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MINI-REVIEW article

An overview of therapeutic qualities and various applications of *Centella asiatica*

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Abstract: A useful therapeutic herb in the old and new worlds, *Centella asiatica* (L.), is a perennial creeper with a subtle scent. It can be found all across the world's tropical and subtropical regions. Its useful functional qualities are primarily responsible for the rise in its use in food and drink over time. Numerous reports have demonstrated its potential for antioxidant, antimicrobial, cytotoxic, neuroprotective, and other activities. These activities are essentially closely linked to the characteristics and mode of action of the plant's bioactive constituents, which include flavonoids, other phenolic compounds, triterpenic acid (asiatic acid and madecassic acid), and triterpenic saponin (madecassoside and asiaticoside). Several applications have been supported by science, which has confirmed the bioactive components. This review evaluated the ancient literature that is available in search of C. asiatica's therapeutic efficacy to give a concise overview of this plant.

Introduction

Historically, most natural products used as drugs are derived from plants. Man discovered the poisonous or healing properties of plants in his search for food. Some plants had dramatic effects on the body and some were found to cure certain diseases. Traditional herbs were regarded as drugs in the medical system and an enormous amount of information was provided by numerous traditional medical systems and folk medicine [1, 2]. Each medicinal plant and crude drug contains active or major chemical constituents with a characteristic profile that can be used for pharmacological effect and clinical use. *Centella asiatica* (Linn.) (C.A.) urban system synonym hydrocotyle asiatica Linn., also called Indian Pennywort, is a member of the Apiaceae family, which has formerly been known as Umbelliferae. Primarily referred to as a "Brain food" in India, C.A. is a key plant for healing wounds, alleviating skin issues, and reviving nerves and brain cells [3]. Because of Centella's numerous health benefits, including its anti-inflammatory, antioxidant, wound-healing, and memory-enhancing qualities, its use in food and drink has grown throughout time. In recent years, Centella's potential as a plant-based natural antioxidant has significantly expanded, as has its ability to defend against age-related alterations in the brain's antioxidant defense system [4]. In Africa, Oceania, India, Sri Lanka, China, and Southeast Asia, the plant has long been utilized as a vegetable. Many illnesses, such as skin disorders, rheumatism, inflammation, syphilis, mental illness, epilepsy, hysteria, dehydration, and diarrhea, have been treated with it for a long time in Southeast Asia [5, 6]. In the global medicinal plant trade, C.A. is one of the most significant medicinal plants. Due to extensive and unrestricted extraction, limited cultivation, and a lack of efforts to replace it, the wild stock of this plant species has nevertheless significantly been

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reduced. Furthermore, it is currently categorized as both an endangered species and a threatened plant species by the International Union for Conservation of Nature and Natural Resources (IUCN) [7-9]. C.A., often known as gotu kola, is used in Indian medical systems to treat nervous system disorders, skin ailments, and memory impairment [10]. Based on experience and traditional remedies, C.A. has been used for thousands of years to cure minor and chronic illnesses, and this is why they continue to receive a lot of attention. Screening medicinal plants is essential to identify novel chemicals that may be used therapeutically [11]. Due to the plant's numerous applications in the treatment of illnesses, scientific organizations have recently been quite interested in it.

Phyto-chemicals: The plant has long been used to cure a wide range of illnesses in folk medicine discovered through chemical means, resulting in medicinal qualities. In addition to being abundant in flavonoids and terpenoids, the main components that give it its pharmacological significance include asiatic acid, asiaticoside, and madecassoside [12]. The term "centelloid" was used to describe a variety of plant-produced secondary metabolite ingredients, primarily pentacyclic triterpenoid saponins [13]. Upon investigation using gas chromatography-mass spectrometry, it was discovered that P-cymene (44.0%) and other volatile chemicals were present in significant amounts in the essential oil of C.A., (**Figure 1**), [14]. C.A. and centellicin were separated from the plant's aerial portion, and a 2D nuclear magnetic resonance approach was used to ascertain their structures [15].

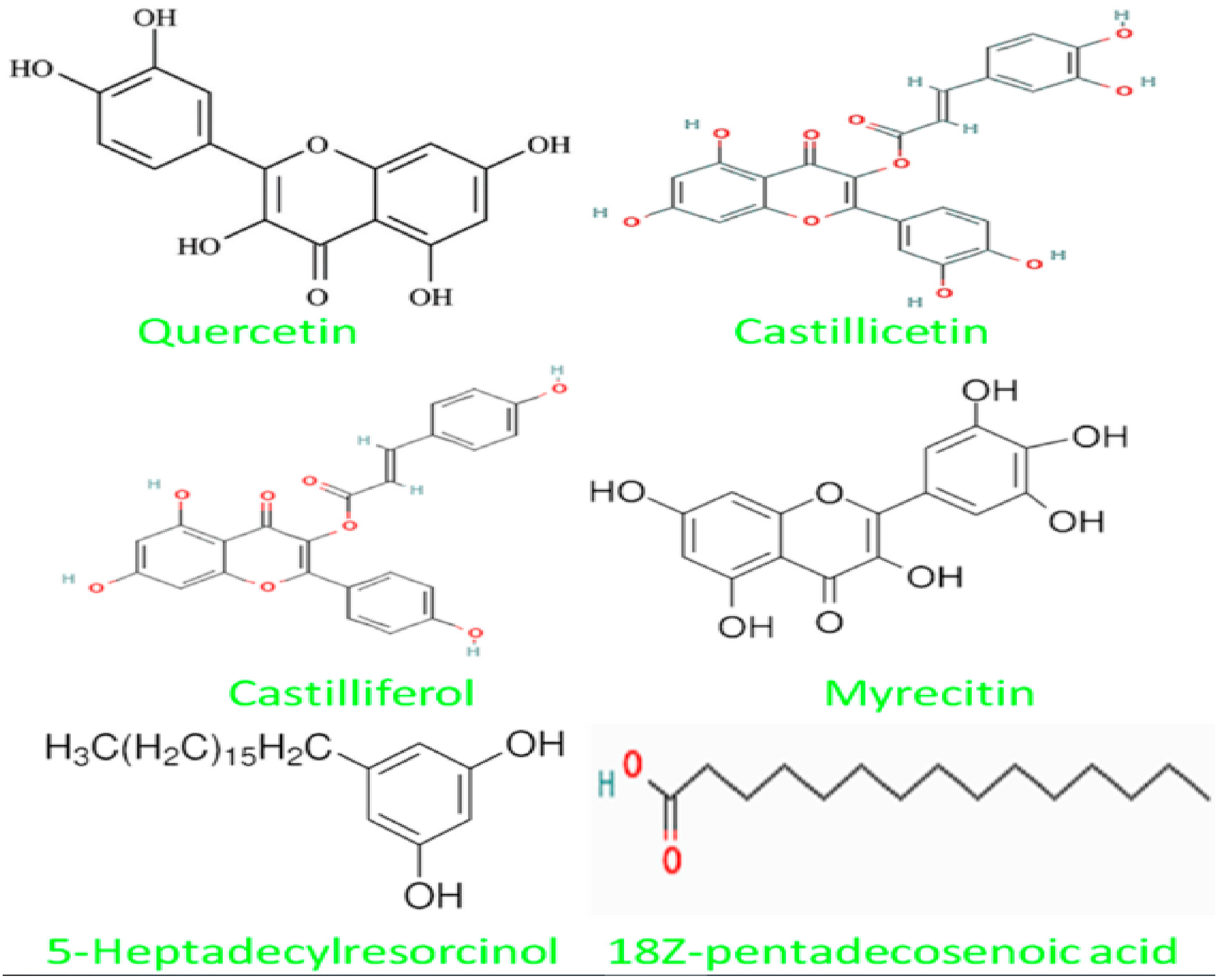

Figure 1: A few chemicals isolated from *Centella asiatica*

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Madecassoside, asiaticoside, madecassic acid, and asiatic acid were detected in a significant quantity from plant extract that was subjected to high-performance liquid chromatography to find bioactive components [16]. According to a quantitative assessment of triterpenoids, leaf samples gathered in the Mangoro region had the greatest asiaticoside level (6.42%) [17]. Two novel triterpenes, a saponin, and 2α,3β,23-trihydroxyurs-20-en-28-oic acid together Spectral methods were used to characterize the structures of O-α-l-rhamno-pyranosy-(1→4)-O-β-dglucopyranosyl(1→6)-O-β-dglucopyranosyl ester, which was isolated from the aerial section of C.A. [18]. Flavonoids including quercetin, kaempherol, catechin, rutin, apigenin, and naringin, as well as volatile oils like caryophyllene, farnesol, and elemene, contribute to its high total phenolic contents in addition to terpenoids [19, 20]. In comparison to the petioles and roots, the leaves had the highest concentration of phytochemicals, according to Zainol et al. [21]. Centella is also rich in vitamin C, vitamin B1, vitamin B2, niacin, carotene, and vitamin A. The total ash contains chloride, sulphate, phosphate, iron, calcium, magnesium, sodium, and potassium [22, 23].

Botanical description: C.A., a clonal perennial herbaceous creeper belonging to the Umbellifere (Apiceae) family, grows in moist places up to 1,800 meters in elevation throughout India. In most tropical and subtropical countries, including parts of India, Pakistan, Sri Lanka, Madagascar, South Africa, the South Pacific, and Eastern Europe, it grows in swampy areas. About 20 species related to C.A. grow in rocky, higher elevations and most tropical or wet pantropical areas, including rice fields [24]. It grows small oval fruits and has white, light purple-to-pink, or white flowers, as well as tiny green leaves shaped like a fan (**Figure 2**). All parts of the plant are used as medicine [10]. It is a flavorless plant with a faintly bitter taste that grows close to water [25]. It is commonly used to treat high blood pressure, prolong life, enhance memory, and purify the blood. C.A. is one of the most important herbs in Ayurveda for revitalizing brain cells and neurons. Eastern healers thought that emotional illnesses like depression had a physical root, so they utilized C.A. to treat them [26, 27]. The plant has garnered significant interest from scientific groups in recent years due to its many uses in the treatment of ailments.

Figure 2: Leaf of *Centalla asiatica*

Antioxidant properties: Due to the growing trend of using natural antioxidants instead of synthetic ones, researchers and the food sector are very interested in the antioxidant qualities of essential oils and other extracts from a wide variety of plants [28]. It is commonly known that C.A. exhibits strong antioxidant properties [29]. C.A. has extremely strong potential to be investigated as a source of natural antioxidants [30] and exhibits antioxidant activity that is comparable to that of sage and rosemary. According to Hashim et al. [31], the antioxidant content of Centella (84.0%) is similar to that of grape seed extract (83.0%) and vitamin C (88.0%). According to Gupta and Prakash [32], C.A. grown in India exhibited strong antioxidant activity,

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as determined by the ferrous ion chelating capacity, DPPH, and reducing power techniques. Moreover, they discovered that C.A. is a good source of antioxidants, including total and beta carotene, ascorbic acid, and total phenolics. Their regression study revealed a significantly substantial correlation between antioxidant levels and antioxidant activity. The antioxidant activity and content of C.A. grown in India were investigated by Subhasree et al. [33]. Their findings demonstrated that C.A. was a good source of antioxidant substances and had good antioxidant activity. When compared to other plant parts, the leaves of C.A. exhibited the best antioxidant activity and the largest phenolic levels, according to Zainol et al. [34]. This finding implies that the main source of C.A.'s antioxidative properties is phenolic chemicals. However, ethanol extract of C.A.'s root showed the highest activity, according to Abdul-Hamid et al. [35], even though it did not differ much from the leaves. Different components of C.A. may have antioxidative properties by chelation of metal ions, reduction of hydroperoxides, or inactivation of free radicals. According to Dasgupta [36], out of the eleven edible Indian green leafy vegetables they examined, C.A. possesses the best total antioxidant capacity and the strongest DPPH radical scavenging activity based on gallic acid and ascorbic acid equivalent. Centella possesses good lipid peroxidation prevention as well as hydroxyl and superoxide radical scavenging capabilities. In addition, it contains more total flavonoids and phenols than other green vegetables. Odhav and others [37] reported that out of the 20 traditional leafy vegetables grown in South Africa, C.A. leaves exhibited the highest amount of antioxidant activity. Here, the methonolic plant extracts generated from the fresh leaves were used to express the antioxidant activity as a percentage of their scavenging capability. Relative activity to rutin was represented by the other results, while the activity obtained for flavonoid rutin was taken as 100% (positive control). In C.A. plants grown in Thailand and South Africa, respectively, Nanasombat and Teckettuen [38] and Akula and Odhav [39] similarly reported higher levels of antioxidant activity.

Wound healing capacity: Research has recently provided greater evidence in favor of the use of C.A. extracts (C.A.E.) for wound healing [40]. Over 24 days, rats with open wounds received three daily applications of an aqueous C.A.E. in various formulations (ointment, cream, and gel). Collagen content and tensile strength rose at the wound site, indicating greater cellular proliferation and collagen synthesis [41]. When applied topically to guinea pig punch wounds, a 0.2% asiaticoside solution increased hydroxyproline by 56.0%, tensile strength by 57.0%, collagen content by 56.0%, and epithelization by 57.0%. By applying a 0.4% asiaticoside solution topically to punch wounds in streptozotocin-diabetic rats, which slowed down the healing process, the hydroxyproline content, tensile strength, collagen content, and epithelization all improved. When given orally at a dose of 1.0 mg/kg, Asiaticoside demonstrated efficacy in the guinea pig poke wound model. In the chick chorioallantoic membrane model, it stimulated angiogenesis at a concentration of 40/disc. One study evaluated the effects of an alcoholic extract of C.A. administered topically and orally on the healing of cutaneous wounds in rats [42].

Anti-inflammatory properties: C.A.E. reduced rats' acute radiation reactivity, which had anti-inflammatory properties. By inhibiting NO formation, C.A. water extract and its active ingredient asiaticoside have anti-inflammatory properties that promote ulcer healing [43]. Rat paw edema occurred because of the anti-inflammatory properties of C.A. crude extract triggered by prostaglandin E2. The anti-inflammatory properties of the crude extract may be due to the presence of bioactive terpene acids like Asiatic acid and madecassic acid [44].

Hepatoprotective activity: When diabetic control rats were given deionized water, their liver concentrations of interleukin-1, MCP-1, and tumor necrosis factor-alpha dropped to 68.0%, 75.0%, and 63.0% of normal control rats' liver concentrations, respectively. This study assessed the impact of C.A. methanolic extract on Type 2 diabetes mellitus [45]. The functional group of Asiatic acid changed at positions C2, C3, C23, and C28. Compound 9 showed moderate hepatoprotective efficacy against CCl_4-induced hepatotoxicity (20.7% protection at 50.0 M) and high hepatoprotective effects against GaIN-induced hepatotoxicity (66.4%

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protection at 50 M) [46]. By starting to inhibit TGF-beta/Smad-assisted fibrogenesis in a Smad7-dependent way, Asiatic acid protects against liver damage. Thus, new hepatoprotective compounds that could be created as pharmacological entities may be found in botanicals that have historically been used to treat liver failure in humans [47].

Antiulcer activity: In a published laboratory study, an aqueous extract of C.A. was found to be effective in avoiding stomach ulcers caused by the ingestion of ethanol [48]. Animal studies showed that C.A.E. reduced stomach ulcers in rats caused by stress from cold and confinement. There was a comparison between the antiulcer activity and the H2-antagonist famotidine and the antiepileptic or antiseizure medication sodium valproate. Apart from the antiulcer effect of famotidine, the medications, and the herb extract decreased stomach ulcers in a dose-dependent way that could be reversed with the use of the particular $GABA_A$ antagonist bicucullin methiodide [49]. As per one study, the anti-inflammatory characteristics of C.A. and its constituent asiaticosides stem from the inhibition of nitric oxide, which facilitates the healing of ulcers [50].

Antibacterial activity: With Minimum Inhibitory Concentration (MIC) values ranging from 0.039 to 1.25 mg/ml, an essential oil extract showed antibacterial activity against Gram-positive (Bacillus subtilis, and S. aureus) and Gram-negative (Escherichia coli, Pseudomonas aeruginosa, and Shigella sonnei) bacteria [51]. *Bacillus cereus* and *Listeria monocytogenes* 10403S were selected to examine the antibacterial activity in C.A. under normal and osmatic stress settings. Extracts of 9.05% ethanol showed twice as much antibacterial activity under osmotic stress. The MIC for C.A. against *Bacillus cereus* was 16 l/ml, while the MIC for L. monocytogenes 10403S was 8.0 l/ml [52].

Memory-enhancing capacity: While reducing brain levels of dopamine, norepinephrine, serotonin, and its metabolites, the herb's aqueous extract markedly enhanced learning and memory [53]. C.A. contains brahminoside, brahmside, isobrahmic acid, and brahmic acid. It has psychotropic, anti-convulsant, and sedative properties. It helps with dementia, mental diseases, and anxiety. A polyherbal formulation helps children with learning impairments by enhancing memory, attention, and concentration through the combined action of all the herbs.

Antidiabetic activity: Methanolic and ethanolic extracts demonstrated the plant's anti-hyperglycemic effectiveness in type II diabetic rats by considerably lowering blood glucose levels to normal levels in a tolerance test [54].

Conclusion: With many medicinal applications, *Centella asiatica* is a promising herb. The neuroprotective qualities of plants and their positive effects on brain development are widely accepted. The aforementioned text states that plants have shown reduced toxicity and increased effectiveness in clinical treatment, with noteworthy properties including antidepressant, anticancer, antibacterial, antifungal, anti-inflammatory, neuroprotective, antioxidant, and wound healing. The therapeutic potential of the plant in terms of its effectiveness and adaptability seems to necessitate further thorough research.

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Author contribution: Both authors conceived, designed the study, collected the data and performed data analysis. IKR drafted the manuscript/revising it for important intellectual context. Both authors approved the final version of the manuscript and agreed to be accountable for its contents.
Conflict of interest: The author declares the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Ethical issues: The author completely observed ethical issues, including plagiarism, informed consent, data fabrication or falsification, and double publication or submission.