Are sage, rosemary and lemon balm effective interventions in dementia? A narrative review of the clinical evidence

Item Type Journal Article

Author Noriko Shinjyo

Author Julia Green

Abstract Dementia is a common, progressive disorder impairing brain function and affecting both sufferers and caregivers' wellbeing. The number of dementia patients will increase as the population ages. Rosmarinic acid is a natural compound with choline esterase inhibitory potency found in members of the botanical family lamiaceae, including sage, rosemary, and lemon balm, and has been suggested as having potential efficacy as a dementia intervention. This study aimed to evaluate effectiveness of these herbs based on a review of randomised controlled trials. Database searches were conducted separately for each herb using PubMed, the Cochrane Library, and ScienceDirect for clinical evidence for sage (Salvia officinalis L. or S. lavandulaefolia Vahl), rosemary (Rosmarinus officinalis L.), and lemon balm (Melissa officinalis L.), administered individually. Database searching identified 235, 112, and 177 articles for sage, rosemary, and lemon balm, respectively. From these, eight studies for sage, five for rosemary and eight for lemon balm met the inclusion criteria. Trials were analysed based on the study designs and summarized as narrative synthesis as data were heterogeneous in terms of the target populations, herbal preparations and administration methods. Studies suggested sage spp. could improve cognitive performance and alertness. Rosemary could improve cognitive performance and alertness. Among eight articles identified on lemon balm, seven studies found it effective in improving mood or cognition. One study found no effect. Some clinical evidence supports the benefit of these herbs in dementia intervention. However, methodological heterogeneity and variable trial quality made information synthesis difficult. Further research is required to determine dosage and intervention periods.

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Cognition enhancing effect of panax ginseng in Korean volunteers with mild cognitive impairment: a randomized, double-blind, placebo-controlled clinical trial

Item Type Journal Article

Author Kee Hyung Park

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Author Renhua Zheng

Author Sehyun Kim

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Author Bo-Hyung Kim

Author Sung-Vin Yim

Abstract This study aimed to investigate the cognition-enhancing effect of Panax ginseng. A randomized, double-blind, placebo-controlled clinical trial was conducted to address the cognition-enhancing effects of Panax ginseng. A total of 90 Korean volunteers with mild cognitive impairment participated in this study. All subjects were allocated randomly into 'Ginseng' group or 'Placebo' group. All subjects were administered 3g of Panax ginseng powder or starch (placebo) for 6 months. The Korean version of the Mini-Mental Status Examination (K-MMSE), Korean version of Instrumental Activities of Daily Living (K-IADL), and Seoul Neuropsychological Screening Battery (SNSB) were used to assess the changes in cognitive function at the end of the 6 month study period. The subjects of the 'Ginseng' group improved significantly on the Rey Complex Figure Test (RCFT) immediate recall (P = 0.0405 and P = 0.0342 in per-protocol (PP) and intention-to-treat (ITT) analysis, respectively) and on the RCFT 20-min delayed recall (P = 0.0396 and P = 0.0355 in PP and ITT analysis, respectively) compared with 'placebo' group throughout the 6 months of Panax ginseng administration. There were no serious adverse events. These results suggest that Panax ginseng has a cognition-enhancing effect.

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Effects of American ginseng (Panax quinquefolius) on neurocognitive function: an acute, randomised, double-blind, placebo-controlled, crossover study

Item Type Journal Article

Author Andrew Scholey

Author Anastasia Ossoukhova

Author Lauren Owen

Author Alvin Ibarra

Author Andrew Pipingas

Author Kan He

Author Marc Roller

Author Con Stough

Abstract Over the last decade, Asian ginseng (Panax ginseng) has been shown to improve aspects of human cognitive function. American ginseng (Panax quinquefolius) has a distinct ginsenoside profile from P. ginseng, promising cognitive enhancing properties in preclinical studies and benefits processes linked to human cognition. The availability of a highly standardised extract of P. quinquefolius (Cereboost™) led us to evaluate its neurocognitive properties in humans for the first time. This randomised, double-blind, placebo-controlled, crossover trial (N = 32, healthy young adults) assessed the acute mood, neurocognitive and glycaemic effects of three doses (100, 200 400 mg) of Cereboost™ (P. quinquefolius standardised to 10.65% ginsenosides). Participants' mood, cognitive function and blood glucose were measured 1, 3 and 6 h following administration. There was a significant improvement of working memory (WM) performance associated with P. quinquefolius. Corsi block performance was improved by all doses at all testing times. There were differential effects of all doses on other WM tasks which were maintained across the testing day. Choice reaction time accuracy and ‘calmness’ were significantly improved by 100 mg. There were no changes in

blood glucose levels. This preliminary study has identified robust working memory enhancement following administration of American ginseng. These effects are distinct from those of Asian ginseng and suggest that psychopharmacological properties depend critically on ginsenoside profiles. These results have ramifications for the psychopharmacology of herbal extracts and merit further study using different dosing regimens and in populations where cognition is fragile.

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Ginsenoside Rh2 attenuates microglial activation against toxoplasmic encephalitis via TLR4/NF-κB signaling pathway.

Item Type Journal Article
Author Xiang Xu
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Author Tong Jiang
Author Ying Lu
Author Fumie Aosai
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Author Guanghua Xu
Author Cheng Jin
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Abstract Ginsenoside Rh2 (GRh2) is a characterized component in red ginseng widely used in Korea and China. GRh2 exhibits a wide range of pharmacological activities, such as anti-inflammatory, antioxidant, and anticancer properties. However, its effects on Toxoplasma gondii (T. gondii) infection have not been clarified yet.The effect of GRh2 against T. gondii was assessed under in vitro and in vivo experiments. The BV2 cells were infected with tachyzoites of T. gondii RH strain, and the effects of GRh2 were evaluated by MTT assay, morphological observations, immunofluorescence staining, a trypan blue exclusion assay, reverse transcription PCR, and Western blot analyses. The in vivo experiment was conducted with BALB/c mice inoculated with lethal amounts of tachyzoites with or without GRh2 treatment.The GRh2 treatment significantly inhibited the proliferation of T. gondii under in vitro and in vivo studies. Furthermore, GRh2 blocked the activation of microglia and specifically decreased the release of inflammatory mediators in response to T. gondii infection through TLR4/NF-κB signaling pathway. In mice, GRh2 conferred modest protection from a lethal dose of T. gondii. After the treatment, the proliferation of tachyzoites in the peritoneal cavity of infected mice markedly decreased. Moreover, GRh2 also significantly decreased the T. gondii burden in mouse brain tissues. These findings indicate that GRh2 exhibits an anti-T. gondii effect and inhibits the microglial activation through TLR4/NF-κB signaling pathway, providing the basic pharmacological basis for the development of new drugs to treat toxoplasmic encephalitis.

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Herbal Extracts and Phytochemicals: Plant Secondary Metabolites and the Enhancement of Human Brain function

Item Type Journal Article
Author David N. Kennedy
Author Emma L. Wightman
Abstract Humans consume a wide range of foods, drugs, and dietary supplements that are derived from plants and which modify the functioning of the central nervous sytem (CNS). The psychoactive properties of these substances are attributable to the presence of plant secondary metabolites, chemicals that are not required for the immediate survival of the plant but which are synthesized to increase the fitness of the plant to survive by allowing it to interact with its environment, including pathogens and herbivorous and symbiotic insects. In many cases, the effects of these phytochemicals on the human CNS might be linked either to their ecological roles in the life of the plant or to molecular and biochemical similarities in the biology of plants and higher animals. This review assesses the current evidence for the efficacy of a range of readily available plant-based extracts and chemicals that may improve brain function and which have attracted sufficient research in this regard to reach a conclusion as to their potential effectiveness as nootropics. Many of these candidate phytochemicals/extracts can be grouped by the chemical nature of their potentially active secondary metabolite constituents into alkaloids (caffeine, nicotine), terpenes (ginkgo, ginseng, valerian, Melissa officinalis, sage), and phenolic compounds (curcumin, resveratrol, epigallocatechin-3-gallate, Hypericum perforatum, soy isoflavones). They are discussed in terms of how an increased understanding of the relationship between their ecological roles and CNS effects might further the field of natural, phytochemical drug discovery.
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Natural Products and Derivatives Affecting Neurotransmission Relevant to Alzheimer’s and Parkinson’s Disease

Item Type Journal Article
Author Peter J. Houghton
Author Melanie-Jayne R. Howes
Abstract The two major neurodegenerative diseases Alzheimer's disease (AD) and Parkinson's disease (PD) are characterised by low levels in the brain of the neurotransmitters acetylcholine (ACh) and dopamine (DA), respectively. Clinical treatment of these two conditions is palliative and relies, in most cases, on improving stimulation at the relevant receptors by either increasing levels of the endogenous neurotransmitter or by the use of substances which have a similar agonist response. Natural products continue to provide useful drugs in their own right but also provide templates for the development of other compounds. The major advances in the treatment of AD have been the use of acetylcholinesterase inhibitors such as galantamine, huperzine A, physostigmine and its derivatives to increase the levels of ACh rather than the use of cholinergic compounds, although compounds with nicotinic properties have attracted some interest. In contrast, the treatment of PD has relied on the elevation of DA levels by use of L-DOPA, its precursor, and by the administration of dopaminergic agonists, especially the ergot alkaloid derivatives. The use of inhibitors of enzymes that cause breakdown of DA is an avenue which is being explored. As well as the major natural products of clinical interest, the paper discusses the chemistry, activity and usage of the constituents of plants used in traditional medicine for the treatment of diseases presenting symptoms similar to those characteristic for Alzheimer's or Parkinson's disease.
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Pharmacological properties of Salvia officinalis and its components

Item Type Journal Article
Author Ahmad Ghorbani
Author Mahdi Esmaeilizadeh
Abstract Salvia officinalis (Sage) is a plant in the family of Labiatae/Lamiaceae. It is native to Middle East and Mediterranean areas, but today has been naturalized throughout the world. In folk medicine, S. officinalis has been used for the treatment of different kinds of disorders including seizure, ulcers, gout, rheumatism, inflammation, dizziness, tremor, paralysis, diarrhea, and hyperglycemia. In recent years, this plant has been a subject of intensive studies to document its traditional use and to find new biological effects. These studies have revealed a wide range of pharmacological activities for S. officinalis. Present review highlights the up-to-date information on the pharmacological findings that have been frequently reported for S. officinalis. These findings include anticancer, anti-inflammatory, antinociceptive, antioxidant, antimicrobial, antimutagenic, antidementia, hypoglycemic, and hypolipidemic effects. Also, chemical constituents responsible for pharmacological effects of S. officinalis and the clinical studies on this plant are presented and discussed.

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Plant-derived nootropics and human cognition: A systematic review

Item Type Journal Article
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Author María Mulet
Author Catalina Arévalo-Caro
Author M. C. Sanchez
Author Ainhoa Perez
Author María Perrino
Author Anna Bach-Faig
Author Antonio Aguilar-Martínez
Author Elisabet Vilella
Author Xavier Gallart-Palau
Author Aida Serra
Abstract Substances with modulatory capabilities on certain aspects of human cognition have been revered as nootropics from the dawn of time. The plant kingdom provides most of the currently available nootropics of natural origin. Here, in this systematic review, we aim to provide state-of-the-art information regarding proven and unproven effects of plant-derived nootropics (PDNs) on human cognition in conditions of health and disease. Six independent searches, one for each neurocognitive domain (NCD), were performed in parallel using three independent scientific library databases: PubMed, Cochrane and Scopus. Only scientific studies and systematic reviews with humans published between January 2000 and November 2021 were reviewed, and 256 papers were included. Ginkgo biloba was the most relevant nootropic regarding perceptual and motor functions. Bacopa monnieri improves language, learning and memory. Withania somnifera (Ashwagandha) modulates anxiety and social-related cognitions. Caffeine enhances attention and executive functions. Together, the results from the compiled studies highlight the nootropic effects and the inconsistencies regarding PDNs that require further research.Supplemental data for this article is available online at https://doi.org/10.1080/10408398.2021.2021137.
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Protective effects of ginseng on neurological disorders

Item Type Journal Article
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Author Tahira Farooqui
Author Hwee-Ling Koh
Author Akhlaq A. Farooqui
Author Eng-Ang Ling
Abstract Ginseng (Order: Apiales, Family: Araliaceae, Genus: Panax) has been used as a traditional herbal medicine for over 2000 years, and is recorded to have antianxiety, antidepressant and cognition enhancing properties. The protective effects of ginseng on neurological disorders are discussed in this review. Ginseng species and ginsenosides, and their intestinal metabolism and bioavailability are briefly introduced. This is followed by molecular mechanisms of effects of ginseng on the brain, including glutamatergic transmission, monoamine transmission, estrogen signaling, nitric oxide (NO) production, the Keap1/Nrf2 adaptive cellular stress pathway, neuronal survival, apoptosis, neural stem cells and neuroregeneration, microglia, astrocytes, oligodendrocytes and cerebral microvessels. The molecular mechanisms of the neuroprotective effects of ginseng in Alzheimer's disease (AD) including β-amyloid (Aβ) formation, tau hyperphosphorylation and oxidative stress, major depression, stroke, Parkinson's disease and multiple sclerosis are presented. It is hoped that this discussion will stimulate more studies on the use of ginseng in neurological disorders.
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Salvia officinalis induces antidepressant-like effect, anxiolytic activity and learning improvement in hippocampal lesioned and intact adult rats.

Item Type Journal Article
Author Zineb El Gabbas
Author Kenza Bezza
Author Jawad Laadraoui
Author Rachida Makbal
Author Rachida Aboufatima
Author Abderrahman Chait
Abstract The anxiolytic and antidepressant like effects of Salvia officinalis extract (50, 100 and 200 mg/kg) were evaluated using marble burying, forced swimming and open-field tests in intact and hippocampal lesioned rats. Additionally, S. officinalis was evaluated on rat's memory using conditioned learning test. and we screened the methanolic extract for anti-oxidant activity, phytochemical and high performance liquid chromatography analyses. The administration of sage extract showed a significant reduction of immobility time in lesioned and intact animals during the forced swim test and anxiolytic effect in marble burying test. In the case of conditioned learning paradigm, memory enhancement was observed in sage treated group which indicates a cognition improvement. These activities seem to be related to the anti-oxidant capacity and the phytochemicals

(phenolic, flavonoid, and tannin) detected into the extract of S. officinalis. The findings show that the methanolic extract of sage possess antidepressant-like effect, anxiolytic activity and also may contain bioactive compounds that stimulate learning in rat.

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Withania somnifera reverses Alzheimer's disease pathology by enhancing low-density lipoprotein receptor-related protein in liver

Item Type Journal Article
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Author Alok Gupta
Author Rupanagudi Khader Valli
Author Shanker Datt Joshi
Author Jessica Mills
Author Edith Hamel
Author Pankaj Khanna
Author Subhash C. Jain
Author Suman Thakur
Author Vijayalakshmi Ravindranath
Abstract A 30-d course of oral administration of a semipurified extract of the root of Withania somnifera consisting predominantly of withanolides and withanosides reversed behavioral deficits, plaque pathology, accumulation of β-amyloid peptides (Aβ) and oligomers in the brains of middle-aged and old APP/PS1 Alzheimer's disease transgenic mice. It was similarly effective in reversing behavioral deficits and plaque load in APPSwInd mice (line J20). The temporal sequence involved an increase in plasma Aβ and a decrease in brain Aβ monomer after 7 d, indicating increased transport of Aβ from the brain to the periphery. Enhanced expression of low-density lipoprotein receptor-related protein (LRP) in brain microvessels and the Aβ-degrading protease neprilysin (NEP) occurred 14–21 d after a substantial decrease in brain Aβ levels. However, significant increase in liver LRP and NEP occurred much earlier, at 7 d, and were accompanied by a rise in plasma sLRP, a peripheral sink for brain Aβ. In WT mice, the extract induced liver, but not brain, LRP and NEP and decreased plasma and brain Aβ, indicating that increase in liver LRP and sLRP occurring independent of Aβ concentration could result in clearance of Aβ. Selective down-regulation of liver LRP, but not NEP, abrogated the therapeutic effects of the extract. The remarkable therapeutic effect of W. somnifera mediated through up-regulation of liver LRP indicates that targeting the periphery offers a unique mechanism for Aβ clearance and reverses the behavioral deficits and pathology seen in Alzheimer's disease models.
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