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A Comprehensive Review on *Centratherum anthelminticum* for its Pharmacognosy and Biological Activities

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ABSTRACT:

Centratherum anthelminticum is a well-known medicinal herb in Indian sub-continent and it is commonly called as KaliJiri (bitter cumin). The study was focused on investigating the effect of *C.anthelminticum*. It is an ethno-medicinal plant in India and a common ingredient in ayurvedic medicine. To date, many scientific studies have been carried out, but a comprehensive review on this plant is lacking. This review aims to cover the biological activities and the active compounds derived from *C. anthelminticum*. The phytochemical analysis revealed the presence of alkaloids, flavonoids, tannins, Gallo tannins, phenols, resins, saponins, and steroids. Many of these active compounds were derived from the seeds and have been evaluated for a variety of biological activities like Antimicrobial, Anticancer, Antidiabetic, Anti-inflammatory, Analgesic, Antipyretic, Diuretic, Larvicidal, Anti Filarial, Antioxidant, Anti-tumour, Wound healing, Diuretic activities.Despite the encouraging results demonstrated by these studies and the traditional use as nutraceutical agent, clinical trials of *C. anthelminticum* extracts or derivates are absent. Thus, a systematic documenting review would provide more insights and spur further research that would lead to production of safer and economical alternative medicine from *C. anthelminticum*.

Keywords: *Centratherum anthelminticum*, antimicrobial, larvicidal, antifilarial, cytotoxic

I. Introduction:

Centratherum anthelminticum or *Vernonia anthelmintica* belongs to the family *"Asteraceae"* (Ayurtimes, 2019), . The seed of this plant is called as black cumin / wild cumin and in urdu it is called as kalijeeri (OSADHI, 2025). *C. anthelminticum* is native to Indian subcontinent and cultivated in Pakistan and Bangladesh. In India, it is grown in Gujarat, Rajasthan and other parts of northern India. This plant is well suited for tropical and subtropical climates of the Indian subcontinent and is often cultivated for its potential medicinal properties (Hina Akram Mudassir, 2015 and Mohammad Javad Paydar, 2013).

The seed of this plant have been reported for many pharmacological activities like Antimicrobial, Anticancer, Anti-diabetic, Anti-Inflammatory, Anti-oxidant, Analgesic, Antipyretic, Diuretic, Larvicidal Activities and also wound healing effects (Deepak Singh, 2014). Seeds were reported to be astringent and cure intestinal colic, flatulence, skin disease and ulcers cough. The aerial part of the plant shows mild laxative, smooth muscle relaxant, anthelmintic and mild hypotensive effects of an aqueous alcoholic decoction and the flowers are purgative and used for the treatment of kidney trouble, Asthma, inflammatory swellings, fruits and tonic, diuretic and antiseptic (Amir, 2011). Traditionally the plant is useful for its anthelmintic (worm-expelling) properties (Ulhep. P, 2022). Besides its anthelmintic properties, this plant has been employed for a

range of other medicinal purposes. It is sometimes used for digestive issues, as a mild diuretic, and even for its potential anti – inflammatory and antioxidant effects. Medicinally seeds are very important. Seeds are stimulants, antiseptic and anthelmintic, destroy worms and promote urination, use to treat skin disease. Seeds contain Delta-7-avenesterol, Verne sterol and demanolide (Daksh Bhatia, 2008). The food value of *Centratherum anthelminticum* was evaluated by estimating the contents of proteins such as albumins, globulins, gluteins and certain other free amino acids.

II. Pharmacognostical Studies on Seeds of *Centratherum anthelminticum*:

The study revealed the presence of patches of rounded to polygonal stone cells, trachieds showing pitting, thick-walled cells, abundant covering and glandular trichomes, aleurone grains and brown tannin content. In fluorescence analysis no specific fluorescence was observed. HPTLC profile was also established for successive extracts of the seed using camag HPTLC system (Daksh Bhatia, 2008).

III. PHARMACOLOGICAL ACTIVITY

a. Anti-Inflammatory Activity:

The process inflammation is mediated by various components in different phases. Early stage of inflammation is mainly mediated by the release of histamine, serotonin and bradykinin, while prostaglandin level will increase in later stage showed that both petroleum ether and alcohol extracts of *C. anthelminticum* were effective on oedema reduction after 3 hours, with percentage inhibition of 46.15 and 41.54%,respectively, in carrageenan-induced oedema rats. The finding was comparable to the standard drug, sodium diclofenac (50.77%). The standard sodium diclofenac has been reported to inhibit prostaglandin synthethase indicating that the extracts could have similar prostaglandin release inhibition activity. Another possibility of anti-inflammatory activity of *C. anthelminticum* could be mediated by inhibiting polymorphonuclear cells (PMNs) such as neutrophils, monocytes and macrophages in sub plantar areas. The level of MPO correlates to the degree of inflammation. In Ashok's et al study, the petroleum ether and alcohol extracts of *C. anthelminticum* exhibited anti-inflammatory activity by MPO inhibition and reducing the infiltration of inflammatory cells (Javad Paydar, 2013 and Rajani Srivastav, 2014).

b. Larvicidal Activity:

Srivastava et al. investigated the larvicidal activity of the petroleum ether extracts of *Centratherum anthelimínticum* against anopheles *stephensi*, the primary mosquito vector of malaria. They reported significant larvicidal activity of both leaf and fruit extracts against instar larvae. The findings indicated that the petroleum ether extracts *Centratherum anthelimínticum* fruits can serve as an active agent to control *Anopheles* larvae (Rajani Srivastav, 2014).

c. Antifilarial Activity:

Lymphatic filariasis commonly known as elephantiasis is a tropical disease caused by the nematode parasites *Brugiamalayi, Brugiatimori and Wuchereria bancrofti*. There are claims of anti-filarial activity of *C. anthelminticum* plant seeds; the study demonstrated anti-filarial activities of the aqueous and alcoholic extract of *C. anthelminticum* seeds on *Setariacervi*. Nisha et al. showed in vitro macrofilaricidal activity of *C. anthelminticum* seeds against adult *S.digitata*, the cattle filarial worm (Rajani Srivastav, 2014).

d. Diuretic Activity:

Diuretics are therapeutic agents that can adjust the composition and volume of body fluids by increasing the rate of urine flow and sodium extraction. The petroleum ether, chloroform and alcohol extracts exhibited significant diuretic activity, compared to the standard drug, spironolactone. Both extracts significantly increased Na^+ excretion and surprisingly, decreased k^+ excretion, drastically. This finding indicated the potential of *C. anthelminticum* as a new source of potassium-sparing diuretic (Rajani Srivastav, 2014).

e. Wound Healing Activity:

The wound healing property of *C. anthelminticum* seeds on excision and incision wounds in Wistar albino rats. The aqueous methanol extract of *C. anthelminticum* seeds was prepared in ointment form with two concentrations, 5% W/W and 10% W/W. The results showed that 10% W/W *C. anthelminticum* ointment and standard drug, nitrofurazone ointment exhibited complete healing of the wound. Whereas lower healing activity was observed with 5% (W/W) *C. anthelminticum* ointment application (Rajani Srivastav, 2014).

f. **Antimicrobial & Anti-Fungal Activity:**

The antimicrobial potential of different extracts of *C. anthelminticum* seeds was first investigated by Sharma and Mehta, using filter paper method. They reported significant inhibitory effects of the extracts against several bacteria and fungi. Later, other studies on the antimicrobial activity of various extracts of *C. anthelminticum* indicated that it could serve as a potential antimicrobial agent against a number of pathogenic bacterial and fungal strains [10]. Thirty-fourmedicinal plants, belonging to twenty-eightdifferent families, screened for potential antibacterial activity against six bacterial strains belonging to Enterobacteriaceae, viz *Enterobacter aerogenes* ATCC13048, Escherichia coli ATCC25922, *Klebsiella pneumoniae* NCIM2719, *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 Pneumonia, while the most resistant bacteria were *S. typhimurium* and *E. coli*. From the screening experiment, *Woodfordia fruticose Kurz*. showed best antibacterial activity. This plant may be used further to isolate and evaluate the therapeutic antimicrobials (Nida Baig, 2022).

g. Analgesic & Antipyretic Activity:

Analgesic and Antipyretic activities of petroleum ether and alcohol extracts of *C. anthelminticum Kuntze* seeds evaluated in brewer's yeast induced fever model in rats, acetic – 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. The results suggested that the petroleum ether and alcohol extracts possessed analgesic and antipyretic activities (Rajani Srivastav, 2014).

h. Antioxidant Activity:

Anti-oxidants are compounds that prevent damage cell structures caused by chemical reactions involving free radicals. However, serious side effects of synthetic anti-oxidants, including their carcinogenic potential, led to a general desire to replace them with natural anti-oxidants.The anti-oxidant activity of different extracts of *C. anthelminticum* seeds was determined by 1, 1-Dipheny1-2-picry1hydrazy1 (DPPH), ABTS radical scavenging and phosphomo1ybdenum reducing assays. The extracts showed significant anti-oxidant activity against DPPH and ABTS radicals (Rajani Srivastav, 2014). No toxicity and mortality due to *C. anthelminticum* fixed oil and its hexane chloroform, and ethanol fractions were observed within 24-48 hours and for 15 days there-after (Rajani Srivastav, 2014 and Anees Ghosi, 2017). The extracts of Centratherum anthelminticum and Withania coagulans showed the improvement in the lipid profile and oxidative stress in Triton X-100 induced Hyperlipidemic rabbits (Nida Baig, 2022).

i. Anti-Anxiety Activity:

The methanolic extract of *C. anthelminticum* shows significant anti-anxiety activity in elevated plus maze apparatus and light dark test. The plant containing carbohydrates flavone glycosides, phenolic compound, flavonoids and sterols were identified. Flavonoids may be responsible for the neuropharmacological activity of the plant. In the present study, use of EPM and light dark model of anxiety to evaluate the anxiolytic effects of the methanolic extract of *C. Anthelminticum.* Diazepam shown significant increase in time spend and in number of entries into the open arms and light chamber. Diazepam also increased the total number of entries. These data are in agreement with the results of other studies, where diazepam and other benzodiazepines have been shown to produce anxiolytic effects in variety of anxiolytic screening procedures, including EPM and light dark model (Anees Ghosi, 2017) (Chung Yeng Looi, 2013).

j. Anti Tumour Activity:

In 2012 group demonstrated that the chloroform fraction of *C. anthelminticum* (CACF) possessed higher anti-cancer activity compared to methanol and hexane fractions. CACF effectively inhibited growth of A549(lung), PC-3 (prostate), MCF-7 (breast) cancer cells with IC50 values of 31.42+/- 5.4, 22.61+/- 1.7 and 8.1+/- 0.1ml, respectively (Chung Yeng Looi, 2013). The powdered seeds of *C. anthelminticum* were extracted successively with hexane, chloroformand methanol in a Soxhlet apparatus for 24 hours. The resultant extracts were filtered using Whatman No.1 filter paper and dried under vacuum to yield respectively of the extracts. Then the dried fractions were kept at -2^0C until further use. Determined the cytotoxic effect of CACF on cell

survival using a well-characterised human breast cancer cell line, MCF-7.MTT assay was used to determine cell viability. The survival of MCF-7 decreased significantly in a concentration dependent manner with IC50 value at 6.8-1.2 MCA/ml. No significant cell inhibitory effect was observed in DMSO (solvent)-treated samples. As a positive control, we treated MCF-7 cells with doxorubicin, a cancer chemotherapy drug, which showed IC50. To verify MTT results, we found comparable results between MTT and Alamar blue staining assays.

k. **Anti Diabetic Activity**:

The present findings conclude that hypoglycaemic effect of ESEt of *C. anthelminticum* in fructose - induced type to diabetic rabbits may be due to correcting insulin resistance by inhibiting either fructose absorption in intestine or triglycerides synthesis in liver. Thereby enhancing receptor sensitivity for insulin and correcting carbohydrate utilization in body cells. *C. anthelminticum* was effective in decreasing blood glucose level. Several phytoconstituents of this plant including Flavonoids, alkaloids, phenols, saponins, steroids which were detected in ESEt. Certain naturally occurring flavonoids, such as quercetin, kaempferol, luteolin, quercetagetin, and scutellarein act as inhibitor of human alpha amylase, which makes them promising candidates for controlling the digestion of starch. Flavonoids are integral parts of human diet providing potential antioxidant benefits for managing diabetes by also preventing the progressive impairment of pancreatic beta – cell function due to oxidative stress. They cannot be synthesized by the human body, and play beneficial roles in human life (Md.Ali Asgar, 2013).

l. Cytotoxic Activity:

The *C. anthelminticum* chloroform fraction (CACF) has profound cytotoxic activity against human melanocytes, by inducing apoptosis through modulation of anti – and pro –apoptotic signalling pathways. CACF induces intracellular reactive oxygen species (ROS) generation, which causes DNA damage, increased membrane permeability and activation of mitochondria - dependent caspase cascade. These effects induce up-regulation of P35 and down-regulation of Bcl-2, which commit cells to apoptosis. In addition, CACF also inhibit pro-survival signalling by preventing NF-KB nuclear translocation. Together, our findings further support the development of CACF as an alternative therapeutic agent melanoma malignancy (Chung Yeng Looi, 2013 and Aditya Arya, 2012).

m. Hypolipidemic Activity:

The important and initiating factor of atherosclerosis is hyperlipidemia, a disorder of lipid metabolism manifested by elevated levels of triglycerides and bad cholesterols and low level of good cholesterol in serum. Among the acquired factors, diet having high fat and low Fiber contents contribute hyperlipidemia which inturn induce oxidative stress by producing reactive oxygen species (ROS) that accelerates lipid peroxidation (LPO) thereby affecting many body organs particularly heart. Ethyl-acetate,acetone,methanol, and water extracts of *C. anthelminticum* shows hypolipidemic activity (Tooba Lateef ,2016).

n. Anthelmintic Activity:

Helminthiasis is the most common cause of the intestinal infestation. Aqueous extracts from the seeds of *C. anthelminticum* were investigated for their anthelmintic activity against Earthworm (*Eisneia Fetida*). Mebendazole is used as the standard drug. Extract was studied in the bioassay a 100 mg/ml, which involved determination of time of paralysis and time of death of worms. Anthelmintic from natural sources may play a key role in the treatment of parasitic infestation (Santosh J Gutte, 2022).

o. Anti-Asthmatic Activity:

Antiasthmatic activity by Histamine induced pre-convulsion dyspnoea (PSD), Mast cell de-granulation (MSD) BY Compound 48/80 and Egg albumin induced asthma at different dose levels. In PCD Animals were divided into three groups and % increase in time of PCD was recovered. InMCD, Animals were divided into seven groups and % protection of mast cell was measured. In egg albumin induced asthma, animals were divided into five groups. Broncho-alveolar fluid was collected and evaluated. Dunnett's t-test and post hoc test were used for statistical analysis. The Methanolic Extract of *C. anthelminticum* significantly decreased bronchospasm induced by histamine and protected the mass cell de-granulation as compared to the control group. It also significantly decreased the total leukocyte and different WBC count in egg albumin induced asthma. Anti-asthmatic action of *C. anthelminticum* could be due to its anti-histaminic, mast cell stabilizing property and preventive effect on infiltration of inflammatory cells (Samirshah, Kintu Patel, 2022).

p. Hepatotoxicity Activity:

To evaluate the hepatoprotective effect of ethanolic seeds extract (ESEt) of *C. anthelminticum* carbon tetrachloride induced liver injury. The test doses (600 and 800 mg/kg) of same extract were found effective in their respective test groups by improving the body and liver weights, serum alanine and aspartate transaminases,y-glutamyl transpeptidase, alkaline,phosphatase, total proteins,albumin, total bilirubin, especially indirect bilirubin and uric acid levels as compared to CCl4 induced hepatotoxic control group. In addition, decreased percent inhibitions of antioxidant parameters includingcatalase, superoxide dismutase and reduced glutathione accompanied with increased percent inhibition of lipid peroxidation observed in both test groups.Histopathological studies also proved the liver regenerating property of ESEt by showing decrease in fatty deposition, necrosis and inflammation around the central vein of liver lobules. Therefore, the ESEt was found to be hepatoprotective in nature (Shamim A. Qureshi, 2016).

q. **Anti Nephrolithiatic Activity**:

Antinephrolithiatic activity of 70% methanolic extract of *C. anthelminticum* seeds (CAE) was evaluated in vitro on nucleation and aggregation of calcium oxalate crystallization. Calcium oxalate crystallization was induced by the addition of 0.01 M sodium oxalate solution in synthetic urine. The effect of CAE (100, 200, 300, 400, 600, 800, 1000 mcg/ml) was studied by the measurement of turbidity in presence or absence of extract at 620 nm of a spectrophotometer. The rates of nucleation and aggregation were evaluated by comparing the turbidity of a control system with that of one exposed to the extract. Crystals in the urine were also analysed by light microscopy. From photomicrography, it is confirmed that CAE inhibited the nucleation of calcium oxalate crystals, decreasing their number and size. Also, percentage inhibition of crystals aggregation increased as the concentration of CAE increased. The result of the present study indicated that 70% methanolic extract of *C. anthelminticum* seeds has the higher capacity to inhibit the crystal formation and aggregation. These suggested possible anti-nephrolithiatic activity of *C. anthelminticum* seeds against calcium oxalate stones (Varsha J. Galani, 2014).

r. Ameliorating Effect:

Polycystic ovary syndrome (PCOS) in females is an endocrine pathological condition of reproductive age which is usually caused by insulin resistance, hyperlipidemia, and oxidative stress. The research was aimed at evaluating the therapeutic effect of the *C. anthelminticum* seed extract (CA) against PCOS in rodents as it is traditionally used to treat diabetes, inflammation, and gynaecological problems. The CAwas chemically characterised by high-performance liquid chromatography-diode array detection (HPLC-DAD). For the induction of PCOS, a high-fat diet (HFD) WAS given to all female Wistar rats for nine weeks except the normal control group, which was given a normal chow diet. Estradiol valerate was given to all rats except normal control. After the induction of PCOS, oral metformin (300 mg/kg) was given to the standard group, while CA was orally administered to diseased rats at 250, 500, and 750 mg/kg/day for 28 days.

HPLC-DAD analysis revealed that kaempferol-3-pcoumaroylglucoside was present in the highest amount (146.8 -1.8 mg/g) of the extract followed by ferulic acid and cholesterol and triglyceride levels in CA treatment groups. A significant rise is observed in progesterone and follicle stimulating hormone with a decrease in luteinizing hormone in the treatment groups as compared to disease control, which indicated normalization of the estruscycle. Overall, the results confirmed the efficacy of CA against PCOS- in treating estradiol –HFD- induced PCOS due to its antidiabetic, anti-inflammatory, antihyperlipidemic, and antioxidant properties (Moonis Shoaib,2023).

s. Neuropharmacological Activity:

The effect of oral dosing of methanolic extracts of *C. anthelminticum* on Neuro pharmacological activities OF Mice. Methanolic extracts of *Centratherum anthelminticum* were soluble in Dimethyl sulphoxide (DMSO) i.e., organic solvent, so it is used in this study.Screening for anxiolytic and Anti-depressant effects were performed using open field test, head dip test, stationary rod test, cage crossing test, light and dark box and swimming-induced depression test. Twenty animals were divided into 2 groups of 10 animals each and numbered as 1 (control, on DMSO) 2 (on methanolic extract Of *C. anthelminticum*). The extract and DMSO were administered orally for 60 days. Any possible change in animal behaviour was evaluated on day15, 30 and 60 of dosing. The group 2 showed significant increase in open field activity and light and dark box test respectively, while significantly decreased activity was observed in head dip and cage crossing activity after 60 days of dosing. Based on above findings, it is suggested that the extract of *C. anthelminticum* have antidepressant and anxiolytic potential with sedative effects (Raana Mahmood, 2019).

IV. Research and Future Directions:

Encourage students to consider areas of research related to *C. anthelminticum* including clinical trials, drug development, and phytochemical analysis. Emphasize the potential for innovative pharmaceutical solutions.

V. Conclusion:

To summarize the significance of *C. anthelminticum*, the drug emphasizes its diverse pharmacological properties and potential pharmaceutical applications due to its rich phyto-constituents. A call of action required to explore the plants deep therapeutic potential future and clinical evidences.

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