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Phytochemical, Pharmacological and Pharmacognostical Profile of *Vernonia anthelmintica*: An Overview.

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Review Article

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ABSTRACT

The aim of this review is to analyze published data on the pharmacological, Phytochemical and Pharmacognostic profile of plant *Vernonia anthelmintica* Willd genus. This will help to identify the state of knowledge in regard to this plant species and to propose future research priorities. Material and Method-The major scientific databases including Science direct, cab direct, CeRA, Proquest and Google Scholar were queried for information on *Vernonia anthelmintic* using various keyword combinations. The International Plant Name Index was also used to verify the names of the plant. Result-The Vernonia genus has about one thousand species and members of the genus are widely used as food and medicine. A total of 109 Vernonia species were reported in the literature to have medicinal properties. *Vernonia anthelmintica* Willd belongs to the family Compositae and has been used for curing asthma, hiccough, inflammatory swellings, sores, and itching of the eyes. Conclusion-On the basis of results from a combination of pharmacological, phytochemical and pharmacognostic studies reported, *Vernonia anthelmintica* holds the most promise for development into against diabetes and potential against cancer and inflammatory conditions. Vernodalidimers A and B is so far the most promising agent from the plant that has potential for development into an anti-cancer agent. Vernoanthelcin A–I effects on estrogen biosynthesis in human ovarian granulosa-like cells. The *Vernonia anthelmintica* and isolated compounds require further studies to ascertain its medicinal potentials.

INTRODUCTION

The Vernonia genus has about one thousand species and members of the genus are widely used as food and medicine. A total of 109 Vernonia species were reported in the literature to have medicinal properties. *Vernonia anthelmintica* Willd belongs to the family Compositae and has been used for curing asthma, hiccough, inflammatory swellings, sores, and itching of the eyes.

Vernonia (Asteraceae) is the largest genus in the tribe Vernoniae with close to 1000 species. The genus Vernonia is named after William Vernon, an English botanist who collected and identified this genus in Maryland in thelate1600sbeforehisdeathin1711 [1]. As the scientific name of the plant indicates, Vernonia *anthelmintica* Willd contains compounds that can be used as valuable anthelmintic medicine. This plant is also used for the treatment of asthma, hiccough, inflammatory swellings, sores, and itching of the eyes [2].

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Vernonia anthelmintica seeds

Pharmacological Profile

Anti-inflammatory activity and anti-arthritic activity

Anti-inflammatory activity and anti-arthritic activity of ethanolic extract of seeds of *Vernonia anthelmintica* (EVA) evaluated in different experimental paradigms. The seeds were extracted by soxhlet method using ethanol (99.9%) and subjected to the preliminary phytochemical and acute toxicity studies. The effect of EVA was evaluated for acute inflammation in carrageenan induced rat paw edema and xylene induced ear edema in mice and for chronic inflammation in complete Freud's adjuvant (CFA) induced arthritis in rats. Further, the biochemical, histopathological and radiographic evaluation was performed. Additionally, ulcerogenic potential of EVA in rats was evaluated. The phytochemical evaluation revealed the presence of alkaloids, flavonoids, steroids, triterpenes and polyphenols in EVA. In acute toxicity test, no signs of toxicity and mortality were observed on oral administration of EVA in mice up to a dose of 5000 mg/kg. In acute study, pretreatment with EVA (250, 500 & 750 mg/ kg, p o) was significantly inhibited the carrageenan induced rat paw edema and xylene-induced ear edema in mice. In chronic study decreased paw volume and paw thickness; increased liver weight and decreased spleen weight; decreased serum SGOT and increased serum TP level and inhibition of histopathological changes and soft tissue swelling destruction of the knee joints in radiographic examination were evident after treatment with EVA(250&500 mg/kg, p o). Further, in the animals treated with EVA (500 mg/kg, p o) ulceration was not evident. The results of present study were revealed the effectiveness of EVA in acute as well as chronic inflammatory conditions without ulcerogenic potential. The EVA may possibly act by preventing production of nitric oxide from nitric oxide synthase or by preventing neutrophilic infiltration thereby decreasing the generation or release of chemotactic factors and inflammatory T cell mediators such as IL, TNF-á and LTs. These effects may be attributed to phytochemicals present in EVA [3].

Anti-bacterial and anti-fungal activities

Antibacterial and antifungal activities evaluated on Methanolic extracts of *Thuja occidentalis, Vernonia anthelmintica, Dryopteris chrysocoma* and *Trachyspermum ammi.* Extracts were tested *In vitro* for their antibacterial and antifungal activities.Antibacterial study performed against six bacteria viz., *Escherichia coli, Citrobacter, Shigella flexenari, Yersinia aldovae, Staphylococcus aureus* and *Pseudomonas aeruginosa* indicated that has potent activity against all microorganisms. The antifungal activity of these extracts was performed against six fungi, viz., *Saccharomyces cereviciae, Aspergillus parasiticus, Trichophyton rubrum, Macrophomina, Fusarium solani* and *Candida albicans*. The extracts showed significant results against different fungal strains [4].

Thirty four medicinal plants, belonging to twenty eight different families, screened for potential antibacterial activity against six bacterial strains belonging to Enterobacteriaceae, viz. *Enterobacter aerogenes* ATCC13048, *Escherichia coli* ATCC25922, *Klebsiella pneumoniae* NCIM2719, *Proteus mirabilis* NCIM 2241, *Proteus vulgaris* NCTC8313, *and Salmonella typhimurium* ATCC23564. Antibacterial activity of aqueous and alcoholic extracts was tested by the agar disc diffusion and agar well diffusion methods. The ethanol/methanol extracts were more active than aqueous extracts for all the plants studied. The most susceptible bacterium was *K. pneumoniae*, while the most resistant bacteria were *S. typhimurium* and *E. coli*. From the screening experiment, *Woodfordia fruticosa* Kurz. showed best antibacterial activity. This plant may be used further to isolate and evaluate the therapeutic antimicrobials [5].

Anti-hyperglycemic activity

Ethanolic extract prepared from the seeds of *Vernonia anthelmintica* evaluated for its anti hyperglycemic activity in STZ (Streptozotocin) induced diabetic rats. Administration of ethanolic extract at a dosage of 0.50 g/kg b w produced the maximum fall (82%) in the blood glucose levels in diabetic rats after 6 h of treatment. Bioassay-directed fractionation using silica gel column chromatography was performed. Among the five fractions (A1, B1, C1, A2 and B2) obtained, of an initial chromatographic separation of the ethanolic extract, fraction A2 (100 mg/kg b.w.)

showed the maximum anti hyperglycemic activity which is significantly higher than that of the reference drug glibenclamide (20 mg/kg b.w.). Administration of the active fraction (100 mg/kg b.w.) for 45 days resulted in significant reduction in plasma glucose, HbA1C, cholesterol, triglycerides, LDL, VLDL, free fatty acids, phospholipids and HMG-CoA reductase in STZ diabetic rats. In addition to that, significant decrease in plasma insulin, protein, HDL and hepatic glycogen observed in STZ diabetic rats, was normalized after 45 days of treatment with the active fraction of V. anthelmintica seeds. From the present study, it is evident that, the seeds of V. anthelmintica possess significant antidiabetic and anti-hyperlipidemic property without evident toxic effects [6] .

Diuretic agent

This review articles identify the plant extracts which promotes diuresis and also to identify the research needed area. A number of genus and species reporting diuretic effects. *Xylopia aethiopica* (dunal) and *Alepidea amatymbica* eckl. & zeyh, *Steganotaenia araliacea* hochst, *Carissa edulis* (forssk) vahl, *Oxystelma esculentum, Tylophora indica, Centratherum anthelminticum* (l.) kuntze, *Opuntia ficus indica* (l.) mill., *Spergularia purpurea* pers., *Spilanthes acmella* murr., *Raphanus sativus*var nigra l., *Lagenaria siceraria*(mol.) standl, *Equisetum bogotense* tea (platero herb) [7].

Analgesic and antipyretic

Analgesic and antipyretic activities of petroleum ether and alcohol extracts of *Centratherum anthelminticum* (L) Kuntze (family: Asteraceae) seeds (100 and 200 mg/kg, p. o.) evaluated in brewer's yeast-induced fever model in rats, acetic acid-induced writhing and Eddy's hot plate methods in mice. Both petroleum ether and alcohol extracts showed significant decrease in number of writhes in acetic acid-induced writhing and increase in paw licking time to heat stimuli in the hot plate method. The maximum analgesic activity was observed at 90 min after dosing when compared to control. Both the extracts showed significant inhibition of elevated body temperature when compared to corresponding control. These results suggested that the petroleum ether and alcohol extracts possessed analgesic and antipyretic activities [8].

Larvicidal activity

Crude extracts of fruits and leaves of *Centratherum anthelminticum* in different solvents were tested for larvicidal activity against *Anopheles stephensi*, the vector of malaria. The petroleum ether crude extract of both fruits and leaves exhibited significant larvicidal activity against III instars larvae with LC50 values of 162.60 ppm and 522.94 ppm, respectively after 24 hr. The petroleum ether extract of fruit was 11.66, 2.15 and 1.32 times more toxic than that of leaf extract after 24, 48 and 72 hr, respectively at LC90 level. However, at LC50 level the corresponding values were 3.22, 1.83 and 1.19, respectively. The petroleum ether extract of C. anthelminticum fruits is a promising source for the control of Anopheles larvae [9].

Anti-bacterial activity

Thirty-four Indian medicinal plants belonging to 28 different families were screened for potential anti-bacterial activity against 3 Staphylococcus species, namely *Staphylococcus aureus, Staphylococcus epidermidis,* and *Staphylococcus subflava*. Antibacterial activity of aqueous and alcoholic extracts was performed by agar disc diffusion method and agar well diffusion method. The alcoholic extracts were more active than aqueous extracts for all the plants studied. The most susceptible bacterium was S.aureus. The methanol extract of *Woodfordia fruticosa* showed the best antibacterial activity. The in vitro susceptibility testing of the studied staphylococcus strains was done against standard antibiotics [10].

Phytochemical Profile

Nine new highly oxygenated stigmastane-type steroids, vernoanthelcin A–I (fig 1–9), and two new stigmastane-type steroidal glycosides, vernoantheloside A and B (fig-10-11) were isolated from the aerial parts of *Vernonia anthelmintica* Willd. The structures of compounds 1–11 were determined on the basis of IR, MS, 1D-NMR, and 2D- NMR, and their absolute configurations were deduced using single-crystal X-ray diffraction and the CD exciton chirality method. Compounds 1, 5, 7, 9 and 10 were tested for their effects on estrogen biosynthesis in human ovarian granulosa-like cells (KGN cells) [11].

A new steroid, vernoanthelsterone A (1), and five known steroids were isolated from the aerial Parts of *Vernonia anthelmintica* Will. Compound 1 possesses a Δ 8(14)-15-one moiety, few steroids with this moiety have been reported before. Compounds 1–6 were tested for their antibacterial activities and their effects on estrogen biosynthesis in human ovarian granulosa-like cells (KGN cells). Compound 2 showed the ability to promote estrogen biosynthesis with EC50 of 56.95 μg/ mL and also exhibited the antibacterial activities against *Bacillus cereus, Staphylococcus aureus, Bacillus subtilis and Escherichia coli* with MICs ranging from 3.15 to 15.5 μg /mL. The structures of 1–6 were determined on the basis of IR, MS, 1D and 2D NMR [12].

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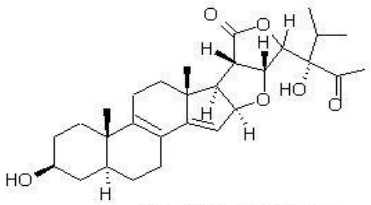

Fig-1 Vernoanthelcin-A

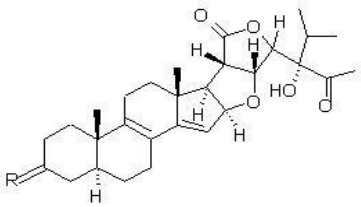

Fig-2 Vernoanthelcin-B
R=Alpha OH, Beta H

Fig-3 Vernoanthelcin-C
R=O

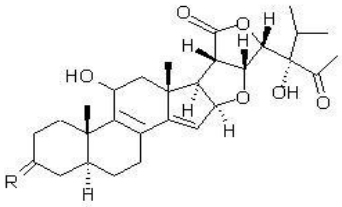

Fig-4 Vernoanthelcin-D
R=O

Fig-5 Vernoanthelcin-E
R=beta OH alpha H

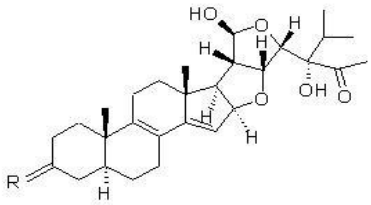

Fig-6 Vernoanthelcin-F
R=O

Fig-7 Vernoanthelcin-G
R=beta OH alpha-H

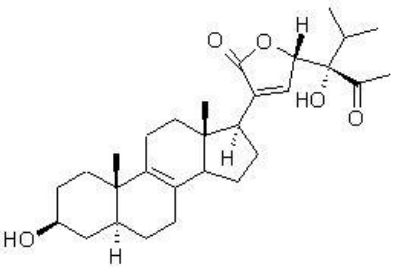

Fig-8 Vernoanthelcin-H

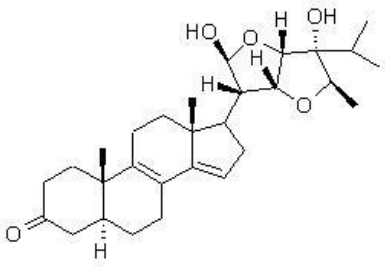

Fig-9 Vernoanthelcin=I

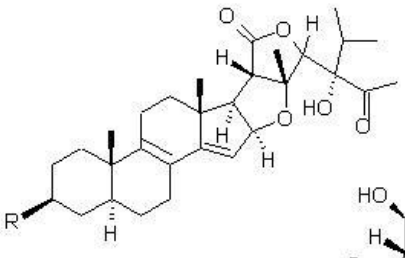

Fig-10 vernoantheloside A
R=OGlc

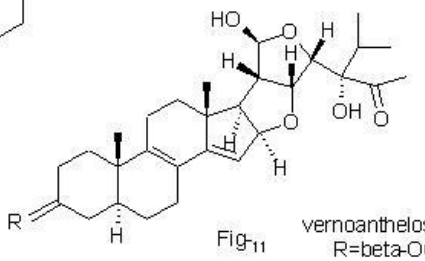

Fig-11 vernoantheloside-B
R=beta-OGlc, alpha-H

Chemical synthesis of two trisaccharides related to the saponin isolated from Centratherum anthelminticum is reported. Stereoselective, high-yielding glycosylation strategies were developed using H2SO4 immobilized on silica for activation of trichloroacetimidate donors, or in conjunction with N-iodosuccinimide for activation of a thioglycoside. A late stage TEMPO-mediated oxidation was performed for the formation of the required uronic acid moiety [13].

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Two novel elemanolide dimers, vernodalidimers A (1) and B (2) were isolated possessing, a rare tri-cyclic ortho ester moiety, from the seeds of *Vernonia anthelmintica*. Their structures were elucidated by 1D and 2D NMR data and CD spectra. Vernodalidimers A (1) and B (2) exhibited potent cell growth inhibitory activity against HL-60 cells (IC50 0.72 and 0.47 l M, respectively) [14].

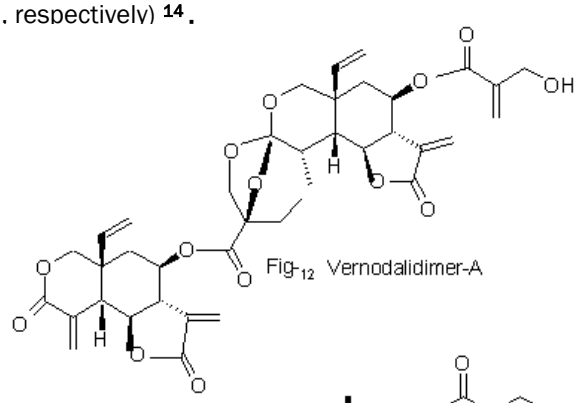

Fig-12 Vernodalidimer-A

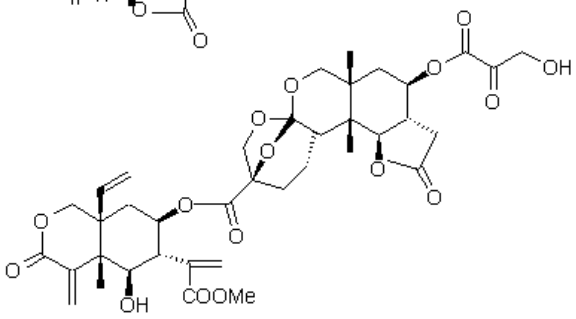

Fig-13 Vernodalidimer-B

Several flavonoids including 2´,3,4,4´-tetrahydroxychalcone, 5,6,7,4´ tetrahydroxyflavone and butin, were separated from the seeds of *Vernonia anthelmintica* Willd by high-speed counter-current chromatography using a two-step operation. Two different types of solvent systems were used: chloroform–dichloromethane–methanol–water (2:2:3:2, v/v) and 1, 2 di-chloro-ethane–methanol–acetonitrile–water (4:1.1:0.25:2, v/v). From 1 kg of seeds of *Vernonia anthelmintica* Willd the method yielded about 45 mg of 2´,3,4,4´-tetrahydroxychalcone, 40 mg of 5,6,7,4´-tetrahydroxyflavone, and 55 mg of butin. Each isolated component showed 95 97% purity as determined by high-performance liquid chromatography analysis. These purified compounds were characterized by MS and NMR [15].

A new glycosylated triterpene has been isolated from the seeds of Centratherum anthelminticum, a medicinally important plant. The structural analysis of its acetylated derivative was performed by ^{1}H, ^{13}C NMR, ^{1}H–^{1}H COSY, HMQC, HMBC and DEPT spectroscopy. The saponin was shown to contain hederagenin and six sugar residues forming two glycosyl chains. The complete structure of the saponin was established as 3-O-[β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranosyl]-28-O-[β-D-glucuronopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)-β-D-glucopyranosyl]-hederagenin [16].

In the present investigation the *In vivo* radiotracer experiments using [1-^{14}C] acetate as the precursor were conducted to investigate the biosynthesis of vernolic acid (12, 13-epoxy-*cis*-9-octadecenoic acid) in the seeds of *Vernonia galamensis*. The acetate precursor radioactively labeled vernolate in phosphatidylcholine (PC), diacylglycerol, and triacylglycerol. Time-course kinetics of the incorporation of the radioactive tracer indicated that vernolate is synthesized while the acyl moiety is esterified to PC. Pulsechase experiments provided additional supporting evidence that vernolate is synthesized while esterified to PC. These results are consistent with the hypothesis that linoleoyl PC is the precursor of vernoleoyl-PC. Subsequently, vernolate is quickly moved from the PC pool to the triacylglycerol pool, where it accumulates [17].

The seed oil of Vernonia anthelmintica on reaction with diols (mono-, di-, tri-, or tetraethylene glycols) in the presence of boron trifluoride etherate, followed by saponification and esterification (methanol/H^{+}), gives the oligoethylene glycol ethers: methyl 12(13)-hydroxy-13(12) [2-hydroxy-ethyl-1-oxy]-octadec-9-enoate; methyl 12(13)-hydroxy-13(12)-[5-hydroxy-3-oxapentyl-1-oxy]-octadec-9-enoate; methyl 12(13)-hydroxy-13(12)-[8-hydroxy-3,6-dioxaoctyl-1-oxy]-octadec-9-enoate; and methyl 12(13)-hydroxy-13(12)-[11-hydroxy-3,6,9-trioxaundecyl-1-oxy]-octadec-9-enoate. Methyl 12, 13-dihydroxyoctadec-9-enoate is a co-product in all reactions [18].

Vernonia anthelmintica (L.) Willd. seed was found to contain enzymes that were active only after the seed was ground. By deactivation of the enzymes, an oil rich in trivernolin (the triglyceride of epoxyoleic acid) was produced, and pure trivernolin was isolated. Acceleration of the enzyme activity altered the composition of the oil as

evidenced by changes in free fatty acid content, iodine values, and oxirane oxygen (epoxy) content. Investigation showed that these changes were due, at least partially, to the conversion of epoxyoleic acid to (+)-*threo*-12, 13-dihydroxyoleic acid, which was isolated in pure form. Pure (−)-*threo*-12, 13-dihydroxyoleic acid was prepared by acetolysis of *V. anthelmintica* seed oil. Neither of these isomers had been obtained previously from mature *anthelmintica* seed [19].

Seed oils of *Euphorbia lagascae Spreng*. and *Vernonia anthelmintica* (L.) Willd. were prepared, refined and deoxidized, trivernolin was prepared from *V. anthelmintica* and also epoxidized. These products were each comparatively evaluated as plasticizer-stabilizers for polyvinyl chloride against commercial controls. Epoxidized Euphorbia and Vernonia oils and epoxidized trivernolin have potential value as primary plasticizers with the added advantage of increased heat and light stability; they could also be used in combination with other plasticizers utilizing the latter properties. Crude and refined Euphorbia and Vernonia oils are not considered suitable primary plasticizers because of poor compatibility and permanence, at low levels they probably could be used as stabilizers [20] .

Pharmacognostical profile

The present study deals with pharmacognostical and preliminary Phytochemical studies on seed of *Centratherum anthelminticum*. All parameters studied regarding the WHO and pharmacopoeial guidelines. The study revealed presence of patches of rounded to polygonal stone cells tracheids showing pitting, thick walled cell, abundant covering and glandular trichomes, aleurone grains, brown tannin content [21].

CONCLUSION

On the basis of results from a combination of pharmacological, phytochemical and pharmacognostic studies reported, *Vernonia anthelmintica* holds the most promise for development into against diabetes and potential against cancer and inflammatory conditions. Vernodalidimers A and B is so far the most promising agent from the plant that has potential for development into an anti-cancer agent. Vernoanthelcin A–I effects on estrogen biosynthesis in human ovarian granulosa-like cells. The *Vernonia anthelmintica* and isolated compounds require further studies to ascertain the its medicinal potentials.

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