



Meta-analysis of randomized controlled trials on cognitive effects of *Bacopa monnieri* extract

Chuenjid Kongkeaw^{a,b,c,*}, Piyameth Dilokthornsakul^{a,b,d}, Phurit Thanarangsarit^a, Nanteetip Limpeanchob^a, C. Norman Scholfield^{a,c}

^a Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok 65000, Thailand

^b Center of Pharmaceutical Outcomes Research, Faculty of Pharmaceutical Sciences, Naresuan University, Thailand

^c Center of Excellence for Environmental Health & Toxicology, Naresuan University, Thailand

^d Center for Pharmacoepidemiology and Pharmacoeconomic Research, College of Pharmacy, University of Illinois at Chicago, Chicago, IL, USA

ARTICLE INFO

Article history:

Received 4 August 2013

Received in revised form

1 November 2013

Accepted 6 November 2013

Available online 16 November 2013

Keywords:

Bacopa monnieri

Brahmi

Cognition

Speed of attention

Nootropic

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.clinicaltrials.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.

© 2013 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

The global shift toward an aging population has brought with it an increase in prevalence of cognitive decline ranging from mild impairment to major dementias (e.g. vascular dementia, Alzheimer's disease) (Forman et al., 2004; Gauthier et al., 2006). Domains of cognition include motor functioning, attention, language, memory, executive control, vision, emotion, sensory functions and consciousness. Mild cognitive impairment is seen in 10–20% of individuals aged ≥ 65 years

Abbreviations: AVLT, auditory verbal learning test; ADHD, attention deficit hyperactivity disorder; MCI, mild cognitive impairment; MMSE, mini mental state examination

* Corresponding author at: Naresuan University, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Phitsanulok 65000, Thailand. Tel.: +66 55 961825; fax: +66 55 963731.

E-mail addresses: chuenjidk@nu.ac.th, chuenjidk@googlemail.com (C. Kongkeaw).

with the reported conversion rates to dementias ranging from 1% to 25% (Bischof et al., 2002; Manly et al., 2008). The World Health Organization estimated that the number of patients suffering from dementias will be approximately 44 million globally by 2030 (World Health Organization, 2006). The burdens of dementias are enormous with 11% of all years lived with this disability (Lin and Neumann, 2012; World Health Organization, 2006). Recent estimates for total cost per dementia patient in Europe for the year 2010 were €16,584 (\$21,538), resulting in a total cost of €105,163 million (\$136,575 million) in the region (Lin and Neumann, 2012). Corresponding excess cost of conversion or progression from mild cognitive impairment to dementias was estimated to be €4389 (\$5700) (Wimo and Winblad, 2003).

Acetylcholinesterase inhibitors (AChEIs) continue to be the first-line nootropics for both Alzheimer's disease and vascular dementia. Although these medications have been shown to be effective for mild to moderate dementia patients, the overall outcomes are often unsatisfactory (May et al., 2009) because of various adverse drug effects and they do not modify the disease

progress in the long term. Thus, when patients discontinue the medication, their symptoms return.

Bacopa monnieri (L.) Wettst. (Synonyms: *Bacopa monniera* (L.) Pennell yes, *Herpestis monniera* L. Kunth; common names: Brahmi, bacopa, water hyssop) is a small herb with oblong leaves and light purple flowers and belongs to the family Scrophulariaceae (Rajani, 2008; Russo and Borrelli, 2005). This plant has been used for more than 3000 years as Indian Ayurvedic medicines for improving memory, increasing brain function, or promoting longevity (Abascal and Yarnell, 2011; Calabrese et al., 2008; Morgan and Stevens, 2010). This medicinal plant has protective effects against β -amyloid toxicity (Limpeanchob et al., 2008) and have beneficial effects on cognitive performance (Abascal and Yarnell, 2011; Calabrese et al., 2008; Morgan and Stevens, 2010; Uabundit et al., 2010).

Complementary and alternative treatments including herbal medicines have increasingly been alternative choices of therapy (May et al., 2009) but evidence about their efficacy as medicines is often weak. A recent systematic review (Neale et al., 2013) showed that *Bacopa monnieri* enhanced memory free recall, thus might be used as a memory enhancer. Similar efficacies were obtained from publications on Panax ginseng and modafinil in healthy, mostly young adults. However, the review did not perform meta-analysis to quantitatively summarize the evidence including those papers showing no effects and did not include the Allied and Complementary Medicine (AMED) database. We have conducted such a formal meta-analysis which aims to examine the efficacy of *Bacopa monnieri* as a treatment for cognitive performance.

2. Methods

2.1. Data sources and search strategies

To identify studies that determined the effects of *Bacopa monnieri* on cognitive performance and/or anxiety, four reviewers electronically searched in MEDLINE, EMBASE, CINAHL, AMED, Cochrane Central of clinical trial, WHO registry, Thai Medical Index, Index Medicus Siriraj library and www.clinicaltrial.gov from the inception date of each database to June 2013. The subject headings were *Bacopa monnieri* or *Bacopa monniera* or *Herpestris monnieri* or *Herpestris monniera* or *Moniera euneifolia* or *Lysimachia monnieri* or Brahmi or coastal water hyssop or water hyssop or thyme leafed gratiola or thyme leaved graticula or thyme leafed graticula with cognitive performance or memory. To ensure thoroughness in our search, we reviewed the reference lists of retrieved articles and, where possible, searched for relevant unpublished works.

2.2. Study selection

Studies that investigated the cognitive effects of *Bacopa monnieri* on both healthy humans and subjects who showed memory impairment were selected by four reviewers using the following criteria: (1) studies were randomized placebo controlled clinical trial; (2) studies determined the effects of *Bacopa monnieri* on neuropsychological tests for cognitive performance; (3) studies reported outcomes after at least 12 weeks of administration; and (4) subjects received a standardized extract of *Bacopa monnieri* whose basoside composition was measured or discoverable. Those which used *Bacopa monnieri* in combination with other active compounds were excluded.

2.3. Data extraction and quality assessment

Data were extracted from each article by independent investigators using a standard abstraction form. The extracted data

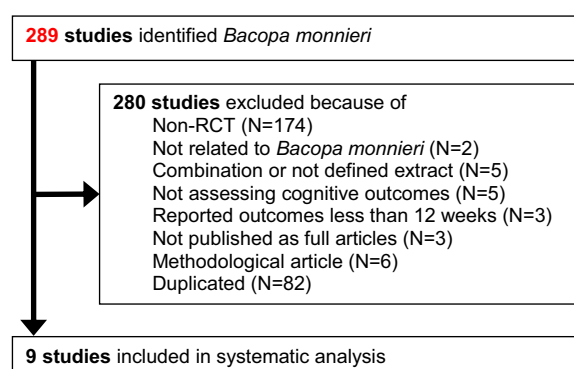


Fig. 1. Flow of included studies.

included the study setting, study design, duration of study, sample size, subject characteristics, methods of product extraction, standardization of product, dosage form, dosage and administration, and outcomes. The relevant cognitive outcomes were pre-specified as shown in Table 2. The methodological quality of studies was assessed using Jadad's quality scales on reporting (Jadad et al., 1996) and Cochrane's risk of bias tool for assessing the internal validity of the study (Deeks et al., 2008). Jadad's overall score of < 3 or ≥ 3 indicates low or high quality of reporting, respectively. In addition, because drop-outs in studies involving complementary alternative medicine may have impacted the overall estimates, we assessed frequency (differential vs. non-differential dropouts) and causes of dropouts (i.e., missing completely at random, missing at random, and missing not at random) to identify attrition bias in each study (Bell et al., 2013; Dumville et al., 2006; Moher et al., 2010). All disagreements among investigators were solved by discussion and consensus.

2.4. Data analysis

The differences of mean scores in each component of neuropsychological tests between treatment and control were outcome measures used for statistical pooling. The weighted mean difference and 95% confidence interval (95% CI) were performed using the random-effects model of the Dersimonian–Laird method (Dersimonian and Laird, 1986). A statistical heterogeneity was tested using the Cochran–Mantel–Haenszel method (Higgins and Thompson, 2002). $p < 0.10$ was considered evidence of heterogeneity (Deeks et al., 2008; Higgins and Thompson, 2002). I^2 -statistics was also performed to determine the degree of heterogeneity across studies. An I^2 of 25%, 50%, and 75% indicates low, medium, and high heterogeneity, respectively (Higgins and Thompson, 2002). Furthermore, clinical heterogeneity was also assessed according to subject, intervention, comparator, and main outcomes as described elsewhere (Thompson, 1994).

3. Results

3.1. Search results

A total of 289 articles were identified. Of these, 280 were excluded because they were non-randomized or uncontrolled clinical trials (174 articles), not related to *Bacopa monnieri* (two articles), combination products (five articles), not assessed in neuropsychological tests for cognitive performance (five articles), had not been published as full papers (three articles), reported outcomes less than 12 weeks (three articles), methodological papers (six articles) or duplicated (82 articles). In total, nine articles remained which met our criteria (Barbhaiya et al., 2008;

Download English Version:

<https://daneshyari.com/en/article/5836849>

Download Persian Version:

<https://daneshyari.com/article/5836849>

[Daneshyari.com](https://daneshyari.com)