



22 September 2021
EMA/HMPC/489143/2020
Committee on Herbal Medicinal Products (HMPC)

List of references supporting the assessment of *Centella asiatica* (L.) Urb., herba

Draft

The European Medicines Agency acknowledges that copies of the underlying works used to produce this monograph were provided for research only with exclusion of any commercial purpose.

Abdul Hamid A, Shah ZM, Muse R, Mohamed S. Characterisation of antioxidative activities of various extracts of *Centella asiatica* (L). Urban. *Food Chem* 2002, 77:465-9

Ahmed AS, Taher M, Mandal UK, Jaffri JM, Susanti D, Mahmood S, et al. Pharmacological properties of *Centella asiatica* hydrogel in accelerating wound healing in rabbits. *BMC Compl Alt Med* 2019, 19:213

Akbar B, Susilo, Nissa RA, Ritonga RF, Lestari S, Astuti Y, et al. Antifertility Effect of the Ethanol Extract of *Centella asiatica* L. Urban Against the White Rat (*Rattus norvegicus* L.) in the Early Post-Implantation. *J Phys: Conf Ser* 2018, 1114(1):012002

Alternative Medicine Review. 2007. *Centella asiatica* internet monograph 12:1, 69-72. Available at: http://www.anaturalhealingcenter.com/documents/Thorne/monos/Centella-asiatica-mono_12.1.pdf

Allegra C, Pollari G, Criscuolo A, Bonifacio M, Tabassi D. [Centella asiatica extract in venous disorders of the lower limbs. Comparative clinico-instrumental studies with a placebo]. *Clin Ter* 1981, 99(5):507-13 [Italian]

Anand T, Naika M, Kumar GP, Khanum F. Antioxidant and DNA damage preventive properties of *Centella asiatica* (L) Urb. *Pharmacogn J* 2010, 2(17):53-58

Arumugam T, Ayyanar M, Pillai YJK, Sekat T. Phytochemical screening and antibacterial activity of leaf and callus extracts of *Centella asiatica*. *Bangladesh J Pharmacol* 2011, 6:55-60

Awad R, Levac D, Cybulski P, Merali Z, Trudeau VL, Arnason JT. Effects of traditionally used anxiolytic botanicals on enzymes of the gamma-aminobutyric acid (GABA) system. *Can J Physiol Pharmacol* 2007, 85:933-42

Barnes J, Anderson LA, Phillipson JD. *Herbal Medicines*. 3rd ed. Pharmaceutical press, London 2007, 371-73



British Herbal Pharmacopoeia. British Herbal Medicine Association. Exeter 1983, 56-57

Bhuyan B, Baishya K. Ethno medicinal value of various plants used in the preparation of traditional rice beer by different tribes of Assam, India. *Drug Invent Today* 2013, 5(4):335-341

Bian D, Zhang J, Wu X, Dou Y, Yang Y, Tan Q, et al. Asiatic acid isolated from *Centella Asiatica* inhibits TGF- β 1 -induced collagen expression in human keloid fibroblasts via PPAR- γ activation. *Int J Biol Sci* 2013, 9(10):1032-1042

Bradwejn J, Zhou Y, Koszycki D, Shlik J. Double-blind, placebo-controlled study on the effects of Gotu Kola (*Centella asiatica*) on acoustic startle response in healthy subjects. *J Clin Psychopharm* 2000, 20:680-4

Brinkhaus B, Lindner M, Schuppan D, Hahn EG. Chemical, pharmacological and clinical profile of the East Asian medical plant *Centella asiatica*. *Phytomedicine* 2000, 7(5):427-448

Centellase® Summary of Product Characteristics

Cesarone MR, Incandela L, De Sanctis MT, Belcaro G, Bavera P, Bucci M, et al. Evaluation of treatment of diabetic microangiopathy with Total Triterpenic Fraction of *Centella asiatica*: A clinical prospective randomized trial with a microcirculatory model. *Angiology* 2001, 52(2): S49-S54

Chandrika UG, Kumarab PAASP. Gotu Kola (*Centella asiatica*): nutritional properties and plausible health benefits. *Adv Food Nutr Res* 2015, 76:125-157

Cheng CL, Guo JS, Luk J, Koo MW. The healing effects of *Centella* extract and asiaticoside on acetic acid induced gastric ulcers in rats. *Life Sci* 2004, 74:2237-49

Cheng CL, Koo MW. Effects of *Centella asiatica* on ethanol induced gastric mucosal lesions in rats. *Life Sci* 2000, 67:2647-53

Chintapanti S, Reddy KP, Reddy PS. Behavioral and neurochemical consequences of perinatal exposure to lead in adult male Wistar rats: protective effect by *Centella asiatica*. *Environ Sci Pol Res* 2018, 25:13173-13185

Chipavat S, Chavalittumrong P, Tantisira MH. Acute and sub-chronic toxicity studies of a standardized extract of *Centella asiatica* ECa 233. *Thai J Pharm Sci* 2011, 35:55-64

Chong NJ, Aziz Z. A systematic review on the chemical constituents of *Centella asiatica*. *RJPBCS* 2011, 2(3):445-459

Corazza M, Virgili A, Toni G, Minghetti S, Tiengo S, Borghi A. Level of use and safety of botanical products for itching vulvar dermatoses. Are patch tests useful? *Contact Dermatitis* 2013, 74(5):289-294

Cosmetic Ingredient Review Expert Panel, 2015. Safety assessment of *Centella asiatica*-derived ingredients as used in cosmetics. Available at: <https://www.cir-safety.org/sites/default/files/centel062015FR.pdf>

Danese P, Carnevali C, Bertazzoni MG. Allergic contact dermatitis due to *Centella asiatica* extract. *Contact Dermatitis* 1994, 31:201

Dantuluri S. Gotu Kola induced hepatotoxicity in a child—Need for caution with alternative remedies. *Dig Liver Dis* 2011, 43(6):500

Das DC, Sinha NK, Chattopadhyay JC, Das M, Samanta P. The use of medicinal plants for the treatment of gonorrhoea and syphilis in South West Bengal of India. *Int J Phytomed* 2013, 5(1):14-17

de Rus Jacquet A, Subedi R, Ghimire SK, Rochet J. Nepalese traditional medicine and symptoms related to Parkinson's disease and other disorders: patterns of the usage of plant resources along the Himalayan altitudinal range. *J Ethnopharmacol* 2014, 153:178-189

Dey A, Gorai P, Mukherjee A, Dhan R, Modak BP. Ethnobiological treatments of neurological conditions in the Chota Nagpur Plateau, India. *J Ethnopharmacol* 2017, 198:33-44

EMEA. The Committee for Veterinary Medicinal Products. *Centella asiatica* extractum - summary report. EMEA/MRL/494 September 1998

ESCOP Monographs 2nd ed. Supplement 2009. *Centellae asiaticae herba*. European Scientific Cooperative on Phytotherapy, editor. Thieme, Stuttgart 2009, 36-44

European Pharmacopoeia 10th ed. *Centella – Centellae asiaticae herba*. Council of Europe 1/2016: 1498

Farhana KM, Malueka RG, Wibowo S, Gofir A. Effectiveness of Gotu Kola extract 750 mg and 1000 mg compared with folic acid 3 mg in improving vascular cognitive impairment after stroke. *E-Based Compl Alt Med* 2016;2795915

Fong SYK, Wong YC, Zuo Z. Alterations in the CNS effects of anti-epileptic drugs by Chinese herbal medicines. *Exp Opin Drug Metab Toxicol* 2014, 10(2):249-267

Gadahad MR, Rao M, Rao G. Enhancement of hippocampal CA3 neuronal dendritic arborization by *Centella asiatica* (Linn) fresh leaf extract treatment in adult rats. *J Chin Med Assoc* 2008, 71:6-13

George M, Joseph L, Ramaswamy. Anti-allergic, anti-pruritic, and anti-inflammatory activities of *Centella asiatica* extracts. *Afr. J. Trad. CAM* 2009, 6(4):554-559

Giribabu N, Srinivasarao N, Rekha SS, Muniandy S, Salleh N. *Centella asiatica* attenuates diabetes induced hippocampal changes in experimental diabetic rats. *E-Based Compl Alt Med* 2014, 2014: 592062

Global Information Hub on Integrated Medicine. *Centella asiatica* (L.) Urban. Malaysian Herbal Monograph, Available at:

https://www.globinmed.com/index.php?option=com_content&view=article&id=102002:centella-asiatica-l-urban&Itemid=143

Gnanapragasam A, Ebenezar KK, Sathish V, Govindaraju P, Devaki T. Protective effect of *Centella asiatica* on antioxidant tissue defense system against adriamycin induced cardiomyopathy in rats. *Life Sci* 2004, 76:585-97

Gomes J, Pereira T, Vilarinho C, da Luiz Duarte M, Brito C. Contact dermatitis due to *Centella asiatica*. *Contact Dermatitis* 2010, 62(1):54-55

Gray NE, Sampath H, Zweig JA, Quinn JF, Soumyanath A. *Centella asiatica* attenuates β-amyloid-induced oxidative stress and mitochondrial dysfunction. *J Alzheimers Dis.* 2015, 45(3):933-946

Gray NE, Harris CJ, Quinn JF, Soumyanath A. *Centella asiatica* modulates antioxidant and mitochondrial pathways and improves cognitive function in mice. *J Ethnopharmacol* 2016, 180:78-86

Gray NE, Zweig JA, Matthews DG, Caruso M, Quinn JF, Soumyanath A. *Centella asiatica* attenuates mitochondrial dysfunction and oxidative stress in Aβ-exposed hippocampal neurons. *Oxid Med Cell Long* 2017, 2017:7023091

Gray NE, Alcazar Magana A, Lak P, Wright KM, Quinn J, Stevens JF, et al. *Centella asiatica*: phytochemistry and mechanisms of neuroprotection and cognitive enhancement. *Phytochem Rev* 2018a, 17:161-194

Gray NE, Zweig JA, Caruso M, Zhu JY, Wright KM, Quinn JF, et al. *Centella asiatica* attenuates hippocampal mitochondrial dysfunction and improves memory and executive function in β-amyloid overexpressing mice. *Mol Cell Neurosci* 2018b, 93:1-9

Gupta YK, Veerendra Kumar MH, Srivastava AK. Effect of *Centella asiatica* on pentylenetetrazole-induced kindling, cognition and oxidative stress in rats. *Pharm Biochem Behav* 2003, 74:579-85

Hamid IS, Widjaja NMR, Damayanti R. Anticancer activity of *Centella asiatica* leaves extract in benzo(a)pyrene-induced mice. *Int J Pharmacogn Phytochem Res* 2016, 8(1):80-84

Hashim P, Sidek H, Helan MHM, Sabery A, Palanisamy UD, Ilham M. Triterpene Composition and Bioactivities of *Centella asiatica*. *Molecules* 2011, 16:1310-1322

Hausen BM. *Centella asiatica* (Indian pennywort), an effective therapeutic but a weak sensitizer. *Contact Dermatitis* 1993, 29:175-79

Heidari M, Heidari-Vala H, Sadeghi MR, Akhondi MM. The inductive effects of *Centella asiatica* on rat spermatogenic cell apoptosis *in vivo*. *J Nat Med* 2012, 66(2):271-278

Herbert D, Paramasivan CN, Prabhakar R, Swaminathan G. *In vitro* experiments with *Centella asiatica*: investigation to elucidate the effect of an indigenously prepared powder of this plant on the acid-fastness and viability of *M. tuberculosis*. *Indian J Lepr* 1994, 66:65-8

Husain GM, Mishra D, Singh PN, Rao CV, Kumar V. Ethnopharmacological review of native traditional medicinal plants for brain disorders. *Pharm Rev* 2007, 1:19-28

Idrus RBH, Chowdhury SR, Manan NABA, Fong OS, Adenan MI, Bin Saim A. Aqueous extract of *Centella asiatica* promotes corneal epithelium wound healing *in vitro*. *J Ethnopharm* 2012, 140:333-338

Idrus RBH, Yunus MHM, Simat SF, Sainik NQAV, Adenan MI, Bin Saim A. Aqueous extract of *Centella asiatica* as a potential anti-keloid agent. *IJPSR* 2018, 9(3):1281-1290

Izu R, Aguirre A, Gil N, Díaz-Pérez JL. Allergic contact dermatitis from a cream containing *Centella asiatica* extract. *Contact Dermatitis* 1992, 26:192-213

Jana U, Sur TK, Maity LN, Debnath PK, Bhattacharyya D. A clinical study on the management of generalized anxiety disorder with *Centella asiatica*. *Nepal Med Coll J* 2010; 12(1):8-11

Jared SR. Enhancement of memory in rats with *Centella asiatica*. *Biomed Res* 2010, 21(4):429-432.

Jenwitheesuk K, Rojsanga P, Chowchuen B, Sarakunprapha P. A prospective randomized, controlled, double-blind trial of the efficacy using *Centella* cream for scar improvement. *E Based Compl Alt Med* 2018, 2018:9525624

Jorge OA, Jorge AD. Hepatotoxicity associated with the ingestion of *Centella asiatica*. *Rev Esp Enferm Dig* 2005, 97:115-24

Joshi K, Chaturvedi P. Therapeutic efficiency of *Centella asiatica* (L.) Urb. An underutilized green leafy vegetable: an overview. *Int J Pharm Bio Sci* 2013, 4(1):135-149.

Kadir MF, Bin Sayeed M, Setu NI, Mostafa A, Mia MMK. Ethnopharmacological survey of medicinal plants used by traditional health practitioners in Thanchi, Bandarban Hill Tracts, Bangladesh. *J Ethnopharmacol* 2014, 155:495-508

Kar A, Pandit S, Mukherjee K, Bahadur S, Mukherjee PK. Safety assessment of selected medicinal food plants used in Ayurveda through CYP450 enzyme inhibition study. *J Sci Food Agric* 2017, 97(1):333-340

Kartnig T. Clinical applications of *Centella asiatica* (L.). *Herbs Spices Med Plants* 1988, 3:145-73

Kartnig T, Hoffmann-Bohm K. *Centella*. In: Hansel R, Keller K, Rimpler H, Schneider G, editors. Hager's Handbuch der Pharmazeutischen Praxis. Springer, Berlin Heidelberg New York 1992, 764-765

Khurshid F, Govindasamy J, Khalilùòah H, Nonami MS, Shahid M, Ain MR, et al. Effect of *Centella asiatica* formulation on the pharmacokinetics of amitriptyline in rats: a herb-drug interaction study. *Lat Am J Pharm* 2018, 37(4):663-670

Kim YJ, Cha HJ, Nam KO, Yoon Y, Lee H, An S. *Centella asiatica* extracts modulate hydrogen peroxide-induced senescence in human dermal fibroblasts. *Exper Dermatol* 2011, 20:998-1003

Kimura Y, Sumiyoshi M, Samukawa K, Satake N, Sakanaka M. Facilitating action of asiaticoside at low doses on burn wound repair and its mechanism. *Eur J Pharmacol* 2008, 584:415-423

Kumari S, Deori M, Elancheran R, Kotoky J, Devi R. *In vivo* and *in vitro* antioxidant, anti-hyperlipidemic properties and chemical characterization of *Centella asiatica* (L.) extract. *Front Pharmacol*. 2016, 7:400

Kunta RK, Vadlapudi V. *In vitro* antibacterial potentiality of *Centella asiatica*. *Biomed. & Pharmacol. J.* 2009, 2(2):293-296

Kwon MC, Choi WY, Seo YC, Kim JS, Yoon CS, Lim HW, et al. Enhancement of the skin-protective activities of *Centella asiatica* L. Urban by a nano-encapsulation process. *J Biotechnol* 2012, 157:100-106

Laerum OD, Iversen OH. Reticuloses and epidermal tumors in hairless mice after topical skin applications of cantharidin and asiaticoside. *Cancer Res* 1972, 32:1463-1469

Lee J, Jung E, Kim Y, Park J, Park J, Hong S, et al. Asiaticoside induces human collagen I synthesis through TDF β Receptor I kinase (T β RI kinase)-independent Smad signaling. *Planta Med* 2006, 72:324-328

Lee JH, Kim HL, Lee MH, You KE, Kwon BJ, Seo HJ, et al. Asiaticoside enhances normal human skin cell migration, attachment and growth *in vitro* wound healing model. *Phytomedicine* 2012, 19(13):1223-1227

Li D, Zheng X, Duan L, Deng S, Ye W, Wang A, et al. Ethnobotanical survey of herbal tea plants from the traditional markets in Chaoshan, China. *J Ethnopharmacol* 2017, 205:195-206

Lou JS, Dimitrova DM, Murchison C, Arnold GC, Belding H, Seifer N, et al. *Centella asiatica* triterpenes for diabetic neuropathy: a randomized, double-blind, placebo-controlled, pilot clinical study. *Exper Dermatol*, 2 Suppl. I, 2018, (6) 20:12-22

Madaus G. Lehrbuch der Biologischen Heilmittel. 1938 *Hydrocotyle asiatica*. Wassernabel. Umbelliferae. Available at: <https://www.henriettes-herb.com/eclectic/madaus/hydrocotyle-asia.html>

Mahanom H, Azizah AH, Suhaila M, Nazamid S, Maznah I, Hair BM. Effect of *Centella asiatica* extract and powder on hydrogen peroxide-treated *Sprague-Dawley* rats. *J. Trop. Agric. Food. Sc.* 2011, 39(1):1-10

Manasa MR & Sachin ID. Anticonvulsant action of aqueous extract of *Centella asiatica* and sodium valproate—A comparative study in pentylenetetrazole-induced seizures. *Nat J Physiol, Pharm Pharmacol* 2016, 6(2):128-131

Marastoni F, Baldo A, Redaelli G, Ghiringhelli L. [*Centella asiatica* extract in venous pathology of the lower limbs and its evaluation as compared with tribenoside]. *Minerva Cardioangiologica* 1982, 30(4):201-207 [Italian]

Mitha KV, Yadav S, Ganaraja B. Improvement in cognitive parameters among offsprings born to alcohol fed female Wistar rats following long term treatment with *Centella Asiatica*. *Indian J Physiol Pharmacol* 2016, 60(2):167-173

Natarajan S, Paily PP. Effect of topical Hydrocotyle Asiatica in psoriasis. *Ind J Dermatol* 1973, 18(4):82-85

Nowwarote N, Osathanon T, Jitjaturunt P, Manopattanasoontorn S, Pavasant P. Asiaticoside induces type I collagen synthesis and osteogenic differentiation in human periodontal ligament cells. *Phytoter Res* 2013, 27(3):457-462

Nurlailly A, Noor Baitee AR, Musalmah M. Comparative antioxidant and anti-inflammatory activity of different extracts of *Centella asiatica* (L.) Urban and its active compounds, asiaticoside and madecassoside. *Med & Health* 2012, 7(2):62-72

Oruganti M, Roy BK, Singh KK, Prasad R, Kumar S. Safety assessment of *Centella asiatica* in albino rats. *Pharmacognosy Journal* 2010, 2(16):5-13

Pan Y, Abd-Rashid BA, Ismail Z, Ismail R, Mak JW, Pook PCK, et al. In vitro modulatory effects on three major human cytochrome P450 enzymes by multiple active constituents and extracts of *Centella asiatica*. *J Ethnopharmacol* 2010, 130(2):275-283

Panmei R, Gajurel PR, Singh B. Ethnobotany of medicinal plants used by the Zeliangrong ethnic group of Manipur, northeast India. *J Ethnopharmacol* 2019, 235:164-182

Paocharoen V. The efficacy and side effects of oral *Centella asiatica* extract for wound healing promotion in diabetic wound patients. *J Med Assoc Thai* 2010, 93(7):S166-S170

Paolino D, Cosco D, Cilurzo F, Trapasso E, Morittu VM, Celia C, et al. Improved in vitro and in vivo collagen biosynthesis by asiaticoside-loaded ultradeformable vesicles. *J Control Rel* 2012, 162:143-151

Paul S, Devi N, Sarma GC. Ethnobotanical utilization of some medicinal plants by Bodo people of Manas biosphere reserve in the treatment of malaria. *Int. Res. J. Pharm.* 2013, 4(6):102-105

PDR for Herbal Medicines – Gotu Kola (*Centella asiatica*), *Medical Economics Company, Inc* 2000, 359-361

Pittella F, Dutra RC, Junior DD, Lopes MTP, Barbosa NR. Antioxidant and Cytotoxic Activities of *Centella asiatica* (L) Urb. *Int. J. Mol. Sci.* 2009, 10:3713-3721

Pointel JP, Boccalon H, Cloarec M, Ledevenhat C, Joubert M. Titrated extract of *Centella asiatica* (TECA) in the treatment of venous insufficiency of the lower limbs. *Angiology* 1987, 38(1):46-50

Prakash A, Kumar A. Mitoprotective effect of *Centella asiatica* against aluminum-induced neurotoxicity in rats: possible relevance to its anti-oxidant and anti-apoptosis mechanism. *Neurol Sci* 2013, 34:1403-1409

Punturee K, Wild CP, Kasinrerk W, Vinitketkumnuen U. Immunomodulatory activities of *Centella asiatica* and *Rhinacanthus nasutus* extracts. *Asian Pac J Cancer Prev* 2005, 6:396-400

Puttarak P, Dilokthornsakul P, Saokaew S, Dhippayorn T, Kongkaew C, Sruamsiri R, et al. Effects of *Centella asiatica* (L.) Urb. on cognitive function and mood related outcomes: A Systematic Review and Meta-analysis. *Sci Rep* 2017, 7(1):10646

Rai N, Agrawal RC, Khan A. Inhibition of DMBA induced mouse skin carcinogenesis by *Centella asiatica* extract. *Pharmacol online* 2011, 3:536-546

Ramesh BN, Indi SS, Rao KSJ. Studies to understand the effect of *Centella asiatica* on A β (42) aggregation *in vitro*. *Curr Trends Biotechnol Pharm* 2010, 4(2):716-724

Randriamampionona D, Diallo B, Rakotoniriana F, Rabemanantsoa C, Cheuk K, Corbisier AM, et al. Comparative analysis of active constituents in *Centella asiatica* samples from Madagascar: application for *ex situ* conservation and clonal propagation. *Fitoterapia* 2007, 78:482-489

Rao SB, Chetana M, Uma Devi P. *Centella asiatica* treatment during postnatal period enhances learning and memory in mice. *Physiol & Behav* 2005, 86:449-457

Saeidinia A, Keihanian F, Lashkari AP, Lahiji HG, Mobayyen M, Heidarzade A, et al. Partial-thickness burn wounds healing by topical treatment: a randomized controlled comparison between silver sulfadiazine and centiderm. *Medicine (Baltimore)* 2017, 96(9):e6168.

Sahu NP, Subodh KR, Mahato SB. Spectroscopic determination of structures of triterpenoid trisaccharides from *Centella asiatica*. *Phytochemistry* 1989, 28:2852-28

Sainath SB, Meena R, Supriya C, Reddy KP, Reddy PS. Protective role of *Centella asiatica* on lead-induced oxidative stress and suppressed reproductive health in male rats. *Envir Toxicol Pharmacol* 2011, 32:146-154

Saokaew S, Suwankesawong W, Permsuwan U, Chaiyakunapruk N. Safety of herbal products in Thailand: an analysis of reports in the Thai Health Product Vigilance Center Database from 2000 to 2008, *Drug Saf* 2011, 34(4):339-350

Sardar AA, Khan Z, Perveen A, Zereen A. Appraisal of ethnobotanical uses of the wetland plants of Punjab, Pakistan. *Afr. J. Trad. CAM* 2015, 12(4):9-13

Savai J, Varghese A, Pandita N, Chintamaneni M. Investigation of CYP3A4 and CYP2D6 interactions of *Withania somnifera* and *Centella asiatica* in human liver microsomes. *Phytother Res* 2015, 29(5):785-790

Sawatdee S, Choochay K, Chanthorn W, Srichana T. Evaluation of the topical spray containing *Centella asiatica* extract and its efficacy on excision wounds in rats. *Acta Pharm.* 2016, 66:233-244

Semenya S, Potgieter M, Erasmus L. Ethnobotanical survey of medicinal plants used by Bapedi healers to treat diabetes mellitus in the Limpopo Province, South Africa. *J Ethnopharmacol* 2012, 141:440-445

Shah GM, Abbasi AM, Khan N, Guo X, Khan MA, Hussain M, et al. Traditional uses of medicinal plants against malarial disease by the tribal communities of Lesser Himalayas-Pakistan. *J Ethnopharmacol* 2014, 155:450-462.

Shukla A, Rasik AM, Jain GK, Shankar R, Kulshrestha DK, Dhawan BN. *In vitro* and *in vivo* wound healing activity of asiaticoside isolated from *Centella asiatica*. *J Ethnopharmacol* 1999, 65:1-11

Siddique YH, Ara G, Beg T, Faisal M, Ahmad M, Afzal M. Antigenotoxic role of *Centella asiatica* L. extract against cyproterone acetate induced genotoxic damage in cultured human lymphocytes. *Toxicol In Vitro* 2008, 22:10-17

Somboonwong J, Kankaisre M, Tantisira B, Tantisira MH. Wound healing activities of different extracts of *Centella asiatica* in incision and burn wound models: an experimental animal study. *BMC Compl Alt Med* 2012, 12:103

Somchit MN, Sulaiman MR, Zuraini A, Samsuddin L, Sonchit N, Israf DA, et al. Antinociceptive and antinflammatory effects of *Centella asiatica*. *Indian J Pharmacol* 2004, 6:377-380

Song J, Dai Y, Zhang H, Xu X, Xia Y, Gong Z. Madecassoside induces apoptosis of keloid fibroblasts via a mitochondrial-dependent pathway. *Drug Devel Res* 2011, 72:315-322

Song J, Xu H, Lu Q, Xu Z, Bian D, Xia Y, et al. Madecassoside suppresses migration of fibroblasts from keloids: involvement of p38 kinase and PI3K signalling pathways. *Burns* 2012, 38(5):677-684

Soumyanath A, Zhong Y, Henson E, Wadsworth T, Bishop J, Gold BG, et al. *Centella asiatica* extract improves behavioral deficits in a mouse model of Alzheimer's disease: investigation of a possible mechanism of action. *Int J Alzheimer's Dis* 2012, 2012(5868):381974

Soyingbe OS, Mongalo NI, Makhafola TJ. *In vitro* antibacterial and cytotoxic activity of leaf extracts of *Centella asiatica* (L.) Urb, *Warburgia salutaris* (Bertol. F.) Chiov and *Curtisia dentata* (Burm. F.) C.A.Sm medicinal plants used in South Africa. *BMC Compl Alt Med* 2018, 18:315

Subathra M, Shila S, Devi MA, Panneerselvam C. Emerging role of *Centella asiatica* in improving agerelated neurological antioxidant status. *Exp Gerontol* 2005, 40:707-715

Suguna L, Sivakumar P, Chandrakasan G. Effects of *Centella asiatica* extract on dermal wound healing in rats. *Indian J Exp Biol* 1996, 34:1208-1211

Sujarwo W, Keim AP, Savo V, Guarerra PM, Caneva G. Ethnobotanical study of *Loloh*: Traditional herbal drinks from Bali (Indonesia). *J Ethnopharmacol* 2015, 169:34-48

Tang B, Zhu B, Liang Y, Bi L, Hu Z, Chen B, et al. Asiaticoside suppresses collagen expression and TGF-b/Smad signaling through inducing Smad7 and inhibiting TGF-bRI and TGF-bRII in keloid fibroblasts. *Arch Dermatol Res* 2011, 303(8):563-572

Thirawarapan SS, Jariyapongsakul A, Suvitayavat W, Muangnongwa S, Sribusarakum A. Anti-hypertensive and cerebral blood flow improving actions of *Centella asiatica* (L.) Urban leaves juice in deoxycorticosterone acetate-salt hypertensive rats. *Pharm Sci Asia* 2019, 46(3):184-192

Umamageswari MS, Latha K, Sathiya Vinhota AT, Rhevanth V, Velarul S, Surapaneni KM. Evaluation of anti-convulsant activity of aqueous leaf extract of *Centella asiatica* in Wistar Albino Rats. *IJPPR* 2015, 7(4):690-695

Veerendra Kumar MH, Gupta YK. Effect of different extracts of *Centella asiatica* on cognition and markers of oxidative stress in rats. *J Ethnopharmacol* 2002, 79:253-260

Visweswari G, Prasad KS, Chetan PS, Lokanatha V, Rajendra W. Evaluation of the anticonvulsant effect of *Centella asiatica* (gotu kola) in pentylenetetrazol-induced seizures with respect to cholinergic neurotransmission. *Epilepsy & Behavior* 2010a, 17:332-335

Visweswari G, Prasad KS, Chetan PS, Lokanatha V, Rajendra W. The antiepileptic effect of *Centella asiatica* on the activities of Na⁺/K⁺, Mg²⁺ and Ca²⁺-ATPases in rat brain during pentylenetetrazol-induced epilepsy. *Ind J Pharmacol* 2010b, 42(2):82-86

Wattanathorn J, Mator L, Muchimapura S, Tongun T, Pasuriwong O, Piyawatkul N, et al. Positive modulation of cognition and mood in the healthy elderly volunteer following the administration of *Centella asiatica*. *J Ethnopharmacol* 2008, 116:325-332

WHO monographs on selected medicinal plants, Herba centellae. Vol 1, World Health Organization, Geneva 1999, 77-85

Williamson EM. Potter's Cyclopaedia of Botanical Drugs and Preparations. The C.W. Daniel Company Ltd, Essex, England 2003, 229-230

Wolfram S. Experiences with Madecassol in the treatment of ulcerative skin changes. *Wien Med Wochenschr* 1965, 115:439-442

Wu F, Bian D, Xia Y, Gong Z, Tan Q, Chen J, et al. Identification of major active ingredients responsible for burn wound healing of *Centella asiatica* herbs. *E Based Compl Alt Med* 2012, 2012(4):848093

Wu Y, Gao S, Yuan T. Enhancement of bleomycin sensitivity in human lung cancer cell line using *Centella asiatica* leaf extract. *Trop J Pharm Res* 2016, 15(2):335-339

Wu X, Bian D, Dou Y, Gong z, Tan Q, Xia Y, Dai Y. Asiaticoside hinders the invasive growth of keloid fibroblasts through inhibition of the GDF-9/MAPK/Smad pathway. *J Biochem Mol Toxicol* 2017, 31(8)

Yadav MK, Singh SK, Singh M, Mishra SS, Singh AK, Tripathi JS, et al. In vivo toxicity study of ethanolic extracts of *Evolvulus alsinoides* & *Centella asiatica* in Swiss albino mice. *Open Access Maced J Med Sci* 2019, 7(7):1071-1076

Yao CH, Yeh JY, Chen YS, Li MH, Huang CH. Wound-healing effect of electrospun gelatin nanofibres containing *Centella asiatica* extract in a rat model. *J Tissue Regen Med* 2017, 11:905-915

Yen GC, Chen HY, Peng HH. Evaluation of the cytotoxicity, mutagenicity and antimutagenicity of emerging edible plants. *Food Chem Toxicol* 2001, 39(11):1045-1053

Yunianto I, Bashah NAK, Noor MM. Antifertility properties of *Centella asiatica* ethanolic extract as a contraceptive agent: preliminary study of sperm proteomic. *Asian Pacific J Reprod* 2017, 6(5):212-216

Zhang CZ, Niu J, Chong YS, Huang YF, Chu Y, Xie SY, et al. Porous microspheres as promising vehicles for the topical delivery of poorly soluble asiaticoside accelerate wound healing and inhibit scar formation *in vitro* & *in vivo*. *Eur J Pharm Biopharm* 2016, 109:1-13