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FILE: ▪Sage (*Salvia officinalis*)
▪Anxiety
▪Cholinesterase inhibitors

HC 050561-305

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RE: Sage Leaf Extract Reduces Anxiety in Clinical Trial

Kennedy DO, Pace S, Haskell C, Okello EJ, Milne A, Scholey AB. Effects of cholinesterase inhibiting sage (*Salvia officinalis*) on mood, anxiety and performance on a psychological stressor battery. *Neuropsychopharmacology*. April 2006;31(4):845-852.

Garden sage (*Salvia officinalis*) has been shown to inhibit cholinesterase enzymes, enzymes that break down acetylcholine (Ach), a chief neurotransmitter. Compounds that inhibit acetylcholinesterase (AChE) may improve mood in some people by helping to maintain optimal levels of Ach and thus brain activity. Lemon balm (*Melissa officinalis*) also has cholinergic properties and has been shown to significantly reduce the negative mood consequences of a psychological stressor battery.[1,2] The authors of this trial used the lemon balm study as a model to evaluate the anxiety and mood modulating capabilities of sage.

Thirty healthy volunteers (mean age: 24 years) participated in this randomized, double-blind, placebo-controlled, crossover study conducted at the University of Northumbria, Newcastle upon Tyne, UK. Participants received placebo, 300, or 600 mg of dried leaf sage extract (MedicHerb UK Ltd, Buckinghamshire, UK) in a counterbalance design with a 7-day washout period between treatments.

Sage leaf and 3 ml of 80% ethanol were placed in a glass container. The mixture was ultrasonically extracted for 10 minutes. The extract was then decanted and filtered. The procedure was repeated twice more. A rotary evaporator was used for 15 minutes to evaporate the solvent, and the flask was weighed to determine the extract's dried weight. The supernatant (clear liquid) was reconstituted with 53% ethanol and assayed.

Subjects underwent a battery of tests and ingested the day's treatment. Then at 1 hour and 4 hour post-dose the participants completed the battery of tests again. The tests included: (1) the Defined Intensity Stressor Simulation (DISS) computerized battery, which rates negative mood, arousal, and stress-related physiological responses; (2) the State-Trait

Anxiety Inventory (STAI), which measures fluctuating levels of anxiety, and (3) the Bond-Lader visual analogue mood scales, which measures the mood effects of anxiolytics. The dried sage leaf extract was also tested in vitro to assess its AChE activity.

In vitro, sage ethanol extract dose-dependently inhibited AChE and butyrlcholinesterase (BuChE), another similar enzyme. The extract more selectively inhibited BuChE than AChE. BuChE is less specific and is found in plasma and liver, while AchE is found in neuronal tissue and RBS. The authors point out that the activity of sage may also involve other properties yet to be discovered.

In the absence of a stressor, both doses of sage had a significant improvement on ratings of mood ($P < 0.05$). The lower dose reduced anxiety, and the higher dose increased alertness, calmness, and contentedness ($P < 0.05$). Both doses of sage modulated the stress-inducing effects of the DISS battery, but the lower dose was associated with increased anxiety and decreased alertness. The stressful situation eliminated the stress reducing capability of the low dose of sage. To this end, the authors believe that the lower dose falls below the treatment threshold required to beneficially modulate mood and performance. They believe the higher dose is within the beneficial therapeutic window.

The dose findings in this study are the opposite of that reported in other studies that used the essential oil or ethanolic extracts. In those studies, the lower dose was within the therapeutic window and the higher dose was not. The authors point out that these divergent findings underscore the lack of current understanding regarding the consequences of different extraction techniques. The authors conclude that a single 600 mg dose of the dry leaf extract preparation can improve mood and cognitive performance in healthy young individuals.

MedicHerb UK markets this sage extract for women who are menopausal and post-menopausal.

—Heather S. Oliff, PhD

References

[1]Kennedy DO, Scholey AB, Tildesley N, et al. Modulation of mood and cognitive performance following acute administration of Melissa officinalis (lemon balm). *Pharmacol Biochem Behav*. 2002;72(4):953-64.

[2]Kennedy DO, Wake G, Savelev S, et al. Modulation of mood and cognitive performance following acute administration of single doses of Melissa officinalis (Lemon balm) with human CNS nicotinic and muscarinic receptor-binding properties. *Neuropsychopharmacology*. 2003;28(10):1871-1881.

The American Botanical Council has chosen not to reprint the original article.