



POTENTIAL MEDICINAL DRUG (INDIAN PENNYWORT)

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ABSTRACT:

Plant-based drug discovery has drawn the attention of researchers, especially the ones used as traditional medicines. *Centella Asiatica* (L.) Urban [Apiaceae], also known as *C. Asiatica* or Indian pennywort. It has been cultivated all over the world, distributed all over India especially concentrated from Haridwar in Himalayan tracts. This plant cures various diseases like Chronic fever, Tuberculosis, Blood purifier, Dermatitis, Purities, Hair fall, Cardiotonic, Cardiac spasm, Hypertension, Asthma, Insomnia, Aging retardant, Female hormonal disorders Alzheimer's disease, ETC. The aerial parts and roots are also used for medicinal purposes, and its chemical constituents have wide therapeutic applications in areas of antimicrobial, anti-inflammatory, anticancer, neuroprotective, antioxidant, and wound healing activities. According to studies, it has been shown that the whole extract and also individual compounds of *C. Asiatica* have a protective effect against various neurological diseases. Most living studies on neuroprotective effects have focused on Alzheimer's disease, Parkinson's disease, learning and memory enhancement, neurotoxicity, and other mental illnesses such as depression and anxiety, and epilepsy. *Centella Asiatica* has the potential as an anti-cancer medicine. Asiatic acid has shown an antiproliferative effect by regulating apoptosis in a variety of human cancer cells. *Centella Asiatica*, a medicinal plant, is individually used for wound healing. Diabetic Mellitus has been reported to affect functions of the hippocampus. The *Centella Asiatica*, a herb traditionally being used to improve memory, prevents diabetes-related hippocampal dysfunction.

KEYWORDS: *Centella Asiatica*, Alzheimer's, diseases, neuroprotective, Parkinson's, antiproliferative, hippocampal.

INTRODUCTION:

Centella Asiatica, the Asiatic pennywort, is an herbaceous perennial indigenous to the southeastern United States. It is also known as Gotu kola, Kodavan (*Centella Asiatica*). It is a Herbaceous, perennial plant in the flowering plant. The name Pennywort is a common term given to 20 species of creeping plants found in marshy

areas of tropical and sub-tropical climates^[1]. *Centella Asiatica* is the common Asian variety that is used in both culinary and medical applications. *Centella Asiatica* is an herb in the parsley family commonly used in ayurvedic medicine. The above-ground parts are used to make medicine. Practitioners claim the medicinal

plant has the power to boost brainpower, heal skin issues, and promote liver and kidney health. It is also used as a culinary vegetable and as a medicinal herb and more than 390,900 plant species known and botanically identified.

Indian pennywort has been used in alternative medicine as a possibly effective aid in treating venous insufficiency. We also need to explore our potential of rich flora so that we may sustainably overcome our problems. According to WHO (World Health Organization), people of developing countries depend upon herbal medicines for primary healthcare^[1]. Moreover, now it has been listed as Threatened plant species by the International Union for Conservation of Nature and Natural Resources (IUCN)², and also as an endangered species^[3]. Consumed for its health benefits, Sri Lankans noticed that elephants, renowned for their longevity, often eat the plant.

India up to an altitude of 600m above sea level. In north-eastern hills, the plant is

found up to 2500 meters. It is a greenish-yellow colour herb with a slightly bitter taste found throughout India and is used as a brain tonic, anabolic, alternative, and anxiolytic. *Centella Asiatica* has gained interest as a potential plant with promising pharmacological properties. It is used in the treatment of several elements. *Centella Asiatica* is mainly used in an ayurvedic system to treat various diseases. This plant holds a reputed position in the indigenous system of medicine and is often misinterpreted as a (*Bacopa monnieri*) Brahmi^[3]. Realising the historical nature of medicinal herbs, we were attracted to scrutinise the pharmacological effects of herb extracts in synergy with the provided cells and scaffolds to further enhance nerve regeneration, and also to improve the utilisation of tissue-engineered nerve grafts and cell therapy in clinical applications for nerve degeneration and injury^[3].





Fig.1 Indian pennywort (Centella Asiatica)

Since the toxicity effects of *C. asiatica* vary according to its geographical distribution, standardizing its bioactive components during extract preparation would be appear to be momentous. The

therapeutic quality, purity, and strength of the plant secondary metabolite depend upon good agriculture cultivation practices (GACP).

DRUG PROFILE:

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.

Moreover, there are some other triterpenes such as : Brahmic acid, centellin, asiaticin, and terminolic acid. Centelloid was a term given for different constituents of secondary metabolites produced by the plant which mainly comprised of pentacyclic triterpenoid saponins. *Centella asiatica* has no known severe interactions with other drugs. *Centella asiatica* moderate interactions with at least 28 different drugs^[4].

Centella asiatica has mild interactions with at least 25 different drugs. *Centella asiatica* has no known serious interactions with other drugs.

They absorbed rapidly, reaching maximum level within 5-15 min after oral administration, but they had poor oral bioavailability, less than 1%. The medicinal property of *C. Asiatica* is becoming popular day by day throughout the world. The plant is beneficial for rheumatism, extra vitality increasing brain power, lowering blood sugar level, skin condition, increased circulation, arthritis, senility, and varicose. According to Ayurveda, the herb has multifunctional properties^[4].

Kingdom:	Plantae
Subkingdom:	Viridiplantae
Infrakindom:	Streptophyta
Superdivision:	Embryophyta
Division:	Tracheophyta
Subdivision:	Spermatophytina
Class:	Magnoliopsida
Superorder:	Asteranae
Order:	Apiales
Family:	Apiales
Genus:	Centella L.
Species:	Centella asiatica(L.)

Figure 1Taxonomical Classification of C.asiatica.

Chemical Composition:

Brinkhaus et al.adequately summed up the chemical composition of *Centella Asiatica*,

discovered as early as 1956. About 0.1% is essential oils, while 1–8% is saponin-

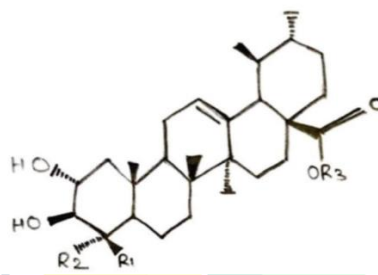
containing triterpene acids and their sugar esters. Further studies on chemical constituents were done on hydroponically grown *C. Asiatica* by Othman^[6]. Centellin, Asiatic, and centellicin were isolated from the aerial part of the plant, and their structures had been determined using the 2D nuclear magnetic resonance technique^[4]. From plant extract using high-performance liquid chromatography to identify bioactive compounds, madecassoside, asiaticoside, madecassic acid, and Asiatic acid were found in a significant amount. The triterpenes of

Centella are composed of many compounds including Asiatic acid, Madecassic acid, Asiaticoside, Madecassoside, Brahmoside, Brahmic acid, Brahminoside, Thankinise, Isothankuniside, Centelloside, Madasiatic acid, Centic acid, and Cenellic acid^[3].

Centella asiatica is reported to have the following types of chemical compounds:-

- ◆ Triterpenoids
- ◆ Volatile and Fatty acids
- ◆ Alkaloids
- ◆ Glycosides
- ◆ Flavanoids
- ◆ Others- Vitamin B, C, G, and some amino acids, etc.

Triterpenoids: Include asiaticoside, centelloside, madecassoside, thankuniside, isothankunic acid, centellose, Asiatic, centelic, and madecassic acids and brahmoside, brahminoside, brahmicacid, the structure of their genin, Brahmic acid (m.p. 293°) have been established as 2,6-hydroxy, 23-hydroxy-methyl ursolic acid. Asiaticoside and madecassoside predominated in the leaves with less in roots³⁰^[8].



	R1	R2	R3
Asiatic acid	H	CH ₂ OH	H
Madecassic acid	OH	CH ₂ OH	H
Madosiatic acid	OH	CH ₃	H
Asiatioside	H	CH ₂ OH	Glucose - glucose - rahmanose
Madecassoside	OH	CH ₂ OH	Glucose - glucose - rahmnose

Volatile and Fatty acids: The fatty oil consists of glycerides of palmitic, stearic, lignoceric, oleic, linoleic, and linolenic acids,

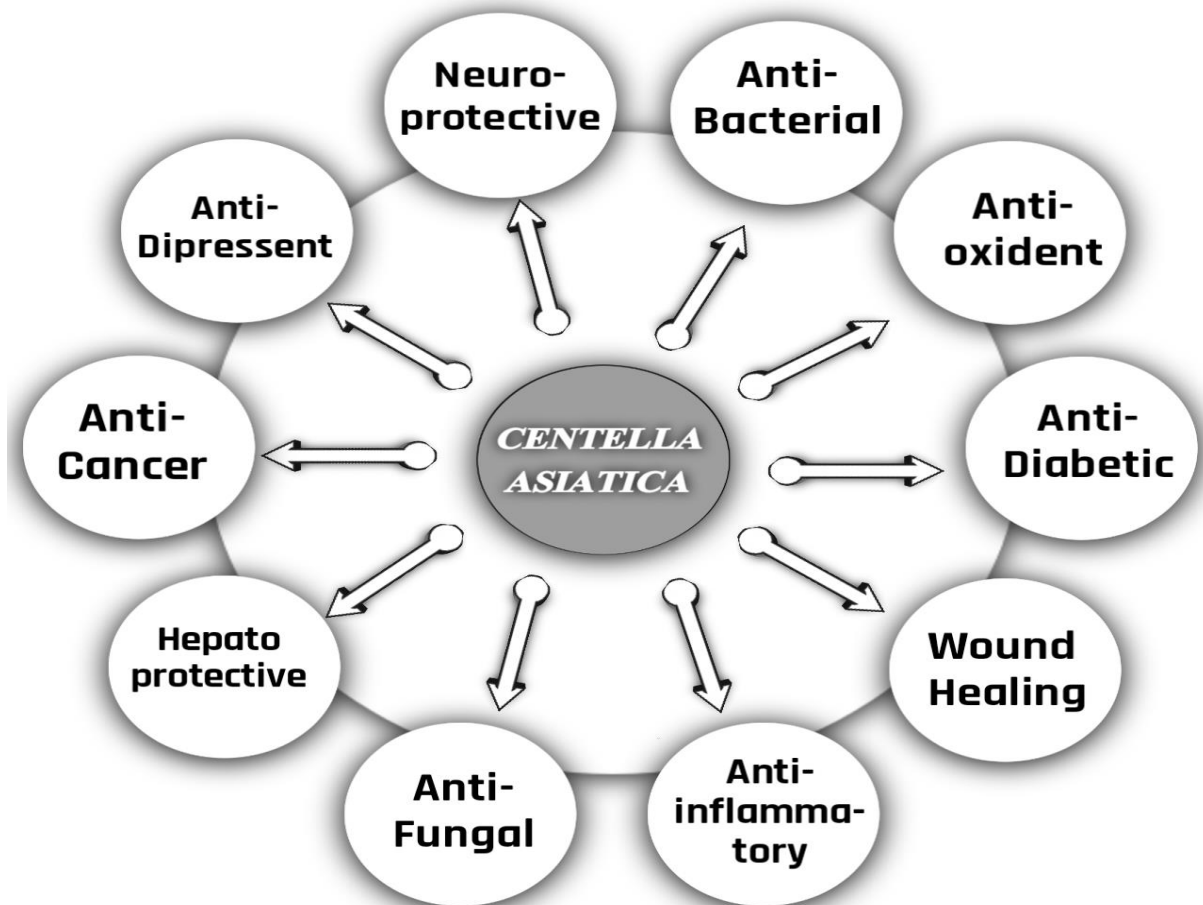
Alkaloids: An alkaloid, hydrocotylin (C₂₂H₃₃NO₈) has been isolated from the dried plants.

Glycosides: Asiaticoside, madecassoside, and centelloside have been isolated from the plant parts. On hydrolysis, these glycosides yield the triterpene acids, Asiatic acid, madegascariac acid³²⁻³⁴, and centellic acid, except this *Centella* acid, all the above are present in free form in the plant.

Flavanoids: Flavanoids, 3-glucosylquercetin, 3- glucosylkaemferol, and 7-glucosylkaemferol have been isolated from the leaves³³. The plant is reported to contain tannins, sugars, inorganic acids³⁵ and resin³¹, amino-acids, viz. aspartic acid, glycine, glutamic acid, α-alanine, and phenylalanine³⁶. The total ash contains chloride, sulfate, phosphate, iron, calcium, magnesium, sodium, and potassium. The leaves are rich in vitamins such as vit. B, vit.C³⁷ and vit.G¹⁸^[8].

The pharmacological activity of Indian Pennywort:

The primary constituents of *C. asiatica* are the triterpene fractions which showed a wide range of defensive and therapeutic effects, most prominently influencing collagen production and deposition in wound healing.



Titrated Extract of *Centella Asiatica* (TECA) is used to treat several microcirculatory problems, skin inflammation (eczema, atopic dermatitis, leprosy, various ulcers, etc.) fever, intestinal problems, and genitourinary conditions. *C. Asiatica* exerts diverse pharmacological activities such as antibacterial, antidepressant, antiemetic, antineoplastic, antioxidant, antithrombotic, anxiolytic, gastroprotective, immunomodulatory, antigenotoxic, nerve degenerative, reproductive, wound healing, etc. due to the presence of several saponin constituents, including asiaticoside, Asiatic acid, madecassic and some other bioactive compounds^[9].

Anticancer:

Cancer is one of the ailments which cannot be completely subdued by chemotherapy. The chemotherapeutic agents though effective against various types of tumors are not totally free from side effects. Many Indian plants like black pepper, asafoetida, pippali, and garlic are quoted to be useful in different types of cancer^[5]. One such plant is "*Jivanti*" (*Leptadenia reticulata*), belonging to the family Asclepiadaceae, well known for its

tonic, restorative, and stimulant property in the Indian system of medicine^[7].

The main constituents reported are stigmasterol, β - sitosterol, flavonoids, pregnane glycosides, and proteins. 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 a major component^[5]. The methanolic extract of *C. Asiatica* (Linn) showed an 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^[7]. The effect of *C. Asiatica* juice was checked on a 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 the human HepG2 cell line. 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 the lung cancer xenograft model. Asiatic acid derived from *C. Asiatica* showed antiproliferative effects on RPMI 8226 cells^[7]. Asiatic acid, asiaticoside, and madecassic acid was the major component of the titrated extract of *C. Asiatica*, and

Neuroprotective:

The nervous system, consisting of the brain, spinal cord, and peripheral nerves, is made of complex and specialized structures which are vulnerable to various diseases and injuries that reduce sensorimotor and cognitive functions, and may also be the cause of life-threatening problems in acute cases. The neuroprotection aspect of *C. Asiatica* mainly involves enzyme inhibition, prevention of amyloid plaque formation in Alzheimer's disease, dopamine neurotoxicity in Parkinson's disease, and reducing oxidative stress^[2]. As synthetic drugs can lead to lung and kidney toxicity, many clinicians and scientists have searched vigorously for other alternatives to treat their patients. Herbal plants which are naturally rich in therapeutic value, more eco-friendly, and have lesser side effects have been subsequently studied for utilization in medical applications^[2]. This has brought *C. Asiatica*, which is known to have memory and cognitive enhancement, into scientific investigations for nerve regeneration and neurological functions before therapeutic use. The research that has been focused on

asiaticoside reduces melanogenesis in B16F10 mouse melanoma by checking tyrosinase mRNA expression. Asiaticoside enhanced anti-tumor activity of vincristine in cancer cells^[13]. Constituents in the methanol extract inhibited the proliferate of human gastric adenocarcinoma (MK-1). Water extracts induced apoptosis in colonic crypts and exerted chemotherapy effect on colon tumorigenesis in male F344rats (Bunpo et al., 2004)^[7]. Asiatic acid-induced apoptosis in human melanoma SK-MEL-2 cells (responsible for skin cancer) and SW480 human colon cancer (Park et al., 2005; Tang et al., 2009). Asiaticoside enhanced the anti-tumor activity of vincristine in cancer cells (Haung et al., 2004). Constituents in the methanol extract inhibited the proliferate of human gastric adenocarcinoma (MK-1), human uterine carcinoma (HeLa), and murine melanoma (B16F10) cells (Yoshida et al., 2005)^[5].

the neurogenerative capacity of *C. Asiatica* on the central nervous system has been widely conducted, focusing on brain cells. In view of *C. Asiatica* as a nerve tonic, it is believed to have therapeutic effects on the peripheral nervous system, too. Water extract of *C. Asiatica* was evaluated on the activity of subtypes of phospholipase A2 (PLA2) in primary cultures of rat cortical neurons, asiaticoside present in extract inhibited cPLA2 and sPLA2 activities^[8]. In male Sprague-Dawley rats, improved learning and memory were observed on acute administration of Asiatic acid^[3]. Neuroprotective potential of modern medicine constituents of the plant includes Asiatic acid, madecassic acid, and brahmaside as well as flavonoids madecassoside and madesiatic acid. The plant is known to utilize neuroprotective effects by attenuating the changes in an animal model such as pathological neurobehavioral and neurochemical properties^[3]. Phosphoinositides-assisted cytodynamics and synaptic function show the neuroprotective effects of asiaticoside in the rat which includes mode of ROT-infused hemiparkinsonism^[8].

Alzheimer:

The present study investigated the effect of *Centella asiatica* (CA) extract in the prevention of sporadic dementia of Alzheimer's type using intracerebroventricular colchicine-induced rats. Salient findings of this study are that pre- and postcolchicine treatment with CA improved cognition, decreased malondialdehyde, and nitrite levels, restored decrease in GSH, increased activities of glutathione-S-transferase, catalase, and SOD^[5]. This illustrates that central administration of colchicine is characterized by progressive deterioration of learning and memory, oxidative stress, and decrease in acetylcholine turnover^[5]. Cytoskeletal disruption has been linked to neurodegeneration in AD. Colchicine is an alkaloid derivative that binds irreversibly to microtubules and causes their depolymerization, thereby inhibiting their assembly^[15]. This leads to impaired intracellular trafficking of neurotrophic factors, synaptic loss, and increased axonal excitotoxicity^[13]. Lipid

peroxidation plays a major role in oxidative damage of lipids. The key metabolites of lipid oxidation are malondialdehyde (MDA) and 4-hydroxynonenal (HNE). A growing body of evidence supports the fact that free radicals are the most likely candidates responsible for producing neuronal changes mediating the behavioral deficits in AD^[13]. In fact, there exists a close correlation between oxidative stress and A β deposition. Although colchicine is one of the major oxidative medication of proteins resulting from peroxynitrite which is associated with free radical and nitric oxide, central administration of colchicine causes oxidative stress by increasing GLU/GABA ratio and increasing NOS production in the brain^[5]. This results in an excessive glutamate activity and NO production thereby resulting in oxidative stress and extensive neuronal damage. NOS-containing neurons are relatively wide spread in AD^[15].

Parkinson:

The role of *Centella asiatica* L. leaf extract was studied on the transgenic *Drosophila* model flies expressing normal human alpha synuclein (h- α S) in the neurons^[13]. The leaf extract was prepared in acetone and was subjected to GC-MS analysis. *C. asiatica* extract at final concentration of 0.25, 0.50, and 1.0 μ L/mL was mixed with the diet and the flies were allowed feeding on it for 24 days^[2]. The effect of extract was studied on the climbing ability, activity pattern, lipid peroxidation, protein carbonyl

content, glutathione content, and glutathione-S-transferase activity in the brains of transgenic *Drosophila*^[15]. The exposure of extract to PD model flies results in a significant delay in the loss of climbing ability and activity pattern and reduced the oxidative stress in the brains of PD flies as compared to untreated PD flies^[2]. The results suggest that *C. asiatica* leaf extract is potent in reducing the PD symptoms in transgenic *Drosophila* model of Parkinson's disease.

Reducing oxidative stress:

Hyperlipidemia and many other metabolic diseases are related to oxidative stress^[15]. *Centella asiatica* is a traditional Chinese medicine whose antioxidant effect in vitro has been reported. We are interested in whether it possesses this effect in vivo and hence modulates lipid metabolism. Therefore, experiments were carried out on mice and golden hamsters regarding its antioxidant and hypolipidemic effect^[17]. We observed that a fraction (CAF3) of the ethanol extract (CAE) of *Centella asiatica* had a cholesterol decrease of

79% and a triglyceride decrease of 95% in acute mice model, so CAF3 was further investigated in high-fat-fed hamster model. It was shown that CAF3 increased SOD and GSH-Px activities and decreased MDA level, and it also improved TC, TG, LDL-C, HDL-C, AST, and ALT levels. L-CAT and SR-BI gene expression in hamsters were increased^[17]. Taken together, our data suggest that the CAF3 fraction of *Centella asiatica* has antioxidant and hypolipidemic properties^[15].

Anti-diabetic:

Diabetes mellitus is a continuously growing health problem, which causes substantial morbidity, mortality and long-term complications even in developed countries. The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030 (Haffner *et al.* 1998). About 150 million or 1.3% people are suffering from diabetes world wide which is almost five times more than the estimates ten years ago and this may double by the year 2030 (Ghosh *et al.* 2004)^[11]. Antidiabetic properties of leaves extract of *C. asiatica* was evaluated in alloxan-induced rat by administering extract at a concentration of 250, 500, and 1000 mg/kg after 3 hrs of ingestion reduction in blood glucose level was noticed by 32.6%, 38.8%, and 29.9%, respectively. Effect of ethanol extract was tested in streptozotocin (50 mg/kg)-induced Wistar rats^[6]. Studying the serum glucose, urea cholesterol, lipid, liver glycogen level, and body weight, the antidiabetic activity of extract at concentration of 200 mg/kg was noticed. Ethanolic and methanolic extracts of *C. asiatica* had shown significant protection and lowered the blood glucose levels to normal in glucose tolerance test carried out in the alloxan induced diabetic rats^[6]. Diabetes Mellitus (DM) is a metabolic disorder that becomes the main problem of the health in all around the world, the prevalence in the world reaches the

number of 382 million people and it is estimated to increase into 592 million people by 2035, while in Indonesia the patients of DM increases from 1.1 percent (1.1 %) in 2007, to 2.1% in 2013 on the basic health research (IDF, 2014; Ministry of Health, 2013) ^[16]. Type 2 Diabetes Mellitus (T2DM) is a complex metabolic disorder that is marked with the case of hyperglycemia as a result of the failure of cell β pancreas so that there is a resistance for the insulin. T2DM happens because of the disturbance of the progressive insulin secretion that becomes the main problem of a resistance to the insulin. Severe hyperglycemia and the disturbance of the insulin secretion cause several indications such as polyuria, polydipsia, polyphagia, and the loss of weight . Severe hyperglycemia that happens to T2DM patients may poison the cell β pancreas with the glucose and the patients may have the apoptosis^[6]. Nganlasom *et al.* treated the wounds of the diabetic induced Male Sprague-Dawley rats with *Centella* plant extract. They found the wounds of the plant extract treated wounds epithelialised faster when compared to control^[11].

In a study, lower inhibitory activities of α -amylase of *C. asiatica* extract and rutin were observed when compared to acarbose and an anti-diabetic drug. Extract of *C. asiatica* led to reducing blood glucose level in dose-dependent manner by 29.4%, 32.8%, 33.6%, and 35.7%, respectively, at

doses of 50, 100, 200, and 400 mg per kg body weight. In alloxan-induced rats, reduction in blood glucose level was observed at a dose level of 50 mg/kg bwt of *C. asiatica* juice^[16]. The effect of intestinal disaccharides and alpha amylase was inhibited, and lowered glucose absorption was observed when

supplemented with plant extract. Plants have been the major source of drug for the treatment of diabetes mellitus in Indian system of medicine and other ancient systems in the world. In diabetic Wistar rat model, asiatic acid showed to preserve and restore beta cell mass^[16].

Wound healing:

An increase in DNA, protein, and collagen content of granulation tissues was observed on supplementation of extract of *C. Asiatica* resulting in collagen synthesis and cellular proliferation at the wound site^[10]. Asiaticoside derived from the plant *Centella Asiatica* is known to possess good wound healing activity. Enhanced healing activity has been attributed to increased collagen formation and angiogenesis^[12].

Since antioxidants have been reported to play a significant role in the wound healing process. Asiaticoside extracted from CA improved hydroxyproline, collagen, tensile strength, and epithelialization rate in a tilt wound model^[12]. Madecassol, an extract of this plant containing

madecassic acid, Asiatic acid, and Asiaticoside accelerates cicatrization and grafting of wounds^[10]. Asiaticoside promotes fibroblasts proliferation and extracellular matrix synthesis in wound healing.

Rats treated with extract showed a better tensile strength of the wound after 7 days of wound infliction when compared with control^[10].

A study on ethanol-induced gastric lesion oral administration of CE (0.05, 0.25, and 0.50 g/kg) before ethanol administration considerably lowered mucosal myeloperoxidase activity checked gastric lesions formation (58% to 82% reduction) and in a dose-dependent manner. Fibroblast division and collagen synthesis were enhanced in the wound on treatment with extract of *C. Asiatica*^[12].

Anti-oxidant:

Free radical and reactive oxygen species (ROS) are the main reason behind aging. All organisms have a mechanism to deal with such reactive groups, free radical scavengers protect the organism^[5]. The analysis of an extract from different parts of *Centella Asiatica* noticed that the leaves of *Centella Asiatica* exhibit higher antioxidant activity compared to other plant parts tested^[12].

Leaves contain a higher concentration of those phytochemicals relative to the petioles and the roots. Essential oil of *C. Asiatica* extracted through steam distillation showed to be an excellent antioxidant for food containing lipids^[1]. Its activity was quite comparable with

the synthetic antioxidant butyl hydroxyanisole (BHA)^[12].

Crude methanolic extract on continuous supplementation for 14 days increased the level of antioxidant enzymes and ascorbic acid level reduced in lymphoma-bearing mice^[5]. Extracts of *C. Asiatica* in different solvents such as chloroform, hexane, acetone, ethyl acetate, methanol, and water were assessed for antioxidant potential. Polyphenol, flavonoid, β -carotene, tannin, Vitamin C, and DPPH compounds are readily found in *C. Asiatica* contributing to significantly higher antioxidant activity in the her^[1].

Anti-inflammatory:

Anti-inflammation is a widely used methodology in experimental oncology which helps to examine the inflammation defensive potential of natural products (betulinic acid, α -amyrin acetate, lupeol acetate, oleanolic acid, and ursolic acid) and synthetic entities^[8]. The overproduction of free radicals increases the risk of oxidative damage to biomolecules, lipids, proteins, and DNA^[9]. Oxidative damage can cause chronic diseases, including degenerative diseases, diabetes mellitus, cancer, and atherosclerosis.

Natural antioxidants and the intake of natural antioxidants, as found in fruits,

vegetables, and medicinal herbs, contain free radical scavenging molecules that can help reduce the risk of degenerative diseases, cardiovascular disease, and diabetes mellitus^[8].

Terpenoid is a major constituent among secondary metabolites secreted by plants. It helps to cope with stress conditions and supports defense activities^[9]. Plants with medicinal properties are rich in these compounds such as ceramide and different forms of terpenoids.

Hypotonicity-induced human red blood cell membrane breakdown was inhibited by *C. Asiatica*^[8].

Anti-fungal:

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^[15]. The control Ketoconazole (10 μ g) showed the inhibition of 12 mm^[3]. 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). 100% ethanolic extract of *C. Asiatica* showed a zone of inhibition of 15.4 mm against *A. niger*^[3]. Against *Candida albicans*, on an average of 5 mm, a zone of inhibition was observed while the standard miconazole nitrate showed inhibition of 20 mm^[15]. The study demonstrated that the ethanolic extract of *Centella Asiatica* has higher antimicrobial activity than petroleum ether and water extract^[3].

Anti-Depressant:

The triterpenoid saponins present in the plant exhibit antidepressant activity by reducing corticosterone levels in serum. Compared to diazepam *C. Asiatica* possesses an antianxiety effect but does not affect behavioral despair^[17]. Total triterpenes and imipramine from *C. Asiatica* were evaluated for antidepressant activity using the forced swimming test, the result showed a reduction in stillness duration and regulated amino acid

levels^[18]. Forced swim test was performed in male Sprague-Dawley rats treated with Asiatic acid and midazolam+asiatic acid, a significant result was observed in the ratio of open-arm time, maximum speed, and time spent in the AA group and the midazolam+AA group ($p < 0.05$)^[17].

The standardized extract showed a reversal of physiological and behavioral changes following OBX-induced depression in rats^[18].

Anti-bacterial:

Methanol hot extract from *C. Asiatica* leaves was taken to check the antibacterial activity which was assessed by the zone of inhibition and minimum inhibitory concentration (MIC) value (2

μ g/disc) by disc diffusion method^[19]. *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^[15].

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. 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^[19].

Precautions:

Although *C. Asiatica* is one of the top-selling herbal medicines due to its remarkable pharmacological effects, some precautions should be taken for this plant. It has been known to be safe when taken at the recommended doses; however, skin irritation and contact dermatitis have been reported in some cases^[19]. In a very early paper in 1969 the total saponoside fraction containing Brahmic acid and its derivatives of the plant was stated to cause fertility in an experiment conducted on human and rat sperms^[18]. The result pointed out the fact that chronic treatment of *C.*

Asiatica might induce a spontaneous abortion in pregnant women. Since the plant may bring about a rise in blood sugar and lipid levels, diabetic and hyperlipidemic patients should consider taking a preparation of *C. Asiatica*^[19]. Briefly, maximum duration suggested for the use of *C. Asiatica* preparations in 6 weeks and at least, a 2-week break is needed after every long-duration use^[17]. Even though no drug interaction has been reported for this plant up to date, pregnancy and breastfeeding are suggested to avoid using this herbal medicine.

Conclusion:

Plants have been used as herbal remedies for decades, and researched as alternative pharmaceutical solutions, for years. This research article highlights the medicinal capacities of *C. Asiatica* and its potential as a therapeutic agent for Alzheimer's disease, memory, diabetes mellitus, wound healing, venous insufficiency and varicose veins, and anti-inflammation, anti-viral, anti-fungal, neuroprotective, anti-depressant, anti-cancer, anti-oxidant, anti-diabetic. Oral use of *C. Asiatica* and

in vitro studies have improved memory and cognition, stabilizing diabetic symptoms, aid topical wounds and alleviate the swelling. In vitro studies in animals have found *C. asiatica* to improve memory and increase reaction time, and assist with the wound-healing process. Dose-dependent amounts of aqueous extract of *C. Asiatica* also decrease the appearance of aging skin, collagen, and topical scars. The plant can be a safer alternative for the formulation of new drugs.

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