



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Paper

A Review on *Centella Asiatica* as A Potential Cancer Activity

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ARTICLE INFO

Published: 24 Apr 2026

Keywords:

Centella asiatica, Herbal
medicine, Skin cancer,
Breast cancer

DOI:

10.5281/zenodo.19730105

ABSTRACT

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. Women with genetic mutation in either BRCA1 or BRCA2 have increased risk of developing breast and ovarian cancer. Evidence for effectiveness of herbal medicine is limited although people find them helpful and their use tends to be based on traditional use rather than scientific research. *Centella asiatica* is medicinal herb that has been widely used in folk medicine to treat various disease. The main constituent for *Centella asiatica*, 'asiatic acid and asiaticoside' is mainly found to show anticancer activity against breast and ovarian cancer. The review shows that, the growth suppression was in concentration dependent manner, relating to cytotoxicity of SKOV-3 and OVCAR-3 cells. *Centella asiatica* show inhibition of cell proliferation in breast cancer cells, MCF-7.

INTRODUCTION

The *Centella asiatica* (L.) Urban, commonly known as Gotu Kola, Indian pennywort, or Asiatic pennywort, is a well-known medicinal herb that has drawn immense pharmacological interest due to its diverse therapeutic potential and long history of use in traditional medicine. Belonging to the family Apiaceae (Umbelliferae), this small, creeping perennial plant is widely distributed in tropical and subtropical regions such as India, China, Sri Lanka, Southeast Asia, Oceania, and Africa, where it grows abundantly in moist, shaded

environments. The plant's aerial parts and roots have been extensively utilized in Ayurveda, Unani, and Traditional Chinese Medicine to treat a wide range of ailments including skin cancer diseases, rheumatism, inflammation, syphilis, mental disorders, epilepsy, hysteria, dehydration, and diarrhea.

The pharmacological value of *Centella asiatica* lies primarily in its rich phytochemical composition, which includes bioactive triterpenoids such as asiaticoside, madecassoside, asiatic acid, and madecassic acid, along with flavonoids, phenolic compounds, sterols, tannins,

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



and volatile oils. These phytoconstituents collectively contribute to the plant's potent biological activities, which have been scientifically validated and continue to be the focus of pharmacological research. Among its various therapeutic actions, the antioxidant, anti-inflammatory, neuroprotective, antimicrobial, wound-healing, and anticancer properties of *Centella asiatica* are particularly noteworthy. Its triterpenoid saponins, known as centellosides, are primarily responsible for stimulating collagen synthesis, promoting tissue regeneration, and enhancing fibroblast proliferation, which make the plant an effective natural remedy for wound healing and skin repair. These compounds also regulate oxidative stress by scavenging free radicals and enhancing endogenous antioxidant defenses through enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, thereby preventing cellular damage and delaying the onset of degenerative diseases. The anti-inflammatory effect of *Centella asiatica* is mediated through the inhibition of cyclooxygenase and lipoxygenase pathways, along with downregulation of pro-inflammatory cytokines and suppression of the NF- κ B signaling cascade, resulting in reduced tissue inflammation and oxidative stress.

Beyond its anti-inflammatory and antioxidant effects, *Centella asiatica* exhibits significant neuroprotective and cognitive-enhancing properties; it improves memory, concentration, and mental clarity by modulating cholinergic neurotransmission, reducing acetylcholinesterase activity, and stimulating the expression of neurotrophic factors such as brain-derived neurotrophic factor (BDNF), which supports neuronal growth and survival.[1] These actions have made it a promising natural agent for the prevention and management of neurodegenerative disorders like Alzheimer's disease and dementia. Furthermore, experimental and clinical studies

suggest that *Centella asiatica* possesses strong antimicrobial activity against various bacteria and fungi, including *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candida albicans*, which supports its traditional use in the treatment of infectious diseases.

The anticancer potential of *Centella asiatica* is another emerging area of pharmacological importance; asiatic acid and madecassoside have been shown to induce apoptosis in tumor cells, inhibit angiogenesis, and suppress cell proliferation by modulating mitochondrial and caspase-dependent pathways, demonstrating their potential as adjuvant agents in cancer therapy. In addition, the plant exhibits hepatoprotective and renoprotective activities by reducing lipid peroxidation, enhancing antioxidant enzyme activities, and stabilizing cellular membranes, thereby mitigating toxin-induced hepatic and renal damage. The pharmacological mechanisms underlying these effects are complex and often synergistic, involving multiple biochemical pathways that together account for the herb's multifaceted therapeutic potential. In Ayurveda, *Centella asiatica* is revered as a "Medhya Rasayana," a rejuvenating herb known to enhance intellect, memory, and longevity, which aligns closely with modern pharmacological findings highlighting its neuroprotective and adaptogenic benefits.

Pharmacokinetic studies reveal that asiaticoside and madecassoside are metabolized in the liver into asiatic and madecassic acids, which are the active forms responsible for systemic pharmacological effects, including their ability to cross the blood-brain barrier and exert central nervous system activity. Toxicological studies affirm that *Centella asiatica* is generally safe at recommended doses, with minimal adverse effects, though excessive consumption may cause mild gastrointestinal discomfort or skin irritation in sensitive individuals. Given its broad safety

margin, the plant has found applications in modern pharmaceuticals, nutraceuticals, and cosmeceuticals, with extracts being incorporated into creams, tonics, and supplements designed to promote wound healing, enhance cognitive performance, and support overall wellness. Despite its widespread traditional use and growing scientific validation, research on *Centella asiatica* continues to evolve, with current investigations focusing on improving the bioavailability of its active compounds through novel drug delivery systems such as nanoparticles, liposomes, and phytosomes. Moreover, efforts are being made to standardize extract formulations to ensure consistent therapeutic efficacy, as variations in geographical origin and environmental conditions can influence the phytochemical profile. As a natural source of multifunctional bioactive compounds, *Centella asiatica* exemplifies how traditional herbal knowledge can guide modern pharmacological innovation. It bridges ancient medicinal wisdom with contemporary biomedical science, offering promising leads for developing safer, plant-based therapeutics that address complex diseases involving oxidative stress, inflammation, and cellular degeneration.

Centella asiatica (Gotu Kola) is used in Indian systems of medicine for enhancing memory and for the treatment of skin cancer diseases and nervine disorders [3]. The plant medicinal properties have long been utilized by the people of Java and Indonesia. In China, it is indigenously called as Gotu kola, and over 2000 years ago, it was one of the documented “miracle elixirs of life” [4]. Herbal medicines can be used as adaptogens, these plant derived drugs either reduce stress reactions in the alarm phase and provide a certain degree of safety against long-term stress [5]. *C. asiatica* (Umbelliferae) syn. *Hydrocotyle asiatica* is used to treat various ailments across India which includes body aches, headaches, insanity, asthma, leprosy, ulcers, eczemas, and wound healing [6].

To find out new potential compounds for therapeutic use, screening of medicinal plant is vital [7]. The plant has significantly drawn the attention of scientific groups in the recent years as it has multiple usages in the treatment of ailments. In Fig. 1, major pharmacological usage in the treatment of ailments has been outlined followed by its detailed description. Furthermore, pharmacological studies have revealed broader implications in biochemical modulation, cellular signaling, and clinical applications, highlighting its importance in contemporary pharmacotherapeutic research.⁷

The plant has long been used as folklore medicine for the treatment of a variety of diseases. Chemically been identified leading to therapeutic properties. Asiatic acid, asiaticoside, and madecassoside form the major constituents responsible for pharmacological value apart from being rich in flavonoids and terpenoids [8]. Centelloid was term given for different constituents of secondary metabolites produced by plant which mainly comprised of pentacyclic triterpenoid saponins [9]. P-cymene-(44%) along with other volatile compounds was found to be in a prominent amount in the essential oil of *C. asiatica* on analysis with gas chromatography-mass spectrometry (GC-MS) [10]. Centellin, asiatic, and centellicin were isolated from the aerial part of the plant, and further, their structures had been determined using 2D nuclear magnetic resonance technique [11]. From plant extract using high-performance liquid chromatography to identify bioactive compounds, madecassoside, asiaticoside, madecassic acid, and asiatic acid were found in the significant amount [12].

A quantitative estimation of triterpenoids showed highest asiaticoside content (6.42%) in leaf samples collected in Mangoro region [13]. New triterpene and a saponin, 2 α ,3 β ,23-trihydroxyurs-20-en-28-oic acid and 2 α ,3 β ,23-trihydroxyurs-20-en-28-oic acid O- α -l-rhamnopyranosy-(1 $\rightarrow$ 4)-O-



β -d- glucopyranosyl(1→6)-O- β -d glucopyranosyl ester, have been isolated from the aerial part of *C. asiatica*, and their structures were determined using spectral methods [14]. Furthermore, pharmacological studies have revealed broader implications in biochemical modulation, cellular signaling, and clinical applications, highlighting its importance in contemporary pharmacotherapeutic research.

On A549 and PC9/G lung cancer, cell line inhibitory concentration 50 (IC₅₀) values of A-3 were 26.03±2.47 and 25.57±0.51, respectively, due to the presence of asiatic acid as major component [15]. Against the cell lines of human breast cancer (MDA MB-231), mouse melanoma (B16F1), and rat glioma (C6), the aqueous extract of *C. asiatica* had shown inhibitory activity with IC₅₀ values of 698.0, 648.0, and 1000.0 µg/mL, respectively [16]. The methanolic extract of *C. asiatica* (Linn) showed inhibitory effect on MCF-7 cell lines, and induced apoptosis in MCF-7 cells as indicated by nuclear condensation, increased annexin staining, loss of mitochondrial membrane potential, and induction of DNA breaks was identified by TUNEL reactivity [17]. The effect of *C. asiatica* juice was checked on human HepG2 cell line using MTT assay, and it showed cytotoxic effects on tumor cells in a dose-dependent manner. At a concentration above 0.1% of juice, a higher amount of DNA damage and apoptotic cell death was observed on human HepG2 cell line [18].

Asiatic acid was evaluated for antiproliferative effect in lung cancer cells using MTT assay. Oral administration of AA inhibited weight and tumor volume significantly in lung cancer xenograft model [19]. In another study, asiatic acid showed induced apoptosis and decreased viability in human melanoma SK-MEL-2 cells in a dose-dependent manner [20]. Asiatic acid derived from *C. asiatica* showed antiproliferative effects on RPMI 8226 cells. It decreased the expression levels of focal adhesion kinase (FAK), and the

probable mechanism of AA may be related to the inhibition of signal transduction mediated by FAK [21]. Asiatic acid, asiaticoside, and madecassic acid was the major composition of titrated extract of *C. asiatica*, and asiaticoside reduces melanogenesis in B16F10 mouse melanoma by checking tyrosinase mRNA expression [22]. In long-term culture at a concentration of 8 µg/ml, partially purified fractions inhibited the growth of mouse lung fibroblast (L-929) cells [23].

Reduction up to 50% in viability was observed in ovarian cancer cells treated with 40 µg/ml concentration of asiatic acid, and it also showed cell cycle arrest at the G₀/G₁ phase and increased apoptosis by 7-10 folds [24]. Induction of apoptosis was observed in A-549 cell line due to presence of asiatic acid which helped in regulation of miR-1290, BCL2 protein level, and cell cycle regulation. Furthermore, pharmacological studies have revealed broader implications in biochemical modulation, cellular signaling, and clinical applications, highlighting its importance in contemporary pharmacotherapeutic research.

Methanol hot extract from *C. asiatica* leaves was taken to check the antibacterial activity which was assessed by zone of inhibition and minimum inhibitory concentration (MIC) value (2 µg/disc) by disc diffusion method. In vitro antibacterial activity of the plant extract against *Staphylococcus aureus* ATCC 25923 and methicillin resistance *S. aureus* (wild type) showed a zone of inhibition of 5 mm and 7 mm respectively. In a study, it was observed that essential oil extract showed antibacterial properties against Gram-positive (*Bacillus subtilis* and *S. aureus*) and Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*, and *Shigella sonnei*) with MIC values ranging from 1.25 to 0.039 mg/ml. *Bacillus cereus* and *Listeria monocytogenes* 10403S were selected to study the antibacterial activity in *C. asiatica* under both normal and osmotic stress condition. At



95% ethanolic extract, antibacterial activity was enhanced twice under osmotic stress condition. The MIC of *C. asiatica* was observed to be 16 µl/ml against *B. cereus* while 8 µl/ml for *L. monocytogenes* 10403S [28]. MS media was used to culture leaf explants, and its antibacterial activity against *B. cereus*, *E. coli*, *S. aureus*, and *P. aeruginosa* was evaluated; methanol extracts of leaf and callus displayed maximum inhibitory effect against the tested organisms [29]. Furthermore, pharmacological studies have revealed broader implications in biochemical modulation, cellular signaling, and clinical applications, highlighting its importance in contemporary pharmacotherapeutic research. The petroleum ether, ethanol, chloroform, n-hexane, and aqueous extract of *C. asiatica* showed activity against *Aspergillus niger* and *C. albicans* with a zone of inhibition of 14, 16, 13, 13, and 11 mm and 13, 15, 15, 11, and 9 mm, respectively. The control Ketoconazole (10 µg) showed the inhibition of 12 mm [30]. Ethanolic extract of *C. asiatica* was checked for antifungal activity against *Aspergillus flavus*, and *Penicillium citrinum* exhibited the strongest antimold activity (percentage mycelial inhibition = 26.3 mm) [31]. 100% ethanolic extract of *C. asiatica* showed a zone of inhibition of 15.4 mm against *A. niger* [32]. Following agar well diffusion method, antimicrobial activity was checked for ethanolic extract of plant against *A. niger* and *Candida albicans*, an inhibition of 16 and 15 mm was observed, respectively, while control ketoconazole (10 µg) gave a inhibition zone of 12 and 10 mm [30]. Against *Candida albicans*, on an average 5 mm, zone of inhibition was observed while the standard miconazole nitrate showed an inhibition of 20 mm [33]. *C. asiatica* is potential herb with an array of health-care applications. It is widely accepted that plant has got neuroprotective activities and helpful in brain improvement. Plants have proved to bear low toxicity and higher

efficacy in clinical treatment with prominent activities such as anticancer, antibacterial, antifungal, anti-inflammation, neuroprotection, antioxidant, wound healing, and antidepressant as mentioned in above manuscript. As *C. asiatica* is an endangered species using plant tissue culture mass propagation major can be helpful, and callus and suspension culture techniques can be harnessed for secondary metabolite extraction. Germplasm conservation could be a possible way to preserve this precious plant. More studies are required to characterize and establish the chemical compounds responsible for a wide range of therapeutic activity. Due to the presence of wide bioactive compound, the plant has vast application.

The plant can be a safer alternative for the formulation of new drugs. Further research is needed to confirm their activities mentioned in ancient scripts followed by clinical studies for their safe application for humans. Furthermore, pharmacological studies have revealed broader implications in biochemical modulation, cellular signaling, and clinical applications, highlighting its importance in contemporary pharmacotherapeutic research.



Figure 1: Centella Asiatic Leaves

CANCER IN SKIN

Cancer is a disease as characterized by the uncontrolled proliferation of cells. It results from a breakdown of the regulatory mechanisms that govern the division, differentiation and survival of individual cells. There are more than 100 distinct types of cancer, and subtypes of tumors can be found within specific organs. Out of many known cancers this study primarily focuses on the tumors caused in the skin. Skin is a shield that protects people from heat or cold, chemicals, UV-radiation and bacteria. Skin cancer is one of the most common of all human cancers and its incidence is increasing rapidly all over the world. Approximately 30% of all newly diagnosed cancer in the world is skin cancer. There has been a progressive increase in the incidence of skin cancers, particularly that of cutaneous melanomas over the last few decades. In India skin cancers constitute about 1-2% of all diagnosed cancers. Various studies from India have consistently reported SCC (squamous cell carcinoma) as the most prevalent skin malignancy. Owing to the large population the incidence of skin cancer in India is lower as compared to the western world. This fact has been established by Deo et al, in 2005.[34] Epidemiological studies have shown that 70-90% of all cancers are environmental. Also, lifestyle related factors are the most important and preventable among the environmental exposures. The risk factors of the major non-communicable diseases like cancer are tobacco, dietary habits, inadequate physical activity and alcohol consumption. Carcinogens in tobacco smoke are classified as human carcinogens with sufficient evidence. These carcinogens include polyaromatic hydrocarbons (PAH), heterocyclic hydrocarbons, N-nitrosamines, aromatic amines, aldehydes, inorganic compounds, and radio- elements such as polonium (Sophia et al., 1986). Benzo(a)pyrene (BaP) and 7,12- dimethylbenz(a)anthracene (DMBA) are polycyclic aromatic hydrocarbons

(PAHs) found in the tar fraction of cigarette smoke, as well as in car exhaust(Lee et al., 2002). Tumor induction studies with many PAH, including dibenzo[a,l]pyrene (DB[a,l]P), 7,12-dimethylbenz[a]anthracene (DMBA), and benzo[a]pyrene (B[a]P) have been studied. It was demonstrated that DMBA is a significantly stronger tumor initiator than B[a]P tested in mouse skin and rat mammary gland. Furthermore, pharmacological studies have revealed broader implications in biochemical modulation, cellular signaling, and clinical applications, highlighting its importance in contemporary pharmacotherapeutic research.

The development of cancer is a complex process during which a normal cell undergoes a progressive series of alterations resulting in the acquisition of an altered proliferative capacity, invasiveness and metastatic potential. These alterations occur in 3 stages: initiation which involves DNA damage leading to mutation(s); followed by promotion, which involves enhanced proliferation and altered cell behavior; and finally, progression results from subsequent genetic changes such as loss of heterozygosity and gene amplification. The present work titled “Antitumor effect of *Trigonella foenum-graecum* on two stage skin papillomagenesis in Rat” aims to deal with the role of these two carcinogens DMBA and TPA in the induction of skin carcinogenesis. Furthermore, the study covers the phytoremediation in cancer treatment with the efficacy of *Trigonella*. Furthermore, pharmacological studies have revealed broader implications in biochemical modulation, cellular signaling, and clinical applications, highlighting its importance in contemporary pharmacotherapeutic research.

DMBA:

Since the emphasis of the report is on the DMBA, a polycyclic aromatic hydrocarbon(PAH), studies



have shown that animals treated with DMBA showed 100% tumor incidence and the tumor was histopathologically confirmed as well differentiated squamous cell carcinoma. It reflects a close relationship between dimethylbenz(a)anthracene and skin carcinogenesis. However DMBA is also responsible for induction of mammary tumors in winstar rats (Margarida et al., 2010). To understand the complex process of carcinogenesis by PAHs sound knowledge is required.[35] 7, 12-Dimethylbenz(a)anthracene is an immunosuppressor and a powerful organ-specific laboratory carcinogen. DMBA serves as a tumor initiator by making necessary mutations. Furthermore, pharmacological studies have revealed broader implications in biochemical modulation, cellular signaling, and clinical applications, highlighting its importance in contemporary pharmacotherapeutic research.

CONCLUSION

In conclusion, *Centella asiatica* stands as a model medicinal plant whose rich chemical diversity and broad pharmacological spectrum have established it as one of the most valuable natural resources in drug discovery and phytotherapy. Its proven effects on wound healing, cognitive enhancement, antioxidant defense, and disease prevention underscore its importance as both a traditional remedy and a modern pharmacological agent with immense potential for future therapeutic development.

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HOW TO CITE: Mahendra Kumar, Richa Agarwal, Rajesh Asija, A Review on Centella Asiatica as A Potential Cancer Activity , *Int. J. of Pharm. Sci.*, 2026, Vol 4, Issue 4, 4068-4075, <https://doi.org/10.5281/zenodo.19730105>

