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Review

Centella asiatica (Gotu kola) as a neuroprotectant and its potential role in healthy ageing

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ABSTRACT

Background: Chronic and degenerative diseases have become major concerns in healthcare and research sectors in the world, especially in hyper-ageing societies. The role of diet in healthy ageing is much emphasised leading to more research on exploring the scientifically backed functional properties of conventional foods. *Centella asiatica* (Gotu kola) is a herbal plant that is highly valued as a medicine and also commonly used in a variety of cuisine as a green leafy vegetable.

Scope and approach: This paper reviews available evidence on health benefits of *C. asiatica* especially emphasising its role as a neuroprotectant, while providing details on its phytochemistry and pharmacological properties.

Key findings and conclusions: Complementing its reputation in traditional medicine as a memory booster, *C. asiatica* possesses wholesome anti-oxidative properties to attenuate oxidative stress, a high anti-inflammatory potent, neuron regenerative ability, potential for neuron damage prevention, neurotoxicity inhibition effect, anti-anxiety and anti-depressive properties, AChE inhibitory potential and ability to reduce accumulation of amyloid plaques. These comprehensive multifunctional properties make it capable of promoting general neuroprotection as well as simultaneously targeting multiple disease pathways to arrest neurodegenerative disorders. However, to be used as a therapeutic agent, a proper evaluation should be done of the active ingredients, presence of any synergistic effects, efficient extraction methods and stabilization of the active ingredients until they are delivered in the body as well as the potential of active ingredients to reach targeted pathological pathways, especially the ability to cross the blood-brain barrier (BBB).

1. Introduction and background

The improvement in life expectancy of the global population over the past years has resulted in the transformation of demographics, from young societies to hyper-ageing societies, especially in developed countries. It is reported that 12.5% (901 million) of the worldwide population were aged 60 and over in 2015 (World Population Aging report, United Nations, 2015). This change may affect economies and social aspirations as well as health and well-being. The emergence of chronic and degenerative diseases and associated costs have become major concerns in healthcare and research sectors in the world. Current trends in research emphasising the role of diet in healthy ageing also reflect and align with these global concerns. The health-conscious consumer demand is ever increasing for functional food and super foods, particularly whole food with exceptional health benefits. The responsibility of researchers is not only to unlock the secrets of functional properties but also to confirm scientifically backed health claims

while ensuring the safety of such foods. Herbal plants are being used as conventional foods for their functional properties which have been evident over the years through experience. Many of these herbs are also explored for their therapeutic potentials in age-related health issues.

C. asiatica (Gotu kola) is one such plant, commonly used as a green leafy vegetable, in traditional societies over the world due to its well-known health benefits. It is highly valued for its use as a medicinal herb since prehistoric times (Brinkhaus, 2000). *C. asiatica* has been used in Ayurvedic, Unani and folk medicine in India, Sri Lanka and South East Asian countries over centuries. Furthermore, it has reported uses in traditional African medicine and traditional Chinese medicine (Jahan et al., 2012). A study conducted by Packer et al. (2012) in collaboration with Yaegl Aboriginal community in Australia has also revealed the native medicinal usage of *C. asiatica* in Australia.

As per Indian Ayurveda, *C. asiatica* is considered as having multifunctional roles (Das, 2011) and a potential “cure-all herb” which has been used in Ayurveda tradition for thousands of years to treat mild and

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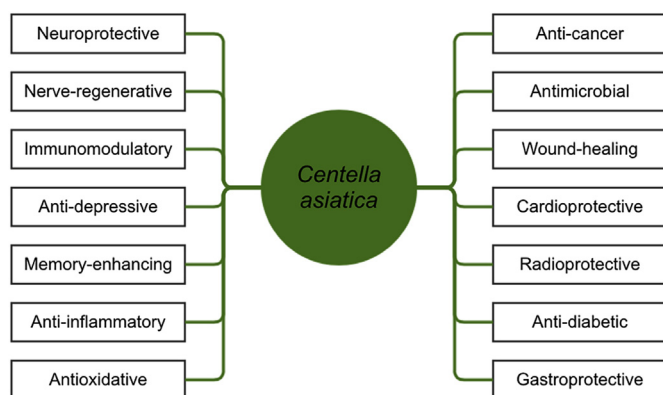


Fig. 1. Pharmacological properties of *Centella asiatica*.

chronic diseases (Gohil, Patel, & Gajjar, 2010). *C. asiatica* is believed to possess diverse pharmacological activities (Fig. 1), such as neuroprotective, nerve regenerative, immunomodulatory, anti-depressive, memory enhancing, gastroprotective, cardioprotective, radioprotective, anti-cancer, antimicrobial, wound healing, anti-inflammatory, anti-diabetic, and antioxidative properties (Bandara, Lee, & Thomas, 2011; Brinkhaus et al., 2000; Das, 2011; Jahan et al., 2012; Roy, Barman, & Shaik, 2013; Zheng & Qin, 2007).

C. asiatica is especially recognised for its traditional use as a memory enhancer (Orhan et al., 2012) and for its ability to revitalise nerves and brain cells (Seevaratnam, Banumathi, Premalatha, Sundaram, & Arumugam, 2012). This traditional use is closely associated with its neuroprotective effect and indicates the potential of its bioactives to cure neurodegenerative diseases such as Alzheimer's disease, senile dementia and Parkinson's disease which are common in ageing societies, such as those found in the industrialised countries. Currently, there are only a few synthetic drugs for the treatment of cognitive dysfunction and memory loss associated with these diseases (Alzheimer's Association, 2017). They are known to have various adverse effects including gastrointestinal disturbances and problems associated with bioavailability, which necessitates finding alternatives from natural resources without these adverse effects. *C. asiatica* is an outstanding candidate with anecdotal evidence in cognitive disorders in traditional medicine.

As emphasised by Brinkhaus, Lindner, Schuppan, and Hahn (2000),

Table 1
Varieties of *Centella asiatica*.

Main group	Constituent	Reference
Triterpenic acids	Asiatic acid, Madasiatic acid, Madecassic acid, Thankunic acid, Indocentoic acid, Euscaphic acid, Terminolic acid, Isothankunic acid, Bayogenin, Centic acid, Betulinic acid, Cenellic acid, Brahmic acid, Idocentic acid	Barnes, Anderson, & Phillipson, 2007; Brinkhaus et al., 2000; Chong and Aziz, 2011; James & Dubery, 2009; Zheng & Qin, 2007
Triterpenic sugar esters	Asiaticoside, Asiaticoside A, Asiaticoside B, Asiaticoside C, Asiaticoside D, Asiaticoside E, Asiaticoside F, Braminoside, Brahmoside, Brahminoside, Thankuniside, Isothankuniside, Centellasaponin A, Centellasapogenol, Sceffoleoside A, Centellasaponin B, Centellasaponin C, Centellasaponin D, Centelloside, Madecassoside	Barnes et al., 2007; Brinkhaus et al., 2000; Chong and Aziz, 2011; James & Dubery, 2009; Jiang et al., 2005; Matsuda et al., 2001; Zheng & Qin, 2007
Triterpenic steroids	Stigmasterol, Sitosterol	Brinkhaus et al., 2000; Chong and Aziz, 2011
Essential oils	β -Caryophyllene, Terpene acetate, Terpinene Pinene, α -Humulene, Bicyclogermacrene, Germacrene B, Elemene, Farnesol, Myrcene	Barnes et al., 2007; Brinkhaus et al., 2000; Chong and Aziz, 2011; Oyedeji & Afolayan, 2005
Flavonoids (polyphenols)	Quercetin glycoside, Kaempferol, Astragalgin, Catechin, Rutin, Naringin	Barnes et al., 2007; Brinkhaus et al., 2000; Chong and Aziz, 2011
Sesquiterpenes	Bicycloelemene, <i>Trans</i> -farnesene, Ermacrene	Brinkhaus et al., 2000; Chong and Aziz, 2011
Vitamines	Ascorbic acid, nicotinic acid, β -carotene	Chong and Aziz, 2011
Minerals	Calcium, phosphorus, iron, potassium, magnesium, manganese, zinc, sodium, copper	Chong and Aziz, 2011
Amino acids	Alanine and serine (major), aminobutyrate, aspartate, glutamate, histidine, lysine, threonine, arginine, leucine, iso-leucine, valine, methionine, tyrosine, mesoinositol, centellose, arabinogalactan	Chong and Aziz, 2011
Other constituents	Hydrocotylin (an alkaloid), vallerine (a bitter compound), phytosterols (e.g. campesterol, stosterol, stigmasterol), resin, 14 different polyacetylenes	Barnes et al., 2007; Chong and Aziz, 2011

"*Centella asiatica* is located at the interface between traditional and modern scientifically oriented medicine". Numerous studies have explored neuroprotective, anti-depressive effects as well as enhancing cognitive performance of *C. asiatica* crude extracts and single or mixture of triterpenic preparations, (Jana, Sur, Maity, Debnath, & Bhattacharyya, 2010; Kumar, Prakash, & Dogra, 2011; Tabassum et al., 2013; Xu et al., 2012). Most of these studies appear to provide evidence to support alternative medicinal claims, thus indicating the necessity for more scientific investigations to examine the traditionally known benefits of *C. asiatica*.

This paper reviews the current literature available on *C. asiatica* as a culinary and medicinal herb and its phytochemistry and pharmacological properties based on epidemiological evidence as well as scientific research. Most importantly, this paper explores the potential use of this herb and its functional properties to benefit healthy ageing especially looking into the treatment of neurodegenerative diseases.

2. Morphology and agro-botany

C. asiatica belongs to the genus *Centella* in the family of Apiaceae which comprises about 50 species including the most abundant species *Centella asiatica* (L.) Urban syn. *Hydrocotyle asiatica* Linn. This plant inhabits warm-climate countries in tropical and subtropical regions such as India, Sri Lanka, Bangladesh, Indonesia, Malaysia, China, Iran, Papua New Guinea, Northern Australia and some parts of Africa and America. It has different common names in many languages: pennywort, marsh pepperwort, Indian water-navelwort (English); asiatisches Wassernabelkraut (German); be'vilaque, coquelariat, violette marron (French); gotu kola (Sri Lanka); brahmi, brahmaduki, karivana, mandookaparni, babassa, thankuni, vallari, vallarai (India); talapetraka, anamanitra, korokorona, silabola (Malagasy); bodila-ba-dinku, tabao en Amhara (African); luo de da and ji xue cao in Chinese (Solet, Simón-Ramiassa, Cosson, & Guignard, 1998).

Solet et al. (1998) mention three varieties of *C. asiatica* (Table 1), in relation to geographic origin, which correlates slight variations in morphology and chemical composition.

C. asiatica is a prostrate, stoloniferous, perennial, creeper herb growing up to an average length of 15 cm (Fig. 2). Its stem is glabrous, striated, rooting at the nodes and the plant is propagating vegetatively by runners (stolons). Leaves are basically kidney shaped 1–5 cm long; 2–6 cm wide with crenate margins and long petioles. Flowers are in fascicled umbels consisting of 3–4 white to purple flowers. The fruit is

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