Scientific References for
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COGNITION

Bacopa

1. **Kongkeaw C1, et al. "Meta-analysis of randomized controlled trials on cognitive effects of Bacopa monnieri extract." J Ethnopharmacol. 2014;151(1):528-35.**
   https://www.ncbi.nlm.nih.gov/pubmed/24252493

ABSTRACT

ETHNOPHARMACOLOGICAL RELEVANCE:
Bacopa monnieri has a long history in Ayurvedic medicine for neurological and behavioral defects. To assess its efficacy in improving cognitive function.

MATERIALS AND METHODS:
MEDLINE, EMBASE, CINAHL, AMED, Cochrane Central of clinical trial, WHO registry, Thai Medical Index, Index Medicus Siriraj library and www.clinicaltrial.gov were searched from the inception date of each database to June 2013 using scientific and common synonyms of Bacopa monnieri, cognitive performance or memory. The reference lists of retrieved articles were also reviewed. Randomized, placebo controlled human intervention trials on chronic ≥ 12 weeks dosing of standardized extracts of Bacopa monnieri without any co-medication were included in this study. The methodological quality of studies was assessed using Cochrane's risk of bias assessment and Jadad's quality scales. The weighted mean difference and 95% confidence interval (95% CI) were performed using the random-effects model of the Dersimonian-Laird method.

RESULTS:
Nine studies met the inclusion criteria using 518 subjects. Overall quality of all included trials was low risk of bias and quality of reported information was high. Meta-analysis of 437 eligible subjects showed improved cognition by shortened Trail B test (-17.9 ms; 95% CI -24.6 to -11.2; $p<0.001$) and decreased choice reaction time (10.6 ms; 95% CI -12.1 to -9.2; $p<0.001$).

CONCLUSION:
This meta-analysis suggests that Bacopa monnieri has the potential to improve cognition, particularly speed of attention but only a large well designed 'head-to-head' trial against an existing medication will provide definitive data on its efficacy on healthy or dementia patients using a standardized preparation.

2. **Kumar N, et al. "Efficacy of Standardized Extract of Bacopa monnieri (Bacognize®) on Cognitive Functions of Medical Students: A Six-Week, Randomized Placebo-Controlled Trial." Evid Based Complement Alternat Med. 2016;2016:4103423. Epub 2016 Oct 10.**
https://www.ncbi.nlm.nih.gov/pubmed/27803728

ABSTRACT

Rationale. Bacopa monnieri, popularly known as Brahmi, has been traditionally used in Ayurveda since ages for its memory enhancing properties. However, data on placebo-controlled trial of Bacopa monnieri on intellectual sample is scarce. Hence this study was planned to evaluate the effect of Bacopa monnieri on memory of medical students for six weeks. Objective. To evaluate the efficacy of Bacopa monnieri on memory of medical students with six weeks' administration. Method and Material. This was a randomized double blind placebo-controlled noncrossover, parallel trial. Sixty medical students of either gender from second year of medical school, third term, regular batch, were enrolled from Government Medical College, Nagpur, India. Baseline biochemical and memory tests were done. The participants were randomly divided in two groups to receive either 150 mg of standardized extract of Bacopa monnieri (Bacognize) or matching placebo twice daily for six weeks. All baseline investigations were repeated at the end of the trial. Students were followed up for 15 days after the intervention. Results. Statistically significant improvement was seen in the tests relating to the cognitive functions with use of Bacopa monnieri. Blood biochemistry also showed a significant increase in serum calcium levels (still within normal range).

3. **Calabrese C, et al. "Effects of a standardized Bacopa monnieri extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double-blind, placebo-controlled trial." J Altern Complement Med. 2008 Jul;14(6):707-13.**
https://www.ncbi.nlm.nih.gov/pubmed/18611150

ABSTRACT

OBJECTIVES:
Study aims were to evaluate effects of Bacopa monnieri whole plant standardized dry extract on cognitive function and affect and its safety and tolerability in healthy elderly study participants.

DESIGN:
The study was a randomized, double-blind, placebo-controlled clinical trial with a placebo run-in of 6 weeks and a treatment period of 12 weeks.

SETTING/LOCATION:
Volunteers were recruited from the community to a clinic in Portland, Oregon by public notification.

SUBJECTS:
Fifty-four (54) participants, 65 or older (mean 73.5 years), without clinical signs of dementia, were recruited and randomized to Bacopa or placebo. Forty-eight (48) completed the study with 24 in each group.

INTERVENTIONS:
Standardized B. monnieri extract 300 mg/day or a similar placebo tablet orally for 12 weeks.

OUTCOME MEASURES:
The primary outcome variable was the delayed recall score from the Rey Auditory Verbal Learning Test (AVLT). Other cognitive measures were the Stroop Task assessing the ability to ignore irrelevant information, the Divided Attention Task (DAT), and the Wechsler Adult Intelligence Scale (WAIS) letter-digit test of immediate working memory. Affective measures were the State-Trait Anxiety Inventory, Center for Epidemiologic Studies Depression scale (CESD)-10 depression scale, and the Profile of Mood States. Vital signs were also monitored.

RESULTS:
Controlling for baseline cognitive deficit using the Blessed Orientation-Memory-Concentration test, Bacopa participants had enhanced AVLT delayed word recall memory scores relative to placebo. Stroop results were similarly significant, with the Bacopa group improving and the placebo group unchanged. CESD-10 depression scores, combined state plus trait anxiety scores, and heart rate decreased over time for the Bacopa group but increased for the placebo group. No effects were found on the DAT, WAIS digit task, mood, or blood pressure. The dose was well tolerated with few adverse events (Bacopa n = 9, placebo n = 10), primarily stomach upset.

CONCLUSIONS:
This study provides further evidence that B. monnieri has potential for safely enhancing cognitive performance in the aging.

4. **Hota SK, et al. "Bacopa monniera leaf extract ameliorates hypobaric hypoxia induced spatial memory impairment." Neurobiol Dis. 2009 Apr;34(1):23-39.**
https://www.ncbi.nlm.nih.gov/pubmed/19154788

ABSTRACT

Hypobaric hypoxia induced memory impairment has been attributed to several factors including increased oxidative stress, depleted mitochondrial bioenergetics, altered neurotransmission and apoptosis. This multifactorial response of the brain to hypobaric hypoxia limits the use of therapeutic agents that target individual pathways for ameliorating hypobaric hypoxia induced memory impairment. The present study aimed at exploring the therapeutic potential of a bacoside rich leaf extract of Bacopa monniera in improving the memory functions in hypobaric conditions. The learning ability was evaluated in male Sprague Dawley rats along with memory retrieval following exposure to hypobaric conditions simulating an altitude of 25,000 ft for different durations. The effect of bacoside administration on apoptosis, cytochrome c oxidase activity, ATP levels, and oxidative stress markers and on plasma corticosterone levels was investigated. Expression of NR1 subunit of N-methyl-d-aspartate receptors, neuronal cell adhesion molecules and was also studied along with CREB phosphorylation to elucidate the molecular mechanisms of bacoside action. Bacoside administration was seen to enhance learning ability in rats along with augmentation in memory retrieval and prevention of dendritic atrophy following hypoxic exposure. In addition, it decreased oxidative stress, plasma corticosterone levels and neuronal degeneration. Bacoside administration also increased cytochrome c oxidase activity along with a concomitant increase in ATP levels. Hence, administration of bacosides could be a useful

therapeutic strategy in ameliorating hypobaric hypoxia induced cognitive dysfunctions and other related neurological disorders.

5. **Simpson T, et al. "Bacopa monnieri as an Antioxidant Therapy to Reduce Oxidative Stress in the Aging Brain." Evid Based Complement Alternat Med. 2015;2015:615384.**
https://www.ncbi.nlm.nih.gov/pubmed/26413126

ABSTRACT

The detrimental effect of neuronal cell death due to oxidative stress and mitochondrial dysfunction has been implicated in age-related cognitive decline and neurodegenerative disorders such as Alzheimer's disease. The Indian herb Bacopa monnieri is a dietary antioxidant, with animal and in vitro studies indicating several modes of action that may protect the brain against oxidative damage. In parallel, several studies using the CDRI08 extract have shown that extracts of Bacopa monnieri improve cognitive function in humans. The biological mechanisms of this cognitive enhancement are unknown. In this review we discuss the animal studies and in vivo evidence for Bacopa monnieri as a potential therapeutic antioxidant to reduce oxidative stress and improve cognitive function. We suggest that future studies incorporate neuroimaging particularly magnetic resonance spectroscopy into their randomized controlled trials to better understand whether changes in antioxidant status in vivo cause improvements in cognitive function.

6. **Kongkeaw C, et al. "Meta-analysis of randomized controlled trials on cognitive effects of Bacopa monnieri extract." J Ethnopharmacol. 2014;151(1):528-35.**
https://www.ncbi.nlm.nih.gov/pubmed/24252493

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ETHNOPHARMACOLOGICAL RELEVANCE:
Bacopa monnieri has a long history in Ayurvedic medicine for neurological and behavioral defects. To assess its efficacy in improving cognitive function.

MATERIALS AND METHODS:
MEDLINE, EMBASE, CINAHL, AMED, Cochrane Central of clinical trial, WHO registry, Thai Medical Index, Index Medicus Siriraj library and www.clinicaltrial.gov were searched from the inception date of each database to June 2013 using scientific and common synonyms of Bacopa monnieri, cognitive performance or memory. The reference lists of retrieved articles were also reviewed. Randomized, placebo controlled human intervention trials on chronic ≥ 12 weeks dosing of standardized extracts of Bacopa monnieri without any co-medication were included in this study. The methodological quality of studies was assessed using Cochrane's risk of bias assessment and Jadad's quality scales. The weighted mean difference and 95% confidence interval (95% CI) were performed using the random-effects model of the Dersimonian-Laird method.

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CONCLUSION:
This meta-analysis suggests that Bacopa monnieri has the potential to improve cognition, particularly speed of attention but only a large well designed 'head-to-head' trial against an existing medication will provide definitive data on its efficacy on healthy or dementia patients using a standardized preparation.

Ganoderma Lucidium

1. **Zhou Y, et al. "Neuroprotective effect of preadministration with Ganoderma lucidum spore on rat hippocampus." Exp Toxicol Pathol. 2012 Nov;64(7-8):673-80.**
   https://www.ncbi.nlm.nih.gov/pubmed/21242065

   ABSTRACT

   The aim of this study was to investigate if preadministration with Ganoderma lucidum spore (GLS) could (1) alleviate oxidative stress and mitochondrial dysfunction in rat hippocampus of intracerebroventricular (ICV) injection of streptozotocin (STZ), (2) protect neurons from apoptosis, and (3) improve cognitive dysfunction. Three groups of Sprague-Dawley rats were preadministrated with GLS at doses of 2.0, 4.0 and 8.0 g/kg, respectively, for 3 weeks before the ICV STZ injury. Thereafter the rats were operated with ICV STZ (1.5 mg/kg) bilaterally on days 1 and 3. The behavioral alterations, oxidative stress indexes, ATP, cytochrome oxidase (CytOx), and histopathology of hippocampal neurons were studied. The results showed that ICV STZ model rats exhibited a significant increase of malondialdehyde (MDA), a significant decrease of glutathione reductase (GR), reduced glutathione (GSH), ATP and CytOx, accompanied with marked impairments in spatial learning and memory, and severe damage of hippocampal neuron. In conclusion, preadministration with GLS at dose of 8.0 g/kg in ICV STZ rats significantly reversed these abnormalities. In conclusion, preadministration with GLS might protect hippocampus from oxidative impairment and energy metabolism disturbance of ICV STZ. This may also provide useful information for future research on the pathogenesis and prevention of Alzheimer's disease (AD).

Ashwagandha

1. **Choudhary D, et al. "Efficacy and Safety of Ashwagandha (Withania somnifera (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions." J Diet Suppl. 2017 Nov 2;14(6):599-612.**

   https://www.ncbi.nlm.nih.gov/pubmed/28471731

ABSTRACT

OBJECTIVES:
Cognitive decline is often associated with the aging process. Ashwagandha (Withania somnifera (L.) Dunal) has long been used in the traditional Ayurvedic system of medicine to enhance memory and improve cognition.

AIM:
This pilot study was designed to evaluate the efficacy and safety of ashwagandha (Withania somnifera (L.) Dunal) in improving memory and cognitive functioning in adults with mild cognitive impairment (MCI).

METHODS:
A prospective, randomized, double-blind, placebo-controlled study was conducted in 50 adults. Subjects were treated with either ashwagandha-root extract (300 mg twice daily) or placebo for eight weeks.

RESULTS:
After eight weeks of study, the ashwagandha treatment group demonstrated significant improvements compared with the placebo group in both immediate and general memory, as evidenced by Wechsler Memory Scale III subtest scores for logical memory I ($p = 0.007$), verbal paired associates I ($p = 0.042$), faces I ($p = 0.020$), family pictures I ($p = 0.006$), logical memory II ($p = 0.006$), verbal paired associates II ($p = 0.031$), faces II ($p = 0.014$), and family pictures II ($p = 0.006$). The treatment group also demonstrated significantly greater improvement in executive function, sustained attention, and information-processing speed as indicated by scores on the Eriksen Flanker task ($p = 0.002$), Wisconsin Card Sort test ($p = 0.014$), Trail-Making test part A ($p = 0.006$), and the Mackworth Clock test ($p = 0.009$).

CONCLUSIONS:
Ashwagandha may be effective in enhancing both immediate and general memory in people with MCI as well as improving executive function, attention, and information processing speed.

2. **Manchanda S, Kaur G. "Withania somnifera leaf alleviates cognitive dysfunction by enhancing hippocampal plasticity in high fat diet induced obesity model." BMC Complement Altern Med. 2017 Mar 3;17(1):136.**

https://www.ncbi.nlm.nih.gov/pubmed/28253924

ABSTRACT

BACKGROUND:
Sedentary lifestyle, psychological stress and labor saving devices in this current society often disrupts the energy gain and expenditure balance leading to obesity. High caloric diet is associated with the high prevalence of cognitive dysfunction and neuropsychiatric disorders in addition to cardiovascular and metabolic abnormalities. The present study was aimed to elucidate the potential beneficial effect of dry leaf powder of Withania somnifera (Ashwagandha) in preventing the cognitive decline associated with diet induced obesity.

METHODS:
Experiments were performed on four groups of young adult female rats: [Low fat diet (LFD) rats fed on regular low fat chow, High fat diet (HFD) rats on feed containing 30% fat by weight, Low fat diet extract (LFDE) rats given regular chow and dry leaf powder of Ashwagandha 1 mg/g of body weight (ASH) and high fat diet extract (HFDE) rats fed on diet containing high fat and dry leaf powder of ASH. All the rats were kept on their respective diet regimen for 12 weeks.

RESULTS:
ASH treated rats showed significant improvement in their working memory and locomotor coordination during behavioral studies as compared to HFD rats. At the molecular level, ASH treatment was observed to restore the levels of BDNF and its receptor TRKB as well as the expression of other synaptic regulators, which are highly implicated in synaptic plasticity. Further, ASH triggered the activation of PI3/AKT pathway of cell survival and plasticity by enhancing the levels of phosphorylated Akt-1 and immediate early genes viz. c-Jun and c-fos.

CONCLUSIONS:
ASH could be a key regulator in maintaining the synaptic plasticity in HFD induced obesity and can serve as a nootropic candidate against obesity induced cognitive impairments.

3. **Pingali U, et al. "Effect of standardized aqueous extract of Withania somnifera on tests of cognitive and psychomotor performance in healthy human participants." Pharmacognosy Res. 2014 Jan-Mar; 6(1): 12–18.**
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3897003/

ABSTRACT

Background:
Withania somnifera is an herbal medicine that has been known to possess memory-enhancing properties. The current study involved an assessment of cognitive and psychomotor effects of Withania somnifera extract in healthy human participants.

Materials and Methods:
In this prospective, double-blind, multi-dose, placebo-controlled, crossover study, 20 healthy male participants were randomized to receive 250 mg two capsules twice daily of an encapsulated dried aqueous extract of roots and leaves of Withania somnifera or a matching placebo for a period of 14 days. Cognitive and psychomotor performance was assessed pre-dose (day 1) and at 3 hrs post-dose on day 15 using a battery of computerized psychometric tests. After a washout period of 14 days, the subjects crossed-over to receive the other treatment for a further period of 14 days as per prior randomization schedule. Same battery of test procedures were performed to assess cognitive and psychomotor performance.

Results:
Significant improvements were observed in reaction times with simple reaction, choice discrimination, digit symbol substitution, digit vigilance, and card sorting tests with Withania somnifera extract compared to placebo. However, no effect can be seen with the finger tapping test.

Conclusion:
These results suggest that Withania somnifera extract can improve cognitive and psychomotor performance and may, therefore, be a valuable adjunct in the treatment of diseases associated with cognitive impairment.

4. **Choudhary D, et al. "Efficacy and Safety of Ashwagandha (Withania somnifera (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions." J Diet Suppl. 2017 Nov 2;14(6):599-612.**
https://www.ncbi.nlm.nih.gov/pubmed/28471731

ABSTRACT

OBJECTIVES:
Cognitive decline is often associated with the aging process. Ashwagandha (Withania somnifera (L.) Dunal) has long been used in the traditional Ayurvedic system of medicine to enhance memory and improve cognition.

AIM:
This pilot study was designed to evaluate the efficacy and safety of ashwagandha (Withania somnifera (L.) Dunal) in improving memory and cognitive functioning in adults with mild cognitive impairment (MCI).

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A prospective, randomized, double-blind, placebo-controlled study was conducted in 50 adults. Subjects were treated with either ashwagandha-root extract (300 mg twice daily) or placebo for eight weeks.

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After eight weeks of study, the ashwagandha treatment group demonstrated significant improvements compared with the placebo group in both immediate and general memory, as evidenced by Wechsler Memory Scale III subtest scores for logical memory I ($p = 0.007$), verbal paired associates I ($p = 0.042$), faces I ($p = 0.020$), family pictures I ($p = 0.006$), logical memory II ($p = 0.006$), verbal paired associates II ($p = 0.031$), faces II ($p = 0.014$), and family pictures II ($p = 0.006$). The treatment group also demonstrated significantly greater improvement in executive function, sustained attention, and information-processing speed as indicated by scores on the Eriksen Flanker task ($p = 0.002$), Wisconsin Card Sort test ($p = 0.014$), Trail-Making test part A ($p = 0.006$), and the Mackworth Clock test ($p = 0.009$).

CONCLUSIONS:
Ashwagandha may be effective in enhancing both immediate and general memory in people with MCI as well as improving executive function, attention, and information processing speed.

Tulsi/Holy Basil

1. **Sampath S, et al. "Holy basil (Ocimum sanctum Linn.) leaf extract enhances specific cognitive parameters in healthy adult volunteers: A placebo controlled study." Indian J Physiol Pharmacol. 2015 Jan-Mar;59(1):69-77.**
   https://www.ncbi.nlm.nih.gov/pubmed/26571987

ABSTRACT

INTRODUCTION:
Ocimum sanctum (OS), known as Holy basil, has been documented to possess neuroprotective, cognition-enhancing and stress relieving effects in animal models. However there is paucity of clinical studies to document these effects.

MATERIALS AND METHODS:
Effect of OS on parameters related to cognition and stress in humans was evaluated with administration of 300 milligram capsules of ethanolic leaf extracts of Ocimum sanctum (EtOS) or placebo per day, over 30 days.

RESULTS:
Intra-group comparison of Sternberg and Stroop test showed improvement in both the placebo and EtOS groups, however, the improvement stabilized after day 15 in the placebo group. Intergroup comparison revealed a significant improvement of the following cognitive parameters in the EtOS as compared to the placebo: reaction time (RT) and error rate (ER) of Sternberg test, RT of neutral task of Stroop, RT and ER of interference task of Stroop. The intra-group comparison of P300 latency, salivary cortisol, and State-Trait Anxiety Inventory showed improvement over time in the EtOS group alone, though the inter-group difference was significant in the P300 latency alone. There were no changes in heart rate (HR), AHR, or galvanic skin response (GSR) or AGSR.

CONCLUSION:
Ocimum sanctum leaf extract seems to have potential cognition-enhancing properties in humans.
PMID: 26571987

2. **Giridharan VV, et al. "Ocimum sanctum Linn. leaf extracts inhibit acetylcholinesterase and improve cognition in rats with experimentally induced dementia." J Med Food. 2011 Sep;14(9):912-9.**
https://www.ncbi.nlm.nih.gov/pubmed/21812651

ABSTRACT

Cognitive disorders such as dementia, attention deficits, and Alzheimer's disease (AD) have been well investigated. However, effective interventions for the promotion and progression of AD are unavailable to date. The present work was undertaken to investigate the effects of the aqueous (300 and 500 mg/kg) and alcoholic (300 and 500 mg/kg) extracts of Ocimum sanctum Linn. leaves as an antidementic and anticholinesterase agent and also as an immunostimulant in rats. Maximal electroshock, atropine, and cyclosporine were used to induce dementia. The passive avoidance task was used for assessing memory. Acetylcholinesterase (AChE) activity was estimated in different parts of the brain, and immune status was studied using dinitrochlorobenzene (DNCB) skin sensitivity tests. In all the three models both aqueous and alcoholic O. sanctum extracts decreased the time taken to reach the shock-free zone and the number of mistakes and significantly decreased the AChE activity in rats. O. sanctum treatment significantly increased the induration in the DNCB skin test. Therefore, O. sanctum was shown to be useful for the management of experimentally induced cognitive dysfunctions in rats.

3. **Jamshidi N, Cohen MM. "The Clinical Efficacy and Safety of Tulsi in Humans: A Systematic Review of the Literature." Evid Based Complement Alternat Med. 2017;2017:9217567.**
https://www.ncbi.nlm.nih.gov/pubmed/28400848

ABSTRACT

Tulsi, also known as holy basil, is indigenous to the Indian continent and highly revered for its medicinal uses within the Ayurvedic and Siddha medical systems. Many in vitro, animal and human studies attest to tulsi having multiple therapeutic actions including adaptogenic, antimicrobial, anti-inflammatory, cardioprotective, and immunomodulatory effects, yet to date there are no systematic reviews of human research on tulsi's clinical efficacy and safety. We conducted a comprehensive literature review of human studies that reported on a clinical outcome after ingestion of tulsi. We searched for studies published in books, theses, conference proceedings, and electronic databases including Cochrane Library, Google Scholar, Embase, Medline, PubMed, Science Direct, and Indian Medical databases. A total of 24 studies were identified that reported therapeutic effects on metabolic disorders, cardiovascular disease, immunity, and neurocognition. All studies reported favourable clinical outcomes with no studies reporting any significant adverse events. The reviewed studies reinforce traditional uses and suggest tulsi is an effective treatment for lifestyle-related chronic diseases including diabetes, metabolic syndrome, and psychological stress. Further studies are required to explore mechanisms of action, clarify the dosage and dose form, and determine the populations most likely to benefit from tulsi's therapeutic effects.

NEUROPLASTICITY

Adaptogens

1. **Choudhary D, et al. "Efficacy and Safety of Ashwagandha (Withania somnifera (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions." J Diet Suppl. 2017 Nov 2;14(6):599-612.**
https://www.ncbi.nlm.nih.gov/pubmed/28471731

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OBJECTIVES:
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AIM:
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METHODS:
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RESULTS:
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Ashwagandha may be effective in enhancing both immediate and general memory in people with MCI as well as improving executive function, attention, and information processing speed.

Ashwagandha

1. **Tohda C, et al. "Dendrite extension by methanol extract of Ashwagandha (roots of Withania somnifera) in SK-N-SH cells." Neuroreport. 2000 Jun 26;11(9):1981-5.**
   https://www.ncbi.nlm.nih.gov/pubmed/10884056

ABSTRACT

Extension of dendrites and axons in neurons may compensate for and repair damaged neuronal circuits in the dementia brain. Our aim in the present study was to explore drugs activating neurite outgrowth and regenerating the neuronal network. We found that the methanol extract of Ashwagandha (roots of Withania somnifera; 5 microg/ml) significantly increased the percentage of cells with neurites in human neuroblastoma SK-N-SH cells. The effect of the extract was dose- and time-dependent mRNA levels of the dendritic markers MAP2 and PSD-95 by RT-PCR were found to be markedly increased by treatment with the extract, whereas those of the axonal marker Tau were not. Immunocytochemistry demonstrated the specific expression of MAP2 in neurites extended by the extract. These results suggest that the methanol extract of Ashwagandha promotes the formation of dendrites.

Bacopa

1. **Konar A, et al. "Bacopa monniera (CDRI-08) Upregulates the Expression of Neuronal and Glial Plasticity Markers in the Brain of Scopolamine Induced Amnesic Mice." Evid Based Complement Alternat Med. 2015;2015:837012.**
   https://www.ncbi.nlm.nih.gov/pubmed/26413129

ABSTRACT

Preclinical studies on animal models have discerned the antiamnesic and memory-enhancing potential of Bacopa monniera (Brahmi) crude extract and standardized extracts. These studies primarily focus on behavioral consequences. However, lack of information on molecular underpinnings has limited the clinical trials of the potent herb in human subjects. In recent years, researchers highlight plasticity markers as molecular correlates of amnesia and being crucial to design therapeutic targets. In the present report, we have investigated the effect of a special extract of B. monniera (CDRI-08) on the expression of key neuronal (BDNF and Arc) and glial (GFAP) plasticity markers in the cerebrum of scopolamine induced amnesic mice. Pre- and postadministration of CDRI-08 ameliorated amnesic effect of scopolamine by decreasing acetyl cholinesterase activity and drastically upregulating the mRNA and protein expression of BDNF, Arc, and GFAP in mouse cerebrum. Interestingly, the plant extract per se elevated BDNF and Arc expression as compared to control but GFAP was unaltered. In conclusion, our findings provide the first molecular evidence for antiamnesic potential of CDRI-08 via enhancement of both neuronal and glial plasticity markers. Further investigations on detailed molecular pathways would encourage therapeutic application of the extract in memory disorders.

2. **Vollala VR, eat al. "Enhanced dendritic arborization of amygdala neurons during growth spurt periods in rats orally intubated with Bacopa monniera extract." Anat Sci Int. 2011 Dec;86(4):179-88**
https://www.ncbi.nlm.nih.gov/pubmed/21409525?dopt=Abstract.

ABSTRACT

Bacopa monniera (BM)--a small, creeping herb-has been classified under Medhya rasayana (medicinal plants rejuvenating intellect and memory) in the ancient Indian system of medicine, viz., Ayurveda. Therefore, this plant has been investigated in several laboratories in India for its neuropharmacological effects. Here, we investigated the role of BM standardized extract on the dendritic morphology of amygdaloid neurons-one of the regions concerned with learning and memory. The rat pups (10 days old) were fed standardized extract of BM (20, 40 and 80 mg/kg) for 2, 4 and 6 weeks. After the treatment period, the rats were killed by decapitation, the brains were removed and amygdaloid neurons were impregnated with silver nitrate (Golgi staining). Amygdaloid neurons were traced using camera lucida. Dendritic branching points (a measure of dendritic arborization) and dendritic intersections (a measure of dendritic length) were quantified. These data were compared with control rats. The results showed a significant increase in dendritic length and dendritic branching points along the length of dendrites of the amygdaloid neurons of rats treated with all doses of BM for longer periods of time (i.e., 4 and 6 weeks). We conclude that constituents present in BM extract have neuronal dendritic growth stimulating properties.

3. **Vollala VR, et al . "Enhanced dendritic arborization of hippocampal CA3 neurons by Bacopa monniera extract treatment in adult rats." Rom J Morphol Embryol. 2011;52(3):879-86.**
https://www.ncbi.nlm.nih.gov/pubmed/21892534

ABSTRACT

OBJECTIVE:
Bacopa monniera (BM), a traditional Ayurvedic medicine has been used in treatment for a number of disorders, particularly those involving anxiety, intellect and poor memory. The current study examined the effects of standardized extract of Bacopa monniera on the dendritic morphology in adult rats of hippocampal CA3 neurons, one of the regions concerned with learning and memory.

MATERIALS AND METHODS:
Adult Wistar (2.5-month-old) rats were designated into 2-, 4- and 6-week treatment groups. Rats in each of these groups were divided into 20 mg/kg, 40 mg/kg and 80 mg/kg dose groups (n=8 for each dose). These rats along with age-matched control rats were then subjected to spatial learning (T-maze) and passive avoidance tests. Subsequent to the T-maze and passive avoidance tests, these rats were killed by decapitation, brains were removed and hippocampal neurons were impregnated with silver nitrate (Golgi staining). Hippocampal CA3 neurons were traced using camera lucida. Dendritic branching points (a measure of dendritic arborization) and dendritic intersections (a measure of dendritic length) were quantified. These data were compared with control rats.

RESULTS AND CONCLUSIONS:
The results showed improvement in spatial learning performance and enhanced memory retention in rats treated with BM extract. There was a significant increase in the dendritic intersections and dendritic branching points along the length of both apical and basal dendrites in rats treated with BM extract for four and six weeks. However, the rats treated with BM extract for two weeks did not show any significant change in hippocampal CA3 neuronal dendritic arborization. We conclude that constituents present in BM extract have neuronal dendritic growth stimulating properties.

Cordyceps Sinensis

1. **Liu Z, et al. "Protective effect of extract of Cordyceps sinensis in middle cerebral artery occlusion-induced focal cerebral ischemia in rats." Behav Brain Funct. 2010 Oct 19;6:61.**
https://www.ncbi.nlm.nih.gov/pubmed/20955613

ABSTRACT

BACKGROUND:
Ischemic hypoxic brain injury often causes irreversible brain damage. The lack of effective and widely applicable pharmacological treatments for ischemic stroke patients may explain a growing interest in traditional medicines. From the point of view of "self-medication" or "preventive medicine," Cordyceps sinensis was used in the prevention of cerebral ischemia in this paper.

METHODS:
The right middle cerebral artery occlusion model was used in the study. The effects of Cordyceps sinensis (Caterpillar fungus) extract on mortality rate, neurobehavior, grip strength, lactate dehydrogenase, glutathione content, Lipid Peroxidation, glutathione peroxidase activity, glutathione reductase activity, catalase activity, Na+K+ATPase activity and glutathione S transferase activity in a rat model were studied respectively.

RESULTS:
Cordyceps sinensis extract significantly improved the outcome in rats after cerebral ischemia and reperfusion in terms of neurobehavioral function. At the same time, supplementation of Cordyceps sinensis extract significantly boosted the defense mechanism against cerebral ischemia by increasing antioxidants activity related to lesion pathogenesis. Restoration of the antioxidant homeostasis in the brain after reperfusion may have helped the brain recover from ischemic injury.

CONCLUSIONS:
These experimental results suggest that complement Cordyceps sinensis extract is protective after cerebral ischemia in specific way. The administration of Cordyceps sinensis extract significantly reduced focal cerebral ischemic/reperfusion injury. The defense mechanism against cerebral ischemia was by increasing antioxidants activity related to lesion pathogenesis.

Neurogenesis

Ashwagandha

1. **Kuboyama T, et al. "Neuritic regeneration and synaptic reconstruction induced by withanolide A." Br J Pharmacol. 2005 Apr;144(7):961-71.**
   https://www.ncbi.nlm.nih.gov/pubmed/15711595

   ABSTRACT

   We investigated whether withanolide A (WL-A), isolated from the Indian herbal drug Ashwagandha (root of Withania somnifera), could regenerate neurites and reconstruct synapses in severely damaged neurons. We also investigated the effect of WL-A on memory-deficient mice showing neuronal atrophy and synaptic loss in the brain. Axons, dendrites, presynapses, and postsynapses were visualized by immunostaining for phosphorylated neurofilament-H (NF-H), microtubule-associated protein 2 (MAP2), synaptophysin, and postsynaptic density-95 (PSD-95), respectively. Treatment with A beta(25-35) (10 microM) induced axonal and dendritic atrophy, and pre- and postsynaptic loss in cultured rat cortical neurons. Subsequent treatment with WL-A (1 microM) induced significant regeneration of both axons and dendrites, in addition to the reconstruction of pre- and postsynapses in the neurons. WL-A (10 micromol kg(-1) day(-1), for 13 days, p.o.) recovered A beta(25-35)-induced memory deficit in mice. At that time, the decline of axons, dendrites, and synapses in the cerebral cortex and hippocampus was almost recovered. WL-A is therefore an important candidate for the therapeutic treatment of neurodegenerative diseases, as it is able to reconstruct neuronal networks.

Bacopa

1. **Kumar S, Mondal AC. "Neuroprotective, Neurotrophic and Anti-oxidative Role of Bacopa monnieri on CUS Induced Model of Depression in Rat." Neurochem Res. 2016 Nov;41(11):3083-3094.**
   https://www.ncbi.nlm.nih.gov/pubmed/27506204

   ABSTRACT

   Major depression is a life threatening neuropsychiatric disorder that produces mental illness and major cause of morbidity. The present study was conducted to evaluate the neuroprotective, neurotrophic and antioxidant potential of Bacopa monnieri extract (BME) on chronic unpredictable stress (CUS) induced behavioral depression in rats. Behavioral tests were carried out for investigation of antidepressant like effects of BME, and potential mechanism was assessed by determining neurotrophin level and hippocampal neurogenesis. Depressive-like behavior was assessed by shuttle-box escape test, forced swim test and tail suspension test. Effect of BME on hypothalamic-pituitary-adrenal (HPA) axis was evaluated by measuring the plasma level of adrenocorticotropic hormone (ACTH) and corticosterone. The expression of brain derived neurotrophic factor (BDNF), neuronal marker doublecortin (DCX) in the hippocampus were

measured and hippocampal neurogenesis was investigated by 5-bromo-2-deoxyuridine/neuronal nuclei (BrdU/NeuN). In addition, effects of BME on oxidative stress markers were also measured in the hippocampus of CUS exposed rats. The results indicated that BME significantly able to attenuate the depressive-like behaviors, normalized the levels of ACTH, corticosterone, and up-regulate the expression of BDNF, DCX and BrdU/NeuN in CUS induced rats compared to BME treated rats. It is also found that BME significantly increased the activity of antioxidant enzymes on CUS induced rats. These findings revealed that BME exerted neuroprotective effects possibly by promoting hippocampal neurogenesis with elevation of BDNF level and antioxidant defense against oxidative stress.

2. **Banerjee R, et al. "Chronic Administration of Bacopa Monniera Increases BDNF Protein and mRNA Expressions: A Study in Chronic Unpredictable Stress Induced Animal Model of Depression." Psychiatry Investig. 2014 Jul; 11(3): 297–306.**
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4124189/

ABSTRACT

Objective

The present study aimed to investigate whether graded doses of Bacopa Monniera (BM) extract could produce antidepressant-like effects in chronic unpredictable stress (CUS) induced depression in rats and its possible mechanism(s).

Methods

Rats were subjected to an experimental setting of CUS. The effect of BM extract treatment in CUS-induced depression was examined using behavioral tests including the sucrose consumption, open field test and shuttle box escape test. The mechanism underlying the antidepressant-like action of BM extract was examined by measuring brain-derived neurotrophic factor (BDNF) protein and mRNA expression in brain tissues of CUS-exposed rats.

Results

Exposure to CUS for 4 weeks caused depression-like behavior in rats, as indicated by significant decreases in sucrose consumption, locomotor activity and escape latency. In addition, it was found that BDNF protein and mRNA levels in the hippocampus and frontal cortex were lower in CUS-treated rats, as compared to controls. Daily administration of the graded doses of BM extract during the 4-week period of CUS significantly suppressed behavioral changes and attenuated the CUS-induced decrease in BDNF protein and mRNA levels in the hippocampus and frontal cortex.

Conclusion

The results suggest that BM extract alleviates depression induced by CUS. Present study also confirms that 80-120 mg/kg doses of BM extract have significantly higher antidepressant-like activity.

Centellia asiatica

1. **Kashmira J, Et al. "Pharmacological Review on Centella asiatica: A Potential Herbal Cure-all." Indian J Pharm Sci. 2010 Sep-Oct; 72(5): 546–556.**
   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3924982/

ABSTRACT

In recent times, focus on plant research has increased all over the world. Centella asiatica is an important medicinal herb that is widely used in the orient and is becoming popular in the West. Triterpenoid, saponins, the primary constituents of Centella asiatica are manly believed to be responsible for its wide therapeutic actions. Apart from wound healing, the herb is recommended for the treatment of various skin conditions such as leprosy, lupus, varicose ulcers, eczema, psoriasis, diarrhoea, fever, amenorrhea, diseases of the female genitourinary tract and also for relieving anxiety and improving cognition. The present review attempts to provide comprehensive information on pharmacology, mechanisms of action, various preclinical and clinical studies, safety precautions and current research prospects of the herb. At the same time, studies to evaluate the likelihood of interactions with drugs and herbs on simultaneous use, which is imperative for optimal and safe utilization of the herb, are discussed.

Ganoderma Lucidium

1. **Vikineswary Sabaratnam et al. "Neuronal Health – Can Culinary and Medicinal Mushrooms Help?" J Tradit Complement Med. 2013 Jan-Mar; 3(1): 62–68.**
   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3924982/

ABSTRACT

Hericium erinaceus a culinary and medicinal mushroom is a well established candidate for brain and nerve health. Ganoderma lucidum, Grifola frondosa and Sarcodon scabrosus have been reported to have neurite outgrowth and neuronal health benefits. The number of mushrooms, however, studied for neurohealth activity are few compared to the more than 2 000 species of edible and / or medicinal mushrooms identified. In the on-going search for other potent culinary and / or medicinal mushrooms, indigenous mushrooms used in traditional medicines such as Lignosus rhinocerotis and Ganoderma neo-japonicum are also being investigated. Further, the edible mushroom, Pleurotus giganteus can be a potential candidate, too. Can these edible and medicinal mushrooms be tapped to tackle the health concerns of the aging population which is projected to be more than 80-90 million of people age 65 and above in 2050 who may be affected by age-related neurodegenerative disorders. Scientific validation is needed if these mushrooms are to be considered and this can be achieved by understanding the molecular and biochemical mechanisms involved in the stimulation of neurite outgrowth. Though it is difficult to extrapolate the in vitro studies to what may happen in the human brain, studies have shown that there can be improvement in cognitive abilities of the aged if the mushroom is incorporated in their daily diets.

Maple Syrup

1. **"Real maple syrup shows promise in protecting brain health."**
   http://www.news-medical.net/news/20160314/Real-maple-syrup-shows-promise-in-protecting-brain-health.aspx

   EXCERPT

   As part of a two-day symposium at the annual meeting of the American Chemical Society, a group of international scientists shared promising results of 24 studies exploring the beneficial effects of natural products on the prevention of neurodegenerative diseases, particularly Alzheimer's disease. For the first time at this symposium, real maple syrup was included among the healthful, functional foods that show promise in protecting brain cells against the kind of damage found in Alzheimer's disease.

   One study presented by Dr. Donald Weaver, from the Krembil Research Institute of the University of Toronto, found that an extract of maple syrup may help prevent the misfolding and clumping of two types of proteins found in brain cells - beta amyloid and tau peptide. When cellular proteins fold improperly and clump together, they accumulate and form the plaque that is involved in the pathogenesis of Alzheimer's and other brain diseases.

   The other research presented at the symposium showed that a pure maple syrup extract prevented the fibrillation (tangling) of beta amyloid proteins and exerted neuroprotective effects in rodent's microglial brain cells. Scientists have found that a decrease in microglial brain cell function is associated with Alzheimer's disease and other neurological problems. The maple syrup extract also prolonged the lifespan of an Alzheimer's roundworm model in vivo. The study was conducted out of the University of Rhode Island, in collaboration with researchers at Texas State University, and was led by Dr. Navindra P. Seeram, the symposium's organizer.

About Sun Horse

The Sun Horse Energy story begins 40 years ago in Jalisco state, Mexico.

Or maybe it starts over 100 years ago in Hungary. Or maybe it begins before time itself?

Depends on how you look at it….

Let's start with Mexico….

The reason Sun Horse Energy has helped so many people is because of a nasty scorpion sting, which took place in the state of Jalisco, in the mid-1970s.

Dan Moriarty, Sun Horse Energy founder, was stung on the left shoulder while fast asleep by a venomous scorpion 'Centruroides Sculpturatus'. He was traveling in Mexico at the time.

He awoke instantly in considerable pain, and within minutes was having extreme difficulty breathing, along with uncontrollable salivation and tunnel vision.

By chance, a local fisherman was in his camp and immediately recognized the gravity of the situation. He knew of a Huichol native living nearby and went to get him on foot.

After a short while, the Huichol native arrived in the camp with a root that he had picked in the jungle (his "medicine chest"). He made a tea from the root, and instructed Dan to drink it while it was very hot.

Upon drinking the tea, Dan was able to breathe freely again within minutes.

"I have no doubt that this man and his plant remedy (guaco) saved my life," Dan swears to this day on his life….

Dan decided right then and there to devote all his energies into learning about herbs from his mother a Hungarian herbalist specializing in Woman's health.

Later in life Daniel chose the Adaptogenic class of herbs to study because of their broad spectrum of healing properties while being non-toxic to the organs. He was inspired to progress his studies based on that threatening incident which happened in Jalisco Mexico that really opened his eyes to the healing nature of plants for the people.

The amazing ability of adaptogenic herbs to help humans adapt to physical, emotional, and environmental stressors has been going on since time immemorial. They have been used by traditional Chinese medicine healers and Ayurvedic practitioners of ancient India, as well as in Tibet and dozens of other traditional societies for at least a few thousand years. And they most likely were used long before these cultures started using them for healing purposes.

Dan's grandmother passed on all her herbal knowledge to Dan's mom, who in turn passed it on to Dan. Dan has been immersed in herbs, especially adaptogenic herbs, for over 40 years.

Saddened and frustrated by the prevalence of "false, unhealthy energy drinks and supplements" on the market, Dan decided to make the safe, effective and non-toxic power of adaptogenic herbs available to everybody in an easy to use, readily-accessible format. The formula for Sun Horse Energy took Dan 8 years to perfect! The stress-regulating, stamina- and focus-boosting formula known as Sun Horse was launched in 2010.

And as of 2016, Sun Horse Energy is the first adaptogenic herbal formula to be available in a liposomal encapsulation. This means that the power of the adaptogenic herbs found in Sun Horse goes directly to your cells and bypasses the lengthy processes of the digestive system.

So, the Sun Horse Energy Story is roughly a decade old. Or 40 years. Or a century. Or … thousands of years. No matter how long the story is, the happy ending of Sun Horse Energy is this:

You will always have stress. But adaptogens are literally here to rescue us. You will not only survive by taking Sun Horse Energy, you will THRIVE! The adaptogenic herbs in our formulas can help you tackle all that our hectic modern society throws your way … and make it seem like it ain't no big thing!