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File: ■ Bacopa (*Bacopa monnieri*)
■ Cognition
■ Meta-analysis

HC 011456-496

Date: May 15, 2014

RE: Meta-analysis of the Cognitive Effects of Bacopa

Kongkeaw C, Dilokthornsakul P, Thanarangsarit P, Limpeanchob N, Scholfield CN. Meta-analysis of randomized controlled trials on cognitive effects of *Bacopa monnieri* extract. *J Ethnopharmacol*. 2014;151(1):528-535.

For more than 3000 years, bacopa (*Bacopa monnieri*) has been used in Ayurvedic medicine to improve memory and brain function, and promote longevity. Many clinical studies have been conducted that evaluate the effect of bacopa on cognitive function; however, according to the authors, there are no published meta-analyses. Hence, the purpose of this study was to conduct a meta-analysis to evaluate the efficacy of bacopa as a treatment of cognitive performance.

The following databases were searched from their inception through June 2013: MEDLINE, EMBASE, CINAHL, AMED, Cochrane Central of Clinical Trial, WHO Registry, Thai Medical Index, Index Medicus Siriraj Library, and www.clinicaltrial.gov. The following search terms were used in combination with cognitive performance or memory: *Bacopa monnieri*, Bacopa monniera, Herpestris monnieri, Herpestrismonniera, Monieraeuneifolia, Lysimachia monnieri, Brahmi, coastal water hyssop, water hyssop, thyme leafed gratiola, thyme leaved graticula, and thyme leafed graticula. In addition, reference lists were hand-searched. Included studies were randomized, placebo-controlled studies, used neuropsychological tests for cognitive performance, had a treatment duration of ≥ 12 weeks, and subjects received a standardized extract of bacopa whose basoside composition was measured or discoverable. Studies that evaluated bacopa in combination with other treatments were excluded. Data were extracted from each article. The methodological quality of each study was evaluated with the Jadad scale (low-quality studies scored < 3) and Cochrane's risk of bias tool for assessing internal validity.

A total of 289 studies were located, but only 9 met the inclusion/exclusion criteria. Of these 9 studies, 7 were conducted in healthy subjects, and 2 were conducted in patients with memory impairment. The most common dose evaluated was 300 mg/day (n = 6 studies), 1 study evaluated 250 mg/day, 2 studies evaluated 450 mg/day, and 1 study evaluated 600 mg/day (1 study evaluated 2 doses). Treatment duration was 12 weeks (n = 6), 13 weeks (n = 1), or 18 weeks (n = 2). The Jadad scores for the 9 studies were 3 (n=2 studies), 4 (n=4 studies), and 5 (n=3 studies), which indicates that the included studies were well designed. Assessment using the Cochrane's tool indicated risk for bias was low or unclear in most

areas; however, 2 studies were at high risk for selective outcome reporting, and 1 study was at high risk for "other sources of bias."

Combining data from all 9 studies, 231 subjects received bacopa, and 206 subjects received placebo. The outcome measures for the meta-analysis were the effects of bacopa on memory function and the effects of bacopa on attention. Six studies collected data on memory function (n = 326 subjects) by evaluating the following parameters: picture recognition, numeric working memory, word recognition, spatial working memory, and auditory verbal learning test. There was high heterogeneity in the results, and on most outcome measures significant correlations between bacopa consumption and improved memory function could not be identified. The authors report that time taken to complete a task was decreased in subjects taking bacopa compared with placebo; however, this conclusion was drawn from only 1 study that examined this endpoint.

Seven studies of those included evaluated attention (n = 303 subjects). While the meta-analysis revealed no effect of bacopa on choice reaction time, sub-group analysis of only studies evaluating 300 mg/day bacopa showed a decreased choice reaction time of 10.6 ms (comparative effects of 450 and 600 mg/day doses not reported).

Eight studies reported no serious adverse events (AEs). AEs commonly reported in the bacopa group were gastrointestinal related (increased stool frequency, nausea, abdominal cramps, and diarrhea). Other AEs reported in subjects taking bacopa were flu-like symptoms, dry mouth, and decrease in the number of dreams.

The authors conclude that bacopa may be beneficial in improving attention. The heterogeneity in the results of the memory assessments could be attributed to the variety of doses and volunteer characteristics (healthy vs. memory impaired). The authors also note that there are many other measures of memory that the included studies did not evaluate. The data from this meta-analysis cannot be generalized to patients with cognitive impairment since the included population was mostly healthy subjects. More well-designed randomized, placebo-controlled studies of bacopa in patients with memory impairment are needed. Perhaps a meta-analysis might be more appropriate when more studies using similar designs are available.

—Heather S. Oliff, PhD

Peer Review Comments:
The authors interestingly indicate that "because attention was improved, the extract might be an appropriate treatment for young patients having attention deficit hyperactivity disorder (ADHD)."

Also intriguing is that the standard tests, particularly for those used in patients with mild cognitive impairment (MCI), have low sensitivity. The current treatments using licensed drugs such as anticholinesterases, including donepezil, generally have little effect on MCI, while the improvements in more advanced disease are highly significant, but their clinical impacts are more questionable. Given that, the effects of bacopa reported here on MCI and non-impaired subjects, although small in absolute terms, suggest that bacopa could be clinically useful.

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