugume et al., 2016). The leaves are used traditionally to induce fertility in women (Adedapo et al., 2014), as laxatives/purgative and enema (Kupcham, 1971). It is used widely to cure several parasitic ailments such as amoebic dysentery and schistosomiasis (Huffman et al., 1996), helminthosis (Nabukenya et al., 2014), hiccups, typhoid fever (Fadimu et al., 2014), yellow fever, (Ene and Atawodi, 2012), stomach-ache, convulsions (Tugume et al., 2016), measles (Sonibare et al., 2009), boils, burns, diabetes (Ajibesin et al., 2008), jaundice (Simbo, 2010), inflammatory diseases (Ogbole et al., 2010), candidiasis (Mustapha et al., 2013), pile (Nwauzoma and Dappa, 2013), cancer, viral diseases (Koubé et al., 2016), bacterial infection, gastrointestinal (GIT) disorders, liver diseases, kidney problems, nausea (Atangwho et al., 2012). Others include diarrhoea, hepatitis (Olorunfemi et al., 2012), eczema, anaemia (Akindahunsi and Salawu, 2005), hypertension, cough (Amira and Okubadejo, 2007), febrile convulsion (Moshi et al., 2010), urinary tract inflammation, wound dressing, menstrual pain, and other sexually transmitted diseases (Farombi, 2003; Fasuyi, 2006). In Southern Ghana, the young fresh leaves are used in treating diabetes, fever, constipation, high blood pressure and as laxative (Asante et al., 2016). The leaves, root and twig of the plant are used for treating wounds, venereal diseases and hepatitis (Nwanjo, 2005; Erasto et al., 2006). The leaves are also used for breast milk enhancement in nursing mothers (Kankara et al., 2015), treatment of fever in poultry (Nalubega et al., 2012), helminthosis in livestock (Nabukenya et al., 2014), mastitis in cattle (Moshi et al., 2010) and cattle de-ticking (Regassa, 2000). More so, the aqueous extract of the leaves is commonly recommended for the treatment of diabetes, induced abrosia nausea, emesis, loss of appetite, dysentery and other gastrointestinal tract problems (Adedapo et al., 2014), scabies, headache, stomach-ache, joint pain associated with AIDS, gingivitis and toothache due to its antimicrobial activity (Akah and Okafor, 1992; Alabi et al., 2005; De Boer et al., 2005; Fasuyi, 2006; Innocent and Deogracious, 2006) by herbalist and naturopathic doctors for their patients.

3.1. Anthelminthic potency of V. amygdalina

Studies towards evaluation of plants' potency against parasitic infections abound since antiquity (Huffman and Seifu, 1989). Traditionally, *V. amygdalina* has shown promising activities in this regards and many scientific studies have been conducted and presently ongoing to consolidate its acclaimed folkloric antiparasitic uses. There are also scientific evidences for the anthelminthic effect of *V. amygdalina* both in human and livestock. The extract of *V. amygdalina* has been tested on different stages of helminths and has shown stage specific effect in some helminths. Alawa et al. (2003) reported the aqueous extract of the leaves of *V. amygdalina* as ineffective in inhibiting egg hatching of *Haemonchus contortus* while Sirama et al. (2015) reported the efficacy of the aqueous and methanol extract of the roots against adult *H. contortus* worms. The raw leaf has also been reported as efficacious against the eggs of several nematodes of economic importance (Leonidas et al., 2013;

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Table 2
Folkloric uses of *Vernonia amygdalina*.

Use in ethnomedicine	Part of plant used	Country or region	Method of extraction	References
Malaria	Leaves	Southern Uganda	Infusion	Njan et al. (2008)
Convulsion, stomachche	Leaves, root	Uganda	Infusion	Tugume et al. (2016)
Worms	Leaves, roots	Uganda	Infusion	Innocent and Deogracious (2006)
Malaria	Leaves	Ethiopia	Homogenization	Asnake et al. (2015)
Wound healing	Leaves	Ethiopia	Concoction, infusion	Yineger and Yewhalaw (2007)
Menstruation pain, wound dressing, urinary tract inflammation and other sexually transmitted diseases	Leaves	Ethiopia		Farombi (2003) and Fasuyi (2006)
Malaria	Leaves and young stem	Nigeria	Infusion	Omosun et al. (2013)
Breast milk enhancement	Leaves	Nigeria	The dried leaves are powdered and taken orally	Kankara et al. (2015)
Yellow fever, hypertension, malaria	Leaves	North-eastern Nigeria	Infusion	Ene and Atawodi (2012)
Stomach ache, vagina itching, laxative, appetizer	Leaves, root	Nigeria	Infusion	Ige (2011)
Pile	Leaves	Nigeria		Nwauzoma and Dappa (2013)
Candidiasis	Leaves	Nigeria	Infusion with lime and potash	Mustapha et al. (2013)
Measles	Leaves	Nigeria	Infusion	
Boils and burns	Leaves	Nigeria	Infusion	Ajibesin et al. (2008)
Diabetes	Leaves	Nigeria	Boiling	Ajibesin et al. (2008)
Malaria	Leaves	Togo		Agbodeka et al. (2016)
Diabetes, cancer and viral diseases	Leaves	Cameroon	Maceration	Koubé et al. (2016)
Malaria, jaundice	Leaves	Cameroon	Decoction	Simbo (2010)
Diabetes, malaria, fever, constipation, and high blood pressure and as laxative	Young leaves	Ghana		Asante et al. (2016)
Induction of uterine mobility and control of post-parturn hemorrhage	Leaves	Malawi		Bullough and Leary (1982)
Diabetes, hypertension and hypercholestrolaemia	Leaves	Malaysia		Atangwho et al. (2013) and Razak et al. (2014)
Febrile convulsions, fever, malaria	Leaves, roots	Tanzania	Squeezing	Moshi et al. (2010)
Liver diseases	Leaves	Rwanda	Crush a handful and boil in 3 L of water and 1 glass of banana wine	Mukazayire et al. (2011)
Voluntary skin depigmentation	Leaves	Rwanda		Kamagaju et al. (2013)
Antihelminth, antiscorbutic	Leaves	West Africa		Jisaka et al. (1992)
Fever	Leaves	East Africa		Kokwaro (1976)
Haematuria caused by *Schistosoma haematobium* infection, and/or stomach troubles caused by *Schistosoma mansoni* infection	Leaves	South Africa		Ojewole and John (2004)
Molluscicide	Leaves	South Africa		Ojewole and John (2004)

Table 3
Ethnoveterinary uses of *Vernonia amygdalina*.

Diseases/uses	Part of plant used	Country or region	Method of extraction	References
Antihelminth	Leaves	Nigeria		Kudi and Myint (1999)
Cattle de-ticking	Leaves	Ethiopia	Infusion	Regassa (2000)
Gastrointestinal nematodes	Leaves	Ethiopia		Scantlebury et al. (2013)
Antiparasitic	Leaves	Rwanda	Raw leaves	Huffman and Seifu (1989) and Leonidas et al. (2013)
Mastitis	Leaves	Tanzania	Leaves	Moshi et al. (2010)
Gastrointestinal parasites	Leaves	Uganda		Nalule et al. (2011)
Heminthosis	Leaves	Uganda	Infusion Boiling Feeding directly on it	Nabukenya et al. (2014)

Adediran et al., 2014). More importantly, the aqueous extract of the plant had been reported to show greater efficacy against many livestock helminths than their treatment mainstay drugs such as ivermectin, levamisole, and albendazole (Adediran and Uwalaka, 2015). However, it has been suggested to avoid the use of hot water *V. amygdalina* extract due to its poor activity against eggs of *H. contortus* and *Trichostrongylus* spp; reason being attributed to degrading of active compounds at high temperature (Alawa et al., 2003). Experimental studies had further showed the antischistosomal activities of *V. amygdalina* leaf extract sesquiterpene lactones and steroid glycosides from the plant (Jisaka et al., 1992, 1993a; Ogboli et al., 2000).

3.2. *Vernonia amygdalina* and snails control

While oftentimes control of parasitic infection through the use of plant products is targeted against the parasite itself, a more productive means can be achieved through vector control. This is particularly important owning to the environmental friendliness of most of plant products. Vector or intermediate host control is very important to break the helminths parasite transmission cycle. This approach is very suitable for control of helminths as many employ invertebrate animals like mosquito or freshwater snails in their developmental cycles. Interestingly few helminths like *Fasciola* in which there has been no report

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on activity of *V. amygdalina* has been targeted at the snail host level using the plant.

As a measure to control schistosomiasis, the molluscicidal effects of the extract of *V. amygdalina* against the mollusk intermediate host of *Schistosoma* and other infectious parasites have been tested. The aqueous and ethanolic extracts of the plant have been reported to be toxic to adult *Biomphalaria pfeifferi* (Asemota et al., 2015) which is the snail intermediate host of *Schistosoma mansoni* as well as *Lymnaea natalensis*, the snail intermediate host of *Fasciola gigantica* (Kela et al., 1989). Adenusi and Odaibo (2010) also reported the molluscicidal effect of the ethanol extracts of the leaves and roots to adult and egg mass of *Biomphalaria pfeifferi,* although a weak activity was reported.

4. Bioactive compounds in *V. amygdalina*

More than thirty compounds belonging to several classes of compounds with differing bioactivities have been isolated and characterized from *V. amagdalina.* Table 4 highlighted the various compounds isolated from *V. amagdalina* and their activities. These include sesquiterpene lactones (Kupchan et al., 1969; Erasto et al., 2006; Owoeye et al., 2010; Luo et al., 2011), steroidal saponins (vernoniosides) (Jisaka et al., 1992), steroid glycosides and flavonoids (Igile et al., 1995). The sesquiterpene lactones are peculiar to *V. amygdalina* (Abay et al., 2015) and have been shown to be the main active compounds responsible for most of the plant's activities (Luo et al., 2011). The isolated compounds have shown activities ranging from antifeedant (Ganjian et al., 1983), antischistosomal (Koshimizu et al., 1994), antiplasmodial (Abay et al., 2015), antioxidant (Erasto et al., 2007a; Sinisi et al., 2016), anti-inflammatory (Sinisi et al., 2016) and anticancer activities (Koshimizu et al., 1994; Owoeye et al., 2010; Luo et al., 2011). While several of the isolated compounds have shown one or more of the activities exhibited by the plant itself, the activities seem to be less in individual isolated compound compared to the parent plant. This implied that the activities shown by the plant occur due to synergistic reactions of the individual components. Hence, the extract(s) of this plant may be standardize for use in alternative medicine, as a preventive or therapeutic agent against the diseases for which its effect has been scientifically established.

4.1. Possible mechanistic anthelminthic pathways of action of *V. amygdalina*

The anthelmintic potency of *V. amygdalina* extracts has been attributed to the variety of secondary metabolites present in the plant. These metabolites are unstable and their biological activity are associated with their structure, physical and chemical properties (Waterman, 1992). Tannins, saponins and alkaloids, the common metabolites from the plant are known to cause parasite paralysis or death (Makut et al., 2008). The metabolites can act individually but their combined interactions have been accredited to be more potent (Kaufman et al., 1999). The addictive, synergistic or antagonistic actions of the bioactive constituents could induce anthelminthic activities at single or multiple target sites (Briskin, 2000; Wynn and Fougere, 2007).

The mechanism of anthelminthic activities of the plant could be similar to that of benzimidazole which cause worms death by interfering with the microtubule system (Schoenian, 2008). The feeding ability of the worms is affected by paralysis thus leading to death as a result of lack of energy (Nalule et al., 2013). Satou et al. (2002) demonstrated the nematocidal activity of alkaloids against the human model nematodes *Strongyloides ratti* and *S. venezuelensis*. However, the alkaloid salts are competitive antagonists preventing acetylcholine binding. They induce cells excitation and neurological dysfunction by their reported physiological activeness, sedative and analgesic properties (Tarnopolsky and Beal, 2001). Saponins like in alkaloids can induce antifeeding behaviour in worms; parasite loses grip on the gut wall as a result of

Table 4
Some isolated compounds from *Vernonia amygdalina* and their reported bioactivities.

Isolated compound	Class of compound	Uses	References
Vernolide	Sesquiterpene lactones	Antimicrobial, antioxidant, antitumoral, antiplasmodial, antischistosomal	Jisaka et al. (1993b), Ohigashi et al. (1994), Koshimizu et al. (1994), Erasto et al. (2006, 2007a,b), Abay et al. (2015) and Sinisi et al. (2016)
Vernodalol	Sesquiterpene lactones	Antimicrobial, antitumoral, antioxidant, antiplasmodial, antischistosomal	Ohigashi et al. (1994), Erasto et al. (2006, 2007a,b), Luo et al. (2011) and Abay et al. (2015)
Vernodalin	Sesquiterpene lactone	Antitumor, antiplasmodial, antischistosomal	Kupchan et al. (1969), Ohigashi et al. (1994), Koshimizu et al. (1994) and Jisaka et al. (1993b)
Hydroxyvernolide	Sesquiterpene lactones	Antiplasmodial, antitumor, antischistosomal	Ohigashi et al. (1994) and Koshimizu et al. (1994)
Vernodalinol	Sesquiterpene lactone	Anticancer	Luo et al. (2011)
Vernomygdin	Sesquiterpene lactone	Anticancer	Kupchan et al. (1969)
Epivernodalol	Sesquiterpene lactone	Anticancer	Owoeye et al. (2010)
11,13-Dihydrovernodalin	Sesquiterpene lactone	Antifeedant	Ganjian et al. (1983)
3′Deoxyvernodalol	Sesquiterpene lactones,	anti-inflammatory and antioxidant	Sinisi et al. (2016)
Luteolin	Flavonoid	Antioxidant, anticancer	Igile et al. (1994) and Galati et al. (2000)
Luteolin 7-O-β-glucuronoside,	Flavonoid	Antioxidant	Igile et al. (1994)
Luteolin 7-O-β-glucoside	Flavonoid	Antioxidant	Igile et al. (1994)
Vemonioside B_1	Steroid Glucosides	Antiplasmodial, antischistosomal	Jisaka et al. (1992), Ohigashi et al. (1994) and Koshimizu et al. (1994)
Vernoamyosides A	Steroid saponins	Anti-inflammatory	Quasie et al. (2016)
Vernoamyosides B	Steroid saponins	Anti-inflammatory	Quasie et al. (2016)
Vernoamyosides C	Steroid saponins	Anti-inflammatory	Quasie et al. (2016)
Vernoamyosides D	Steroid saponins	Anti-inflammatory	Quasie et al. (2016)

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in vivo paralysis leading to the spontaneous expulsion with faeces (Nalule et al., 2013).

Tannins have been well documented for their anthelminthic properties (Molan et al., 2003; Hoste et al., 2006; Forbey et al., 2009). Condensed tannins have shown evidence of activities against nematodes in *in vitro* (Dawson et al., 1999; Ademola and Idowu, 2006) and *in vivo* studies (Butter et al., 2001; Kotze et al., 2009). Tannins being polyphenolic compounds could interfere with energy generation in helminths by uncoupling oxidative phosphorylation; a mechanism similar to niclosamide and oxyclozanide which are synthetic phenolic anthelmintics (Martin, 1997). Tannins also bind to free proteins in the gastrointestinal tract (Hoste et al., 2006) or glycoprotein on the cuticle of the parasite. This impairs nutrient absorption, motility, and reproduction (Githiori et al., 2006).

5. Toxicity studies on *V. amygdalina*

In view of the increasing folkloric uses of *V. amygdalina,* toxicity studies on the plant become necessary. The aqueous and ethanol extract of *V. amygdalina* were non-toxic in mice exposed to up to 1200 and 2000 mg/kg/day of the aqueous and ethanolic extract respectively for 28 days (Njan et al., 2008; Akowuah et al., 2015). A much higher concentration 5000 mg/kg of the plant's leaf aqueous extract was also non-lethal in mice (Yeap et al., 2013). Testicular lesions were observed in male wistar rats exposed to 300 and 600 mg/kg of ethanolic extract for 56 days, these lesions were however not observed in male rats exposed to 100 mg/kg of the ethanol extract for the same duration (Saalu et al., 2013). The methanol and aqueous extracts were also non-toxic to Madin-Darby Bovine Kidney (MDBK) cells *in vitro* (Razak et al., 2014). This altogether suggested that the extracts of *V. amygdalina* are not toxic at lower concentrations but may be harmful at higher concentrations. Hence, the extracts should not be taken at high concentrations.

6. Conclusions and recommendations

Vernonia amygdalina is a multipurpose plant with several preventive and therapeutic potentials. This report has clearly shown its anthelminthic properties. While the efficacy of the plant showed desirable outcomes on helminth parasites, available reports on its use against the corresponding vectors of helminths showed poor activities. Its lack of considerable toxicity makes it a choice plant for further drug discovery. Effort should be made towards standardizing the extract(s) of *V. amygdalina* for use in alternative medicine for treatment of helminth-related diseases. This could either be used alone as preventive or therapeutic agent or as adjuvant either to increase the efficacy or reduce the toxicity of orthodox drugs.

Compliance with ethical standards

Not required.

Conflicts of interest

The authors report no declaration of interest.

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