

Therapeutic Uses and Prospects of *Cyanthillium cinereum* - The Underrated Herb

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<https://dx.doi.org/10.13005/bpj/2473>

(Received: 30 June 2021; accepted: 08 July 2022)

The whole plant of *Cyanthillium cinereum* has several pharmacological properties in treating a broad range of diseases in traditional medicine but underestimated to be used as a commercial drug. As a remedy to several health conditions, phytochemicals of *C. cinereum* can be used as multi-target drugs to treat comorbidity. This review elaborates on the therapeutic benefits of the herb, *C. cinereum* and its prospects in the treatment of diseases.

Keywords: *Cyanthillium cinereum*; Multi-target drugs; Alternative medicine; Phytochemicals; Multi-target drugs.

Cyanthillium cinereum commonly called the little ironweed, belongs to the family of Asteraceae and has become a native to Africa, Australia, tropical and temperate Asia though originally a native of Central America. *C. cinereum* commonly occurs in upland crop areas, gardens, waste places, and along the roadsides and its therapeutic benefits are often underrated. Studies on phytochemical constituents of *C. cinereum* have shown the presence of glycosides, flavonoids, aliphatic acids, terpenoids, sterols, saponins, tannins, fatty oils, triterpenoids, alkaloids, esters, and sesquiterpenes on extraction with different solvents¹. The major phytoconstituents present in the ethanolic extract of *C. cinereum* are lupeol, lupeol acetate, luteolin-7-O-glucoside, stigmaterol- β -D-glucopyranoside, stigmaterol and dotriacontanoic acid, along with several other minor phytochemicals².

The extensive free radical scavenging potential of dried whole plant *C. cinereum* is well studied and established that might contribute to its total phenolic and flavonoid contents resulting in a therapeutic benefit^{3,4}. Extract of *C. cinereum* has been used in the treatment of urinary incontinence and piles. Also, it is given as a decoction to treat diarrhea, stomachache, cough, and bronchitis in traditional medicine, without any adverse effects⁵. *C. cinereum* possesses anti-microbial, anti-bacterial properties and has been used as an alternative source to antibacterial agents^{6,7}. The whole plant has several pharmacological properties in treating a broad range of diseases in traditional medicine but underestimated to be used as a commercial drug. This review elaborates on the therapeutic benefits of the herb, *C. cinereum* and its prospects in treatment of diseases.

Therapeutic uses of *C. cinereum*

Antibacterial, antiviral and antiplasmodial activity

Methanolic extract of leaf exhibited maximum antibacterial activity towards *S. aureus* and hexane extract of the flower against *B. cereus*, accounting for the presence of Saponins, while the whole plant extract showed good anti-bacterial activity against *E. coli* and *Klebsiella pneumoniae* species⁸. Maximum antibacterial activity was shown by the petroleum ether and ethanolic extracts⁹. The methanolic crude extract of the root of *C. cinereum* proved the antistaphylococcal activity. *C. cinereum* have been used successfully in folkloric medicines in the indigenous communities in the Philippines¹⁰.

The methanolic fraction of ethanolic extract of the root of *C. cinereum* exhibited 50 % antiviral activity against the Japanese Encephalitis Virus in vitro (Vero cells). A new flavone glycoside 5,7,4'-trihydroxy 3'-methoxy flavone-4'-O- α -L-rhamnopyranosyl-(1'4)-O- α -L-arabino-pyranosyl-(1'3)-O- β -D-galactopyranoside showed antiviral activity along with luteolin and taxifolin. Nevertheless, methanolic extract of the leaves of *C. cinereum* showed against dengue virus using dengue NS2B-NS3 protease

Among other members of the Asteraceae family, the alkaloid extracts of *C. cinereum* have been proved as a good source for antimalarials¹¹. The crude alkaloid extracts from the whole plant showed good antimalarial effects against the chloroquine-resistant strain K1, with IC₅₀ values 2.56 μ g/ml. *In vitro* anti-plasmodial evaluation showed that the sesquiterpene lactones were active against chloroquine-resistant *Plasmodium falciparum* strain (W2)¹².

Anti-oxidant activity

Phytochemicals of different classes and several plant extracts have been found to have prominent antioxidant activity, among which *C. cinereum* show exiting results^{13,14,15}, owing to the presence of a large number of flavonoids and triterpenoids. The antioxidant properties of *C. cinereum*, evaluated by DPPH radical-scavenging activity, with standard antioxidants, gallic acid and quercetin proved the anti-oxidant potential of the herb⁶. This property would aid in its prospective clinical use as preventive medicine against various degenerative diseases and also tissue aging. Whole

plant hexane, chloroform, methanolic and aqueous crude extracts bear potent antioxidant property. Furthermore, *C. cinereum* has shown anti-oxidant protective effects against oxidative damage to biological molecules such as lipids and DNA¹⁶. Therefore extracts of *C. cinereum* could sustain equilibrium between free radicals and antioxidant systems inhibiting oxidative damage cascade in cells to mitigating degenerative diseases.

Anti-inflammatory activity and Antipyretic activity

Thailand is well known for the traditional application of aerial parts extracts of *C. cinereum* for immune-related remedies and anti-inflammation¹⁷. The alcoholic extract of the flowers of *C. cinereum* caused a reversal of the inflammatory processes in adjuvant arthritic rats¹⁸. Further, leaf extracts of *C. cinereum* have been reported with significant analgesic, anti-inflammatory and antipyretic properties¹⁹. *C. cinereum* is also widely used with quinine for its antipyretic benefit on malarial fever²⁰.

Anti-hyperglycemic activity

Though several plants were reported to lower blood glucose and are used to treat multiple diseases, only a hand full has enormous potency to show direct therapeutic effects²¹. The presence of phytochemical bioactive compounds like glycosides, esters, flavonoids, steroids, tannins and terpenoids in abundance had resulted in the anti-hyperglycemic activity of *C. cinereum*²². Treatment with *C. cinereum* has shown a significant decrease in fasting blood glucose levels and HbA1c levels in diabetic patients in comparison with the placebo group without causing any change in the liver or kidney function²³. Methanolic extracts of stem-bark and leaves extract of *C. cinereum* has caused a time-dependent reduction of the blood glucose levels of the alloxan-induced diabetic rats. With fourteen days of treatment, a decrease in blood glucose levels was seen in alloxan-induced mice than normal mice²⁴.

Anti-cancer activity

Anticancer studies on the methanolic extract of leaves of *C. cinereum* revealed the total growth inhibition (TGI) >10 mg/ml on the cancer cell lines, Hep 2 and HT29, where the relative cell survival progressively decreased in a dose-dependent manner. In addition to that, short term cytotoxicity studies by Trypan Blue exclusion

method also confirmed the anticancer activity of *C. cinereum* (syn. *V. cinerea*) (1mg/ml showed 77% of Cytotoxicity inhibition)²⁵. The ethanolic leaf extract of *C. cinereum* treated cells showed typical features of decrease in cells and cell death at the morphological level such as rounding off cells, cell shrinkage, and detachment from the substrate. In a similar study, the plant extract exhibited a significant reduction in cell viability as compared with control cells. Significant anti tumour activity against Dalton's ascitic lymphoma was observed in the ethanolic and chloroform extracts of aerial parts of *C. cinereum*. A decrease in cancer cell count with a protective effect was concluded by the hematological parameters²⁶. *C. cinereum* extracts inhibited tumor cell invasion and metastasis through stimulation of CMI and regulation of MMPs, VEGF, prolyl hydroxylase, lysyl oxidase, ERK-1, ERK-2, TIMPs, and proinflammatory cytokine gene expression in metastatic lung tissue and thus establishing anti metastasis activity²⁷.

Anti Cataractogenesis

C. cinereum provides protection against the formation of nuclear opacity in selenite-treated Sprague Dawley rat pups and has potential against selenite-induced cataract and could be useful against lens damage caused by ROS generation under oxidative stress²⁸. A drop of the leaf juice instilled in the eye can relieve eye pain²⁹.

Nephroprotective activity

A study on the alcoholic, ethyl acetate and petroleum ether extracts of *C. cinereum* revealed nephroprotective activity in rat-model of cisplatin-induced renal toxicity. The alcoholic extract showed pronounced curative activity, while ethyl acetate extract showed good prophylactic activity, and a petroleum ether extract showed moderate protection in curative and prophylactic models³⁰.

Anticataleptic activity

The anticataleptic effect of ethanolic extract of *C. cinereum* in haloperidol-induced catalepsy in rats and demonstrated the protective effect against symptoms of Parkinson's disease (catalepsy) due to the regulation of neurotransmitters such as dopamine, serotonin, glutamate³¹.

Wound healing activity

C. cinereum has been used as a poultice to treat cuts and wounds. A study was done in Indonesia aiming at the traditional wound healing property of *C. cinereum*. The oil was

prepared by frying the fresh aerial parts plant with sufficient cooking oil and leaving it until the plant is completely fried. Then the oil obtained is applied to the part that is not too close to where the wound occurred about 15 cm from the wound site. The hematological analysis indicated that *C. cinereum* oil could significantly increase the erythrocyte count, hemoglobin concentration, hematocrit, mean cell volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) particularly during the early day of treatment. Thereby potentially accelerate the wound healing by enhancing physiological endurance particularly the erythrocyte and hemoglobin level³².

Smoking cessation activity

A study by Supakit. W *et al* was done by comparing the efficacy and safety of *C. cinereum* with a placebo. The aqueous soluble extract of crushed dried whole plant of *C. cinereum* was prepared in infusion in the tea bag. The study concluded that the plant could be an alternative therapeutic target with low cost for the treatment of tobacco dependence. Moreover, a study of *C. cinereum* and lime in Thailand demonstrated that the herb can reduce smoking urges in two weeks and decrease the number of cigarettes smoked³³.

Immunomodulatory effect

Studies confirm the immunomodulatory effect of *C. cinereum* on peripheral blood mononuclear cells³⁴. The methanolic extract of *C. cinereum* showed an enhancement in the phagocytic activity of peritoneal macrophages. When *C. cinereum* was given along with the antigen, sheep red blood cells (SRBC), an enhancement in the circulating antibody titer and the number of plaque forming cells (PFC) in the spleen increased. The maximum number of PFC (304.16 ± 12.4) was obtained on the 6th day. The proliferation of splenocytes, thymocytes and bone marrow cells both in the presence and absence of specific mitogens *in vitro* and *in vivo* was observed in the study³⁵.

CONCLUSION

The majority of the world population relies on natural remedies to meet their health needs, either as "traditional medicine" or as an "alternative medicine". Many compounds obtained from plant sources have been proved to

possess pharmacological activities. Though these compounds cause therapeutic relief for a variety of diseases and could yield many vital drugs for human use, not many pharmaceutical companies focus on developing natural drugs³⁶. *C. cinereum* lead the list of plants that have been reported to have a wide range of therapeutic use, and have not been used as a commercial drug for the benefit of mankind. The medicinal properties of *C. cinereum* had been studied for several decades and are well known to prevent and treat various conditions. This review highlights the therapeutic importance *C. cinereum* and its prospects of development of drugs from *C. cinereum*. As a remedy to several health conditions, phytochemicals of *C. cinereum* can be used as multi-target drugs to treat comorbidity²¹. Further research in multi-target prospects could yield beneficial outcomes concerning effective treatment.

Conflict of Interest

The authors declare that there is no conflict of interest.

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