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ETHNOMEDICINAL USES, PHYTOCHEMISTRY, AND PHARMACOLOGICAL INSIGHT OF *CYANTHILLIUM CINEREUM* (L.) H. ROB.: A COMPREHENSIVE REVIEW

Karan Singh[1]*, Amit Aggarwal[1]

[1]Maharaja Agrasen School of Pharmacy, Maharaja Agrasen University, Baddi-174103, Distt. Solan,Himachal Pradesh, India.

ABSTRACT

Cyanthillium cinereum is a plant species in the family Asteraceae. It is a common weed that grows in tropical and subtropical regions around the world, including Asia, Africa, and the Americas. In traditional medicine, various parts of the plant have been used to treat a wide range of ailments, including fever, inflammation, pain, and gastrointestinal disorders. The plant is also known to possess various biological activities, such as antioxidant, antimicrobial, and anti-inflammatory properties. Thus, the present review aims to provide updated information on *C. cinereum* botany, ethnomedicinal uses, phytochemistry, pharmacological effects, and toxicity as well as also highlight perspective for future research. Particular emphasis is also given to its antioxidant potential in health promotion. In-depth literature was probed by searching several sources via online databases, texts, websites, and thesis. Many studies have been conducted to investigate the phytochemistry and pharmacological properties of *C. cinereum*, and the results suggest that it contains various bioactive compounds, including flavonoids, alkaloids, terpenoids, and phenolics. These compounds may be responsible for the medicinal properties of the plant. It is important to note that while *C. cinereum* has been traditionally used for medicinal purposes, further research is needed to fully understand its potential benefits and to develop safe and effective treatments based on its bioactive compounds.

Keywords: *Cyanthillium cinereum*, phytochemistry, ethnomedicinal uses, pharmacology, etc.

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INTRODUCTION

Cyanthillium cinereum (L.) H. Rob or Sahadevi was previously known as *Vernonia cinerea* (L.) Less [1] as well as *Conyza cinerea* L. and is commonly known as little ironweed, which is a common annual weed that has a wide range of geographical distribution throughout India, Bangladesh, Sri Lanka, and Malay Islands [2]. This plant has great value in *Ayurveda*. This plant is also known as Sahadevi that has diverse pharmacological activities such as anti-inflammatory, antipyretic, analgesic, anti-bacterial, anti-microbial, diuretic, diaphoretic, alexipharmic, anthelminthic, depurative, lithotriptic, anodyne and stomachic [3]. It is popularly known for its smoking cessation activity that decreases cigarette cravings in smokers. Phytoconstituents responsible for showing these activities have also been identified. *C.cinereum* have shown the presence of flavonoids, terpenoids, glycosides, aliphatic acids, saponins, fatty oils, alkaloids, fatty oils, triterpenoids, esters, and sesquiterpenes after the extraction with different solvents [4]. The paste of its stem and bark is used to treat cuts. Flowers of this plant are used in the treatment of arthritis, conjunctivitis, and rheumatism [5]. To treat the incontinence of urine and piles extract of *C. cinereum* is of great use. In the treatment of stomachache, cough, diarrhea, and bronchitis the decoction of this plant can be used since it has no adverse reactions [4]. The dried whole plant of *C. cinereum* has free radical scavenging activity. *C. cinereum* leaves have antipyretic, analgesic and anti-inflammatory effects [2]. Infusion of the root is used as an antidote for snake venom and scorpion sting [5]. In recent years, the interest in traditional as well as complementary medicine is growing worldwide. *Cyanthillium cinereum* was extensively used in Thailand as a complementary medicine for the cessation of smoking. Since 2012, this plant got enlisted in the National List of Essential Medicines, Ministry of Public Health, Thailand [6].

C. cinereum or little ironweed or poovamkurunnal or poovamkurunnila (in Malayalam) or monara kudumbiya (in Sinhalese) is basically a perennial plant from the sunflower family. The taxonomical classification of *C.cinereum* is **Kingdom:** Plantae, **Clade:** Tracheophytes, Angiosperms, Eudicots, Asterids, **Order:** Asterales, **Family:** Asteraceae, **Genus:** *Cyanthillium*, **Species:** *C.cinereum* [5,6].

BOTANICAL DESCRIPTION

Habitat

C. cinereum is traditionally used in folklore medicine. It is a significant plant in Kerala. This plant is extensively found throughout Andra Pradesh, Karnataka, in all districts of Kerala, Aloka district of Maharashtra, throughout Odisha, and Tamil Nadu. Worldwide *C.cinereum* is mostly

found in Tropical Asia, Africa, Bangladesh, New Zealand, and Australia [7,8]. Figure 1 represent the distribution of *C. cinereum* in India.

Figure 1. Distribution of *C. cinereum* in India. [The shaded areas in yellow represent the natural habitat of *Cyanthillium cinereum* in India.]

Morphological and Microscopical Characteristics

Morphological and microscopical characteristics of *C. cinereum* provide valuable information for the identification and authentication of the plant species. The plant is an annual or perennial herb that can grow up to 1 meter tall. The stem is erect, branching and covered with hairs. The leaves are alternate, simple and vary in shape from elliptic to lanceolate. They are arranged spirally along the stem and have toothed or serrated margins. The flowers are small, pink or purple in color, and arranged in clusters at the end of the branches. They are composed of a

central disk surrounded by numerous ray florets. The fruit is an achene that is 1-2 mm long, brown in color, and covered with fine hairs. Microscopically, the stem of *C. cinereum* shows the presence of a single-layered epidermis with cuticle and unicellular non-glandular trichomes. The cortex contains collenchyma and parenchyma cells. The vascular bundles are arranged in a ring and surrounded by a sclerenchymatous sheath. The leaf of the plant shows a single-layered epidermis with stomata, palisade and spongy parenchyma, and vascular bundles [1,7]. Morphological features of different plant parts are depicted in Figure 2.

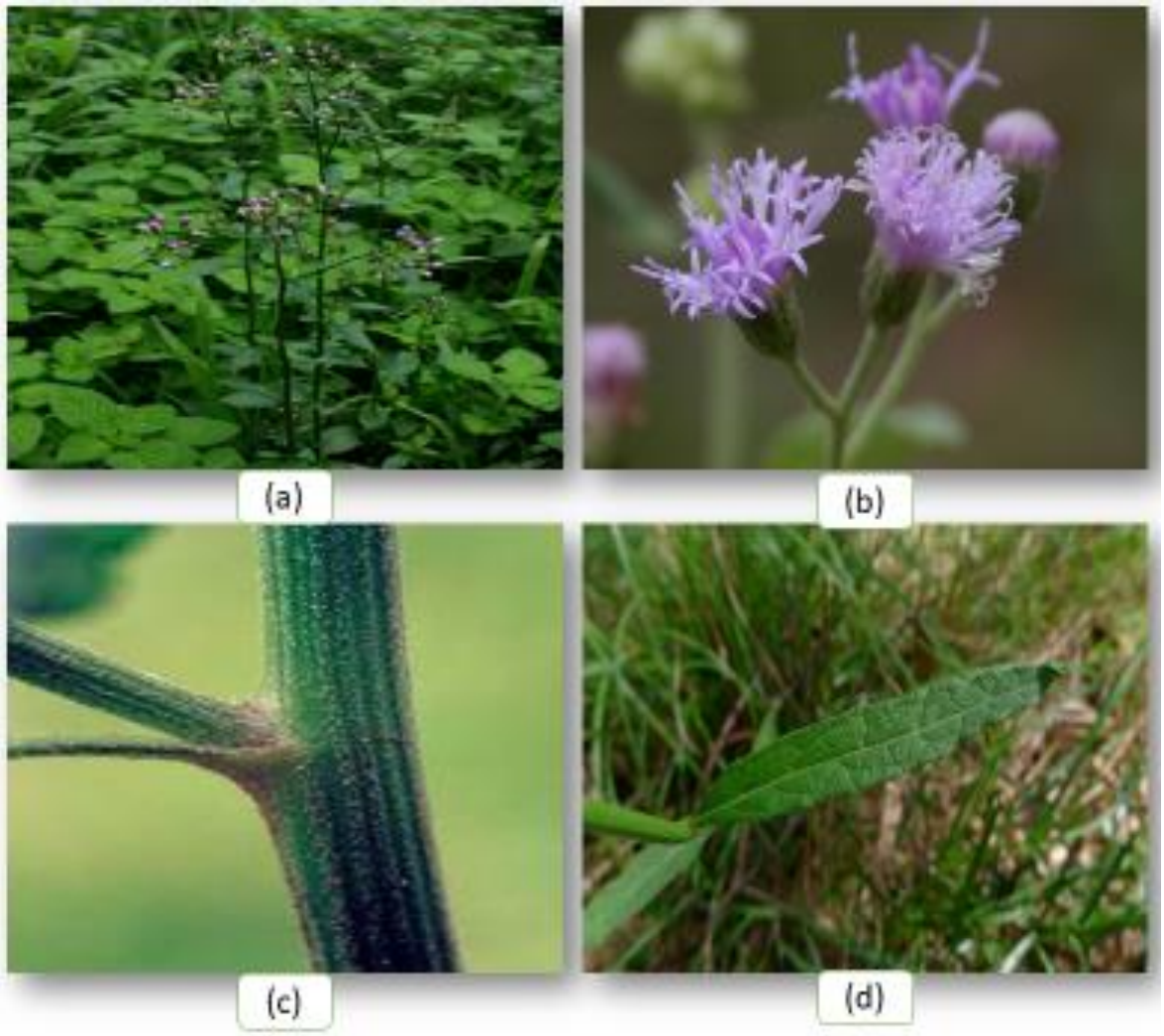


Figure 2. *Cyanthillium cinrereum* (a) Whole plant, (b) Flower, (c) Stem, (d) Leaf.

Ethnomedicinal Uses

C.cinereum is a traditional plant that has several therapeutic benefits of its leaves, seeds, bark, roots, stem, flower, and whole plant. Ethnomedicinal uses of various plant parts are tabulated in Table 1.

Table 1. Ethnomedicinal Uses of *C.cinereum*

Plant Parts	Uses	References
Stem and leaves	Smoking cessation	[6, 8]
Whole plant	Dysentery, Dyspepsia, Stomatitis, Filariasis, Fever, Diarrhea, Abdominal Pain, cough	[2,6,7]
Seeds	Alexipharmic, Anthelminthic, Leprosy, Constipation and Flatulence, Chronic skin disease, Food poisoning	[2,7]
Leaves	Analgesic, Eye disease, Indigestion, Ringworm, Amoebiasis, Elephantiasis, Malarial fever, Antipyretic, Anti-inflammatory	[2,7]
Root	An antidote to Scorpion, Snake Venom, Diabetes,	[7,8]

Physiochemical and Nutritional analysis

Numerous physiochemical and nutritional parameters of *C. cinereum* have been studied, as shown in Tables 2 and 3.

Table 2. Physiochemical Estimation of *C.cinereum*

Parameters	Results				References
Extractive value (%w/w)	**Whole Plant**	**Leaf**	**Stem**	**Root**	
Aqueous Extract	14.61	15.73±0.06	15.48±00.26	11.10±0.23	[1,12,13]
Alcoholic Extract	13.00	18.76±0.11	03.52±0.17	06.25±0.38	
Ethanolic Extract	15.12	-	-	-	
Hydroalcoholic Extract	-	17.03±0.11	08.03±0.65	-	
Chloroform	-	03.21±0.22	0.99±0.16	0.41±0.04	
Petroleum Ether	6	0.1±0.04	0.59±0.07	0.94±0.02	
Ash Value (%w/w)					
Total ash	8	13.83±0.99	06.08±1.00	03.39±0.44	
	-	13.33±0.89	10.33±1.29	09.27±0.44	
Water soluble ash	1.63	06.23±0.26	03.05±0.70	02.22±0.18	
Acid insoluble ash	0.55	01.44±0.27	0.44±0.08	0.33±0.11	
Moisture content	7	-	-	-	
Fibre content	33.13	-	-	-	

Table 3. Mineral content of *C. cinereum*

Parameters	Content present(mg/g)	References
Protein	42.6	[14]
Lipid	11.6	
Chlorophyll a	0.32	
Chlorophyll b	0.86	
Carotenoids	2.64	
Thiamine	4.2	
α tocopherol	1.86	
Ascorbic acid	2.86	
Calcium	85	
Iron	5	
Phosphorus	10	

Phytochemistry

Terpene and Terpenoids

Four sesquiterpene lactones such as 8α-(2′z-tigloyoxy)-hirsutinolide; 8α-(2′z-tigloyoxy)-hirsutinolide-13-*O*-acetate; 8α-hydroxy-13-*O*-hirsutinolide; 8α-(4-hydroxytigloyloxy)-hirsutinolide were extracted from the methanolic extract of *C.cinereum* leaves and stem [15]**.** Roots of *C.cinereum* possessed six crucial triterpenes such as δ -amyrin acetate, α-amyrin acetate, β-amyrin acetate, β-amyrin, and α-amyrin [15-17]. 12-oleanen-3-ol-3β-acetate was found in the leaves of the plant *C.cinereum.* A pentacyclic triterpenoid, Lupeol (3′-hydroxylup-20(29)-ene) was isolated from the ethyl acetate fraction of methanolic extract of the whole plant of *C.cinereum.* The whole plant of *C.cinereum* contained 8α-(2-methylacryloyloxy)-1-O-methylhirsutinolide-13-*O*-acetate, which was regarded as Vernolide K. Vernobockolide B (4′-hydroxypiptocarphin F) was also isolated from the whole plant of *C.cinereum.* Root oil of *C.cinereum* consists of trans-β-bergamotene, β-elemene, β-pinene, cyperene, and germacrene A which are sesquiterpenes. Whereas, Essential oil of *C.cinereum* flower contains trans-β-bergamotene, γ-humulene, β-pinene, (E)-β-caryophyllene, (E)-β-farnesene which are sesquiterpenes. Loliolide and isololiolide are the two terpene lactones that were also found in this plant source [15-20]**.**

Sterols

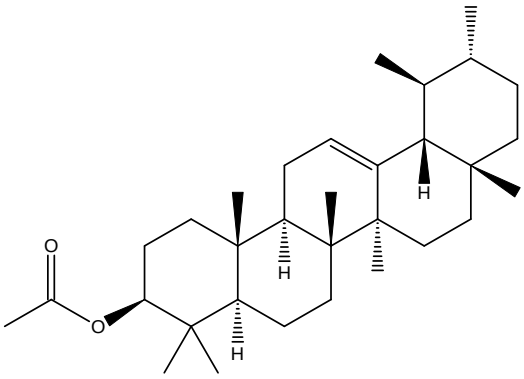
β-sitosterol, stigmasterol, and α-spinasterol were isolated from the whole plant of *C.cinereum* [13,14].

Polyene

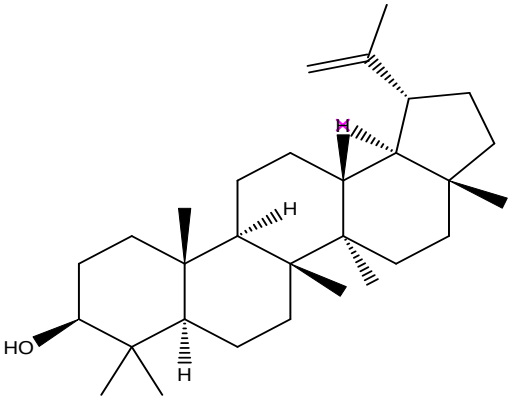
Leaves of *C.cinereum* contains a new polyene compound called urticifolene [6,20].

Carotenoids

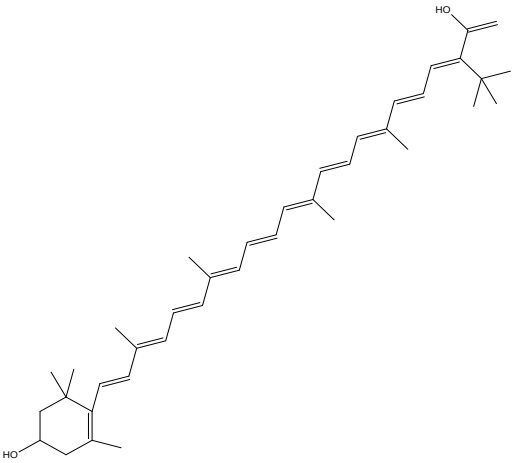
Lutein, a member of carotenoid family was found in the leaves of *C.cinereum* [13]**.** Chemical strudtures of these bioactive compounds are depicted in figure 3.



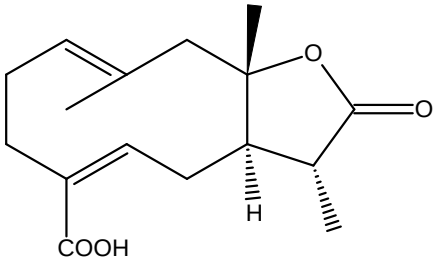
Alpha Amyrene Acetate



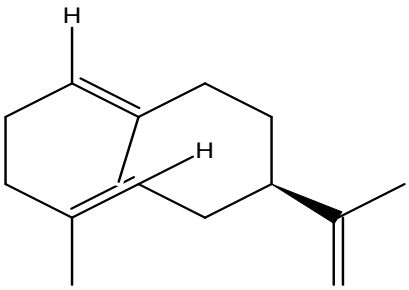
Lupeol



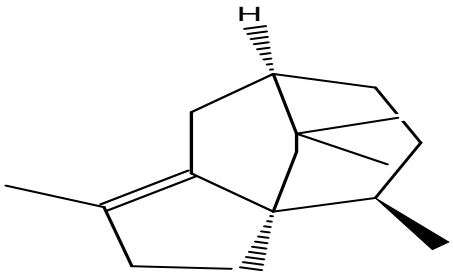
Lutein



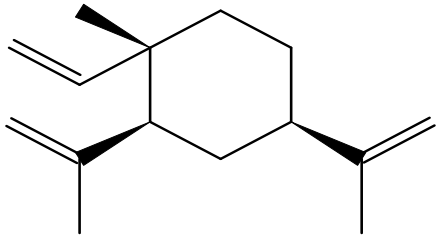
Vernobockolide B



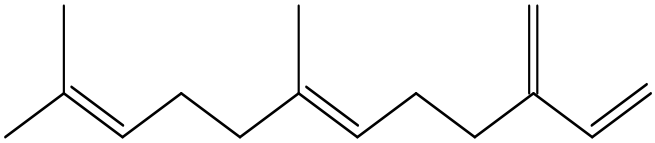
Germacrene A



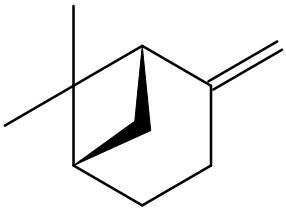
Cyperene



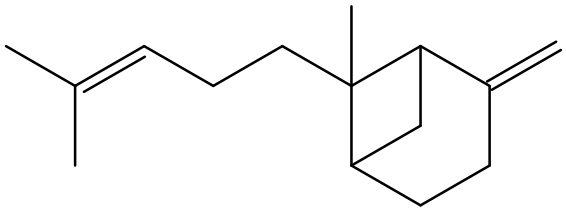
Beta Elemene



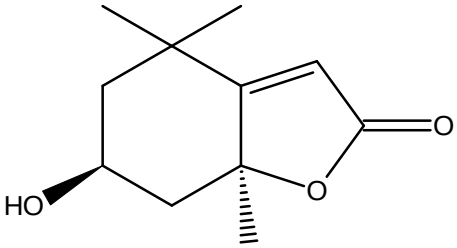
Beta Farnesene



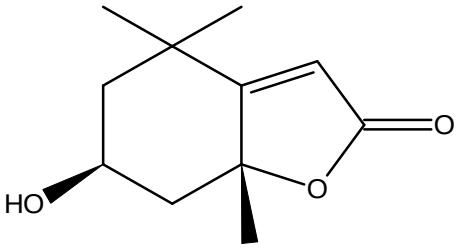
Beta Pinene



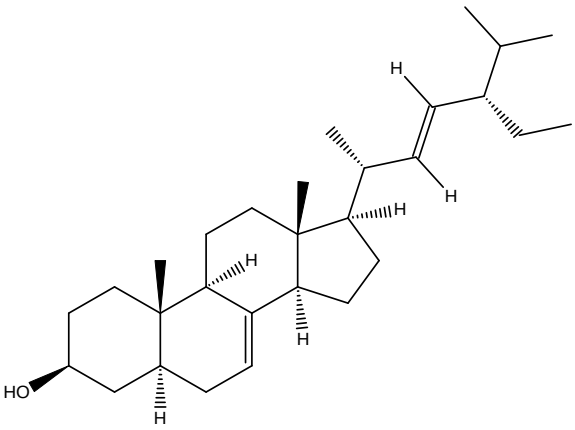
Trans Beta Bergamotene



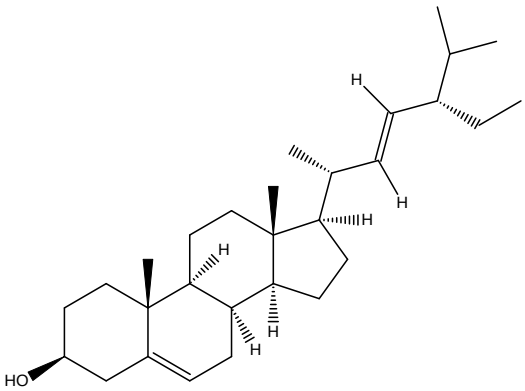
Iso Loliolide



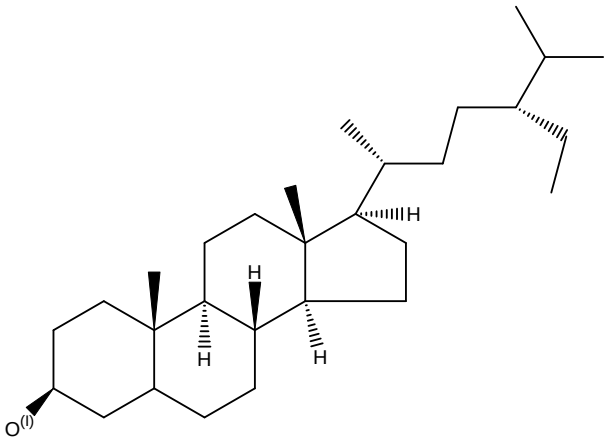
Loliolide



Alpha Spinasterol



Stigmasterol



Beta Sitosterol

Figure 3. Chemical structure of potential bioactive compounds of *C. cinereum*

Pharmacological Activities

Various studies have been done to find out the pharmacological actions of *C. cinereum* such as diabetes, filariasis, malaria, diarrhea, gastrointestinal disorders, liver disorders, fever, and diuretics [21]. *C. cinereum* significantly decreases the level of pro-inflammatory mediators such as TNF-α, IL-6, and IL-1β and inhibits the action of NF-κB [22]. Besides this, the plant inhibits lipid peroxidation in renal slices. Other than down-regulating the production of pro-inflammatory cytokines, this plant also inhibits pro-metastatic genes (MMP-9, lysyl oxidase, MMP-2, VEDF, prolyl hydroxylase, *k-ras*, ERK-1, and ERK-2) as well as up-regulates the expression of antimetastatic genes (TIMP-1, nm23, and TIMP-2) [23,24]. It also helps in decreasing fasting blood glucose, glycosylated hemoglobin, cholesterol, and triglyceride levels [25]. It is a potent antioxidant. *C.cinereum* effectively scavenges the hydroxyl radical, superoxide, and nitric oxide. It also possesses anti-microbial as well as antiprotozoal activity. It also has spasmodic and radioprotection effect [26].

Table3. Pharmacological effects of *C. cinereum*

Part Used	Extract	Dose treated/ Route of Administration	Animals/ Cell Lines	Experimental Models	Result	References
Whole Plant	Aqueous Extract	400mg/kg; i.p	Male albino mice	Cisplatin-induced Renal damage	Reverses renal damage and regenerates renal Epithelial cells.	[27]

Aerial parts	Aqueous and Ethanolic Extract	25-50µg/ml	SW620 and HT29	MTT assay	Antioxidative and Free Radical Scavenging activity	[17]
Whole Plant	Aqueous Extract	250 and 500mg/kg; oral gavage	Mice	High Fat Diet Induced Model	Improves impaired glucose and lipid homeostasis. Manages Insulin resistance related diseases.	[28]
Gold nanoparticles of Leaf and Stem	Aqueous Extract	2mg/ml	*Bacillus subtilis, Chromobacterium violaceum, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pyogenes, Aspergillus niger, Fusarium oxysporum , Rhizopus oryzae, Penicilliu m expansum.*	Disc Diffusion Assay	Higher antimicrobial activity	[29]
		1.28.78µg/ml 2. 30.22 µg/ml		1. DPPH assay 2. ABTS assay	Showed good antioxidant property.	
Whole Plant	Methanolic Extract	25, 50, 100 µg/ml	*Xoo*	Agar Plate assay	An eco-friendly antimicrobial compound.	[30]
Aerial Parts	Ethanolic extract	0-20µM	Human liver microsomal CYPs 1A2, 2A6, 2B6, 2C8, 2C9,	Cocktail inhibition assay	Demonstrates time-dependent inhibition, mechanism-based inactivation towards CYP2A6.	[31]

			2C19, 2D6, 2E1 and 3A4.			
Leaves and stem	Ethanolic extract	40mg/kg; oral gavage	Sprague-Dawley rats	Streptozotocin-induced diabetic model	Significantly restored sperm motility and testosterone concentration and decreased testicular histopathological changes in DM rats.	[32]
Whole Plant	Ethanolic extract	1.18, 0.85, 0.66, 0.71 and 0.45 µM	RAW264.7	In vitro anti-inflammatory assay	Enhances The inhibition of NO production	[18]
Whole Plant	Ethanolic extract	200, 300, 400mg/kg; p.o	Wistar rats	Vincristine-induced painful neuropathy	Shows beneficial effects by exerting antioxidative, neuroprotective, and calcium channel inhibitory actions.	[12]
Whole Plant	Ethanolic extract	200, 300, 400mg/kg; p.o	Wistar rats	Sciatic nerve-induced behavioral hyperalgesia	Shows potential antioxidative, neuroprotective, and calcium channel inhibitory actions.	[33]
Whole Plant	Ethanolic extract	40-60 µg/ml	HeLa, A549, MCF-7, Caco-2	Cytotoxicity assay	Possesses a cytotoxic effect, triggers apoptosis, inhibits MDR transporters, enhances drug uptake, and sensitized cancer cells towards anticancer drug-mediated cytotoxicity.	[34,35]
Leaves	Methanolic extract	30 µg/ml; oral gavage	Sprague-Dawley rats	Selenite induced cataract	Lupeol extracted from VC was found effective in the treatment of cataracts.	[17]

CONCLUSION

India is considered to have a rich heritage system of medicine. *C. cinereum* is an underrated medicine that was used to be considered an alternative medicine for many diseases. But this plant is yet to be explored commercially for the benefit of mankind. The pharmacological properties of *C. cinereum* are continuing to be explored till now. Many areas are still untapped. Since, this plant is a rich source of minerals and beneficial phytocomponents, so it can be hypothesized that

this plant is able to create miracles in the treatment of various complex diseases. Another surprising property of this plant is its multi-target action to treat co-morbidity. Further studies are yet to be done in multi-target prospects. Besides this, it can be anticipated that from the above review, researchers will get help with the usefulness of this plant and further investigation will be done to isolate some novel potential phytocompounds possessing efficacy against various complex diseases.

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***Correspondence Author:** Karan Singh, Maharaja Agrasen School of Pharmacy, Maharaja Agrasen University, Baddi-174103, Distt. Solan,Himachal Pradesh, India.