REVIEW ARTICLE

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Vernonia anthelmintica Willd.: An Overview on Phytopharmacological Properties

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Abstracts: Plants have been one of the important sources of medicines even since the dawn of human civilization. Medicinal plants are the nature's gift to human being to have disease-free healthy life. It plays a vital role to preserve our health. *Vernonia anthelmintica* Willd. (Family- Asteraceae) commonly known as kalijiri, is an important medicinal plant of India. Its medicinal usage has been reported in the traditional system of medicine such as Ayurveda and Unani. It has been used extensively for treatment of some diseases like asthma, kidney troubles, inflammatory swellings, leucoderma, worm infection and convulsion. It has been found to possess various therapeutic activities, viz. anti-inflammatory, anti-arthritic, antidiabetic, anthelmintic, antioxidant, antibacterial, anticancer and many more. The present paper is an overview on scientifically established and published phytopharmacological properties of the plant.

INTRODUCTION

Vernonia anthelmintica Willd. (Syn. *Centratherum anthelminticum* Kuntze or *Ascaradia indica* or *Conyza ascaradia* or *Serratula anthelmintica)* belongs to family *Asteraceae*, is an annual herb distributed throughout India [1, 2].

Taxonomic Classification [3]

- Kingdom : Plantae
- Division : Angiosperms
- Class : Eudicots
- Subclass : Asterids
- Order : Asterales
- Family : Asteraceae
- Subfamily : Cichorioideae
- Tribe : Vernonieae
- Genus : *Vernonia*
- Species : *Vernonia anthelmintica*

Vernacular Names [4]

- **Sanskrit :** Somaraja, Vakuchi, Agnibija, Aranyajiraka, Putiphali, Krishnaphala, Kananajiraka, Tiktajiraka
- **Hindi :** Bakshi, Kalijhiri, Somraj, Vapchi, Buckshi
- **Gujarati :** Kalijiri, Kadvojiri
- **English:** Purple Fleabane
- **Marathi :** Kalajira, Kalenjiri, Kalijiri, Ranachajire
- **Bengali :** Babchi, Bukshie, Hakuch, Kaliziri, Somraj
- **Punjabi :** Bukoki, kakshma, Kaliziri
- **Malayalam :** Kattujirakam, Puvankuruntala
- **Telugu :** Nelavavili, Garitikamma, Vishakantakamula
- **Urdu :** Janglijiri
- **French :** Herbe aux mouches
- **Arabic :** Atarilal, Itrilal, Kamunebari

Botanical Description

Vernonia anthelmintica is an annual, erect and leafy plant about 1.5 m tall. The stems are branched and pubescent. Leaves are 5-9 cm long, 2.5-3.2cm broad, lanceolate or elliptic-lanceolate, acute, coarsely serrate, pubescent on both surfaces, petiolate and with tapering base. Heads are 1.3-2cm diameter, subcorymbose with about 40 flowers and linear bract near the top of the peduncle. Outer involucral bracts are linear, hairy, shorter than those of the inner rows; intermediate bracts with herbaceous hairy tips, linear, acute, equaling or shorter than the innermost; innermost bracts usually the longest, linear, subacute, often tipped with purple. Pappus reddish, the exterior row very short, subpaleaceous, persistent; the inner hairs somewhat flattened, deciduous, much shorter than the glabrous corolla. Achenes are 4.5-6 mm long, oblong-cylindrical, 10-ribbed, pubescent [2, 4].

Traditional Uses

According to Ayurveda, seeds are hot, acrid, astringent, anthelmintic; cure ulcers, vata and kapha; use in skin disease, leucoderma and fever. According to Unani system of medicine, the seeds are anthelmintic, purgative; used for asthma, kidney troubles, hiccough, inflammatory swellings, to remove blood from the liver, sores and itching of the eyes. The seeds are anthelmintic, stomachic, tonic, diuretic and antiperiodic. The powdered seeds are applied externally in paralysis of the legs at Mundas of Chota Nagpur. The juice of the leaf is given to cure phlegmatic discharges from the nostrils. In Ceylon, the plant is used for fever convulsions [1, 2, 3].

PHYTOCHEMICAL STUDIES

Achenes of *Vernonia anthelmintica* contain fixed oil (18.89%), brassicasterol, stigmasterol, resin (2%), myristic acid (7.4), palmitic acid (7%), stearic acid (5.9%), oleic acid (5.7%), linoleic acid (9.6%), vernolic (epoxyoleic) acid (62.4%) and methyl vernolate[2]. The seeds contain the main active principle Delta-7-avenasterol[5], also other sterols 4-alpha-methylvernosterol, vernosterol and avenasterol[2]; main sterol 7,(*Z*)-24(28)-stigmastadienol along other components 5-stigmasten-3β-ol and 7,22-stigmastadienol[5]; 4α-methylsterol[7]; alkaloid vernonine[1]; two flavan glucosides p-hydroxybenzoyl-vernovan and vernovan[8]; bitter principle demanolide lactone[5]; other constituents like vernodalin, vernodalol, butein; 3,4,2',4',5'-pentahydroxy-6'-methoxy-2-methyl-chaltone, β-amyrin, β-sitosterol-β-D-glucoside and

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stigmasterol[8]; Seeds consist flavonoids like 2′,3,4,4′-tetrahydroxychalcone; 5,6,7,4′-tetrahydroxyflavone and butin[9]; elemanolide dimers vernodalidimers A and B[10]. Seed oil of *V. anthelmintica* consist chief component trivernolin and minor components, 1,3-divernolin and vernolic acid [11]. Leaf of *Vernonia anthelmintica* contains abscisic acid [12]. Centratherin and germacranolide were isolated from the leaves and stem [5]. The highly oxygenated stigmastane-type steroids vernoanthelcin A–I; stigmastane-type steroidal glycosides vernoantheloside A and B were isolated from the aerial parts of *V. anthelmintica* [13].

PHAMACOLOGICAL STUDIES

Anti-inflammatory Activity

Petroleum ether and alcoholic extracts of *V. anthelmintica* seeds (100 mg and 200 mg/kg p.o.) showed anti-inflammatory activity in acute and subacute models of inflammation. Both petroleum ether and alcoholic extracts showed significant reduction in paw oedema in carrageenan-induced model. In subchronic inflammatory phase both extracts provoked a significant reduction of transudation phase and too little extent proliferative phase when tested in cotton pellet-induced granuloma model. Both the extracts also reduced alkaline phosphatase activity in serum. The histopathology of granuloma tissue showed significant inhibition of lymphocytes, neutrophils, exudates, necrosis and giant cell when compared with control without ulcerogenic effect. The results suggested that petroleum ether and alcoholic extracts may exert anti-inflammatory activity through prostaglandin inhibition, reduced myeloperoxidase and antitransudation [14].

Antiarthritic Activity

The ethanolic extract of seeds of *V. anthelmintica* EVA (250 and 750 mg/kg) and EVA (500 mg/kg) showed significant ($p<0.05$ and $p<0.01$ respectively) inhibition of paw edema from 1 to6 h as compared to carrageenan control, but the effect was not dose-dependent. EVA 250 mg/kg showed significant ($p<0.01$) prevention of the paw edema on 28th day, whereas the treatment with EVA 500 mg/kg showed significant ($p<0.01$) prevention in the paw edema during 21st and 28th day as compared to the arthritis control. In xylene induced edema treatment with EVA (250, 500 and 750 mg/kg) showed significant ($p<0.01$) decrease in ear thickness as compared to control during the 30 to 60 min[15].

Antidiabetic and Antihyperlipidemic Activity

Ethanolic extract of *Vernonia anthelmintica* seeds showed significant hypoglycemic effect in STZ (Streptozotocin) induced diabetic rats. At a dose of 100 mg/kg body weight of extract showed a significant antihyperglycemic activity in the diabetic treated rats with a maximum fall of 82.3% in the blood glucose level after the 6th hour of treatment when compared with other fractions. Administration of ethanolic extract (100 mg/kg body weight) for 45 days showed significant reduction in plasma glucose, HbA1C, cholesterol, triglycerides, LDL, VLDL, free fatty acids, phospholipids and HMG-CoA reductase in STZ diabetic rats. Also significant decrease in plasma insulin, protein, HDL and hepatic glycogen observed in STZ diabetic rats and that was normalized after 45 days of treatment with the active fraction of *V. anthelmintica* seeds. Thus the seeds of *V. anthelmintica* showed significant antidiabetic and antihyperlipidemic property without toxic effects [16].

Anthelmintic Activity

The seeds of *V. anthelmintica* showed anthelmintic activity. *In-vitro* studies revealed higher anthelmintic effects ($p \geq 0.05$) of crude methanol extract (CME) as compared with crude aqueous extract (CAE) of *V. anthelmintica* seeds on live *Haemonchus contortus* as evident from their mortality. In *in-vivo* studies, seeds of *V. anthelmintica* were administered as crude powder (CP), CAE, and CME to sheep naturally infected with mixed species of gastrointestinal nematodes. *In-vivo* maximum reduction (73.9%) in fecal egg counts per gram (EPG) was recorded in sheep treated with *V. anthelmintica*. CAE at 3 g kg^{-1} body weight on day 5 post-treatment (PT) followed by CP at 3 g kg^{-1} (55.6%) on day 3 PT. CME did not exhibit anthelmintic activity *in-vivo* [17].

Anticancer Activity:

The chloroform fraction of *Centratherum anthelminticum* seeds (CACF) showed cytotoxic effect and TNF-α inhibition activity with NF-κB activation response. The cytotoxicity of CACF was tested using the MTT (methyl thiazolyltet razolium) assay; CACF effective inhibitory concentrations (IC50) for A-549, PC-3, MCF-7, and WRL-68 cells were 31.42 ± 5.4, 22.61 ± 1.7, 8.1±0.9, and 54.93±8.3 μg/mL, respectively. CACF effectively and dose-dependently inhibited TNF-α release, *in-vitro* and *in-vivo*. CACF inhibited TNF-α secretion in stimulated RAW264.7 macrophage supernatants with an IC50 of 0.012μg/mL, without affecting their viability; the highest dose tested reduced serum TNF-α by 61%. Acute toxicity testing in rats revealed that CACF was nontoxic at all doses tested. Matching the cytotoxic activity towards a mechanistic approach, CACF dose-dependently exhibited *in-vitro* inhibitory effects against the activation of NF-κB translocation in MCF-7 cells. Thus these studies revealed the potential of CACF in the treatment of breast cancer and in oxidative stress conditions with associated inflammatory responses [18].

The chloroform and acetone extracts (after removing fats) of *V. anthelmintica* showed antiproliferative property of five tumor cell lines (such as human melanoma cell A-375, mice melanoma cell B-16, human breast tumor cell BCF-7, human gastric carcinoma cell BGC-823 and human liver carcinoma cell HepG-2) *in-vitro* using MTT method. MTT method showed that extracts of *V. anthelmintica* had different effects on tumor cells growth, the acetone extract showed significant growth inhibition on human melanoma A375 cells. There was a concentration-dependent relationship between the *V. anthelmintica* extract and the inhibition of A-375 cells proliferation ($P<0.05$), also change of cell morphology was observed with the *V. anthelmintica* extract [19].

Two novel elemanolide dimers, vernodalidimers A and B, possessing a rare tricyclic ortho ester moiety, were isolated from the seeds of *V. anthelmintica* which exhibited

potent cell growth inhibitory activity against HL-60 cells (IC_{50} 0.72 and 0.47 μM, respectively)[10].

Vernonia anthelmintica significantly enhanced the activity of tyrosinase *in-vitro* and proliferation of B-16 murine melanoma cell. MTT was used to study proliferation of the cell, and melanin was detected by its absorption at 470 nm [20].

Antimicrobial Activity

Methanolic extracts of *V. anthelmintica* showed antibacterial and antifungal activities. Antibacterial study performed against six bacteria viz., *Escherichia coli, Citrobacter, Shigella flexenari, Yersinia aldovae, Staphylococcus aureus* and *Pseudomonas aeruginosa* while the antifungal activity of these extracts performed against six fungi, viz., *Saccharomyces cereviciae, Aspergillus parasiticus, Trichophyton rubrum, Macrophomina, Fusarium solani* and *Candida albicans*. Methanolic extract of the seeds showed significant antibacterial activity against all tested bacterials except *Yersinia aldovae* while showed antifungal activity against only *Trichophyton rubrum* [21].

Antioxidant Activity

Methanol extract (75%) of *V. anthelmintica* was found to be potent inhibitors of lipid peroxide formation and scavengers of hydroxyl and superoxide radicals' *in-vitro*[22]. The chloroform fraction of *V. anthelmintica* demonstrated significant antioxidant activity with DPPH (1, 1-Diphenyl-2-picrylhydrazyl), ORAC (oxygen radical absorbance capacity), and FRAP (Ferric Reducing/Antioxidant Power) assays [18].

Estrogen Biosynthesis Activity

Nine highly oxygenated stigmastane-type steroids, vernoanthelcin A–I (**1**–**9**), and two stigmastane-type steroidal glycosides, vernoantheloside A and B (**10** and **11**) have been isolated from the aerial parts of *V. anthelmintica*. Compounds **1**, **5**, **7**, **9** and **10** were tested for their effects on estrogen biosynthesis in human ovarian granulosa-like cells (KGN cells) [13].

Immunomodulatory Activity

The orally administered seed of *V. anthelmintica* exhibited suppression of Rh-incompatibility of female during pregnancy. Phytochemical study showed that no harmful steroids are present in seeds. These studies reveals that seeds suppressed Rh-incompatibility in patients either by suppressing the sensitivity of B and T cells to the antigens or by blocking both T and B cells to undergo blast formations and did not allow them to differentiate into antibiodies forming cells [23].

Melanogenesis Activity

V. anthelmintica flavone (VAF) stimulated melanogenesis directly on human epidermal melanocytes. Three different concentrations of VAF were incubated with human melanocytes for 72h and then melanin content and tyrosinase activity were respectively measured. The proliferation of melanocytes was most inhibited by VAF at high dose (≥100μg/ml). In the range of experimental dose, VAF increased the activity of the tyrosinase and melanin content significantly in a dose-dependent manner. The increasing protein expression of TRP1 was in a dose-dependent manner. No effect was observed on protein expression of TYR and TRP2. The studies revealed that VAF may stimulate melanogenesis directly on human epidermal melanocytes, which may be induced by increasing expression of TPR1 and post-translational modification of TYR [24].

CONCLUSION

V. anthelmintica is used in traditional system of medicine to treat various physiological conditions. It is an important source of various types of compounds as well as pharmacological activities. Further research in view of fulfilling the need of quality control aspects, standardization of the various constituents and extracts are needed. Also there is a need to explore its maximum potential in the field of medicinal and pharmaceutical sciences for novel and fruitful applications.

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