

***Bacopa Monnieri*, Cognitive and Psychological Outcomes, and Self-Nanoemulsifying Delivery: A Structured Narrative Review of Human Evidence, Formulation Science and Translational Gaps**

Ketham Giribabu¹, Asha Alajangi²

¹Department of Pharmacology, AU College of Pharmaceutical Sciences, Andhra University, Visakhapatnam, Andhra Pradesh, India

²Department of Education, AU Arts College, Andhra University, Visakhapatnam, A.P., India.

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ABSTRACT

Background *Bacopa monnieri* (Brahmi) extracts are widely used for memory and stress-related complaints, yet human trial results are mixed and extracts, doses and cognitive tests differ widely. The main active saponins (bacosides) dissolve poorly in water, which has prompted interest in self-nanoemulsifying drug delivery systems (SNEDDS).

Objective To summarize controlled human evidence on *Bacopa monnieri* and cognitive or psychological outcomes, to appraise the available Bacopa-SNEDDS formulation evidence, and to define what is needed before a SNEDDS formulation is tested in humans.

Methods Structured narrative review of an author-curated set of 67 records, extended by targeted searches and verification against PubMed, publisher and trial-registry pages in October 2026. Eleven randomized controlled trials in adults were summarized. The only Bacopa-SNEDDS study identified was read in full and appraised against a formulation-science checklist.

Results Controlled trials of conventional Bacopa extracts (28 to 90 days; 150 to 450 mg/day) reported improvements in verbal learning, delayed recall, working memory or attention in several studies, but two trials found no cognitive advantage. Psychological outcomes were measured in about half the trials, with lower anxiety, depression, stress reactivity or fatigue reported in some and no effect on sleep. Only one trial enrolled students. The single Bacopa-SNEDDS study (oleic acid, Tween 20, ethanol) reported fast emulsification, a mean droplet size of 33.8 nm, 89% in vitro release at 60 min versus 24% for untreated extract, and higher ex vivo intestinal diffusion. No pharmacokinetic, safety or human data exist for any Bacopa SNEDDS, and the study has important reporting limitations.

Conclusions Evidence for conventional Bacopa extract is suggestive but heterogeneous, mainly for memory and attention, and sparse for stress, well-being and students. For SNEDDS, only laboratory-level proof of concept exists. Improved absorption, safety and clinical benefit remain unproven. A staged pathway from formulation quality to a feasibility pilot is justified.

Keywords: *Bacopa monnieri*; Brahmi; bacoside A; self-nanoemulsifying drug delivery system; cognition; perceived stress; psychological well-being; university students

INTRODUCTION

Bacopa monnieri is a traditional Ayurvedic herb. Its standardized extracts are rich in triterpenoid saponins, chiefly bacoside A, which is used as a marker compound.¹ Randomized trials in healthy and older adults have reported better verbal learning, memory consolidation and delayed recall, together with lower state anxiety, after 12 weeks of 300 mg/day.^{2,3} A 90-day trial of a different extract instead reported better spatial working memory accuracy.⁴

Evidence syntheses are cautious. A systematic review of randomized trials found some support for improved learning and free recall but could not pool results because extracts and tests differed.⁵ A meta-analysis restricted to trials of at least 12 weeks with standardized extracts suggested a possible benefit for speed of attention.⁶ A network meta-analysis of 29 trials in healthy adults (n = 2107) reported better working memory with higher Brahmi doses, while noting that

the lack of direct comparisons limits confidence.⁷ Not all trials are positive: a 12-week trial of 450 mg/day in 72 healthy adults did not reproduce the cognitive or anxiolytic benefits reported earlier, showing only a trend towards lower state anxiety.⁸

Bacosides dissolve poorly in water, which motivates lipid-based delivery. SNEDDS are isotropic mixtures of oil, surfactant and cosurfactant that disperse into nano-sized droplets in gastrointestinal fluid. A bacoside A-loaded SNEDDS was described in 2016,⁹ and bacoside-rich solid lipid nanoparticles have been compared with extract in an animal model of Alzheimer's disease.¹⁰ Whether any Bacopa formulation outperforms a conventional extract in humans is unknown.

Research gap. Three questions remain open: (i) whether any Bacopa SNEDDS has been characterized well enough to support human use; (ii) whether Bacopa affects perceived stress and well-being in young adults such as university students; and (iii) what evidence a future pilot study needs.

Aim and objectives. To (1) summarize controlled human evidence on cognitive and psychological outcomes; (2) describe the Bacopa preparations studied; (3) appraise Bacopa-SNEDDS and related evidence, keeping laboratory, animal and human findings apart; and (4) propose a staged translational pathway.

METHODS

2.1 Design and reporting

This is a structured narrative review, reported with reference to the SANRA quality criteria.¹¹ It is not a systematic review: no multi-database search with duplicate screening was performed, no protocol was registered, and PRISMA flow counts are therefore not reported.

2.2 Sources

The evidence base was a set of 67 records assembled by the authors (66 unique, as two entries were identical). Between October 2026 and the date of submission, trial and review records were checked against PubMed, publisher pages or trial registries, and targeted web searches were used to confirm trial design and to find controlled trials missing from the set. Two trials found this way were added.^{8,12}

2.3 Scope and classification

The human-evidence section covers randomized, placebo-controlled trials in adults reporting cognitive or psychological outcomes. Paediatric studies, uncontrolled studies, trial protocols without results, and entries that could not be traced to a primary source are described but not weighed. Records were classified as human study, protocol, systematic review or meta-analysis, narrative review, preclinical study, formulation study, analytical method, general SNEDDS or nano-delivery literature, or methodological guidance.

2.4 Appraisal and synthesis

The only Bacopa-SNEDDS paper was read in full and appraised against a checklist developed for this review (claims versus data, authorship and conflicts, internal consistency, composition, characterization, performance testing, stability, statistics). The checklist is not a validated instrument. For human trials, design features and results were taken from abstracts, registry records and available full texts, and formal risk-of-bias scoring with RoB 2¹³ was not applied; methodological concerns are instead described qualitatively. Synthesis is narrative, and human, animal and laboratory findings are never combined.

RESULTS

3.1 Composition of the evidence base

Of the 67 supplied records, 13 were human study reports, 3 were trial protocols without results, 9 were systematic reviews or meta-analyses, 10 were narrative reviews, chapters or reference entries, 3 were preclinical Bacopa studies, 1 was a Bacopa-SNEDDS study, 1 an analytical method, 10 concerned nano-delivery or curcumin, 14 concerned SNEDDS or self-emulsifying systems for other compounds, and 4 were methodological guidance (the remaining records are duplicates of the above groups).

Of the 13 human reports, 9 were adult randomized trials,^{2-4,14-19} one was an open-label study in Alzheimer's disease,²⁰ one was a paediatric study, and two could not be traced to a primary source (a web feed entry and an open-label ADHD report without identifiers). With the two trials added from searching, 11 adult randomized trials were summarized. No human study of any Bacopa SNEDDS or other nano-formulation was found.

3.2 Human trials of conventional Bacopa extracts

Study	Population	Intervention	Main reported findings
Stough 2001 ²	46 healthy adults, 18–60 y	Extract 300 mg/day, 12 wk, vs placebo	Faster visual information processing; better learning rate and memory consolidation (AVLT); lower state anxiety; maximal effects at 12 wk
Calabrese 2008 ³	54 healthy adults ≥65 y (mean 73.5)	Extract 300 mg/day, 12 wk after a 6-wk placebo run-in	Better AVLT delayed recall (primary outcome) and Stroop performance; lower depression (CESD-10) and anxiety scores; adverse events mainly stomach upset (9 Bacopa, 10 placebo)
Stough 2008 ⁴	107 healthy adults recruited, 62 completed	KeenMind 2 × 150 mg, 90 days	Better spatial working memory accuracy; fewer false positives on rapid visual information processing
Sathyanarayana n 2013 ⁸	72 healthy urban adults, 35–60 y	Extract 450 mg once daily, 12 wk	Earlier cognitive and anxiolytic benefits not reproduced; trend towards lower state anxiety
Morgan 2010 ¹⁴	Older adults	BacoMind, 300 mg/day (as summarized in ref. ⁸)	Better verbal learning, memory acquisition and delayed recall (AVLT)
Raghav 2006 ¹⁵	Age-associated memory impairment	250 mg/day (as summarized in ref. ⁸)	Better memory and paired-associate learning
Barbhaiya 2008 ¹⁶	Elderly adults	BacoMind, 450 mg/day (as summarized in ref. ⁸)	Better memory, including paired-associate delayed recall
Kumar 2016 ¹⁷	60 medical students, India	Bacognize 150 mg twice daily, 6 wk, 15-day follow-up	Significant improvement in cognitive tests; higher serum calcium, within normal range
Lopresti 2025 ¹⁸	101 adults, 40–70 y, self-reported memory and attention problems (50 vs 51)	Bacumen 300 mg/day, 12 wk	Cognition not better than placebo; greater reduction in stress reactivity ($p = 0.03$) and in fatigue and stress after a demanding task; more adverse reactions (digestive complaints, headaches)
Lopresti 2021 ¹²	100 adults with self-reported poor sleep	Bacognize 150 mg twice daily, 28 days	No better sleep (Bergen Insomnia Scale); better emotional well-being, general health and pain scores; lower salivary sIgA and sAA
Delfan 2024 ¹⁹	62 adults with mild cognitive impairment	Standardized extract for two months, triple-blind	Better overall cognitive performance; no effect on sleep quality (as summarized in secondary sources)

Table 1. Randomized placebo-controlled trials of conventional Bacopa extracts in adults. Findings are as reported by the cited sources; no effect sizes were pooled. AVLT, Auditory Verbal Learning Test; sIgA, salivary immunoglobulin A; sAA, salivary α -amylase.

Several patterns emerge. Extracts differ (KeenMind, BacoMind, Bacognize, Bacumen and others), doses range from 150 to 450 mg/day, and durations from 28 to 90 days. Samples are small, and attrition can be high (62 of 107 completed in one trial⁴). Memory outcomes are reported most often, and positive findings cluster in studies using the Rey Auditory Verbal Learning Test. One open-label study of 300 mg twice daily for six months in 39 patients with Alzheimer's disease reported improved Mini-Mental State scores, but it had no control group.²⁰

3.3 Evidence syntheses

Existing reviews agree on heterogeneity.^{5–7} A systematic review in Alzheimer's dementia and mild cognitive impairment rated the certainty of cognitive outcomes as very low and called for larger trials with clinically meaningful outcomes.²¹ Because syntheses overlap in the trials they include, their conclusions should not be treated as independent confirmations.

3.4 Psychological outcomes and students

Psychological outcomes were measured in about half of the trials. Lower state anxiety was reported in two,^{2,3} lower depression scores in one,³ and lower stress reactivity and fatigue in one.¹⁸ One trial found only a trend for anxiety,⁸ and

sleep did not improve in two trials.^{12,19} Gastrointestinal complaints and headache were the main adverse effects reported.^{3,18} Only one trial enrolled students, and it measured cognitive and biochemical outcomes, not perceived stress or well-being.¹⁷ No trial in this review tested Bacopa for perceived stress in a student sample.

3.5 Bacopa-loaded SNEDDS

Gohel and colleagues optimized a bacoside A-loaded SNEDDS using a D-optimal mixture design with oleic acid, Tween 20 and ethanol and an extract described as containing 45% bacoside A.⁹ Reported findings are in Table 2.

Parameter	Reported value
Optimized composition (% w/w)	Oleic acid 4.52, Tween 20 35.47, ethanol 5.01 (sum 45.00%; the remaining 55.00%, including extract loading, is not stated)
Self-emulsification time	9 s
Refractive index; transmittance	1.33; 98.7%
Z-average droplet size; polydispersity index	33.84 nm; 0.487
Zeta potential	-4.45 mV
Electron microscopy size range	6.12–50 nm
In vitro release (0.1 N HCl)	About 89% (SNEDDS) vs 24% (untreated extract) at 60 min
Ex vivo intestinal diffusion (4 h)	90.14% (SNEDDS) vs 23.65% (untreated extract)

Table 2. Findings reported for the Bacopa-SNEDDS study.⁹ All results are laboratory or ex vivo; no in vivo pharmacokinetic, efficacy or human data are reported.

The study supports formulation feasibility and a dissolution advantage in vitro. Its title and conclusions, however, refer to bioavailability and in vivo evaluation that the reported experiments do not include. Table 3 lists the issues found on appraisal.

Domain	Observation
Claims versus data	Bioavailability is claimed, but no plasma pharmacokinetics (C _{max} , AUC) are reported, and the conclusion mentions in vivo studies that are not presented.
Authorship and conflicts	The byline lists Gohel et al., while the running header and citation line say Patel et al., with different author names and title wording. A co-author is affiliated with the company that supplied the extract ex gratis, yet no conflict of interest is declared.
Internal consistency	The text states eleven design runs, but twelve are tabulated. Dissolution is given as 89% at 60 min in the abstract and more than 80% within 50 min in the text. The coefficient table is titled quadratic while the text describes cubic models.
Sample sizes	The ex vivo figure reports n = 2, dissolution n = 6, and design responses n = 3.
Particle characterization	A Z-average of 33.84 nm sits beside a polydispersity index of 0.487 and a main intensity peak near 64 nm (about 85% of intensity), indicating a broad distribution. A near-neutral zeta potential (-4.45 mV) is interpreted as supporting stability and mucoadhesion, which the data do not show.
Analytical method	Bacoside A in a complex extract was measured by UV spectrophotometry, which is non-specific. A validated chromatographic method exists. ¹
Composition and tolerability	The surfactant fraction is high (about 35% Tween 20) with ethanol; the remaining composition, extract loading and unit dose are not clearly stated. Capsule compatibility, ethanol volatility and gastrointestinal tolerability are not addressed.
Stability	A cloud-point method is described, but no result is reported. No thermodynamic, dilution-robustness or storage-stability data are shown.
Statistics	ANOVA, R ² and lack-of-fit statistics are not shown.
Referencing	Several citations do not match the statements they support (for example, a PLGA microsphere paper cited for emulsification time and zeta potential).

Table 3. Appraisal of the Bacopa-SNEDDS study against the review checklist. C_{max}, maximum plasma concentration; AUC, area under the concentration–time curve.

3.6 Other delivery evidence

Bacoside-rich solid lipid nanoparticles have been compared with extract in vivo in an Alzheimer's disease model.¹⁰ This and the broader SNEDDS and nano-delivery literature for other compounds show which characterization and performance tests are expected, but they concern different compounds and cannot be read as evidence for a Bacopa SNEDDS.

DISCUSSION

Human evidence. Conventional Bacopa extracts have been tested in several randomized trials, and positive findings cluster around verbal learning, delayed recall and attention, particularly at 12 weeks or longer.²⁻⁶ Contradictory trials,^{8,18} small samples, and different extracts and tests limit confidence, and no firm conclusion can be drawn for a specific product.

Psychological outcomes. Anxiety, depression, stress reactivity and sleep have been measured in only some trials, with mixed results.^{2,3,8,12,18,19} Evidence in students is limited to one trial of cognitive outcomes.¹⁷ Conclusions about perceived stress and well-being in young adults would be premature.

Extract versus formulation. Evidence for a conventional extract does not transfer to a SNEDDS. Dose equivalence, bacoside content, excipient effects and absorption could all differ.

Pharmaceutical plausibility versus demonstrated benefit. The Bacopa-SNEDDS study shows that extract can be incorporated into a nano-emulsifying system with rapid emulsification and faster in vitro release.⁹ It does not show better absorption in animals or humans, safety, stability, or any cognitive or psychological effect. Mechanistic explanations offered for improved permeability are speculative.

Safety. Digestive complaints and headache were reported with conventional extract.^{3,18} A formulation with a high surfactant and ethanol fraction needs its own tolerability and toxicology review before human use.

Interdisciplinary relevance. A credible human study needs pharmaceutical quality (standardized extract, characterized and stable formulation) matched with sound psychological measurement (prespecified outcomes, control of practice effects, and a blinding check).

Implications for Future Research

1. Confirm extract identity and standardization with a validated chromatographic bacoside assay.
2. Re-establish formulation performance, including droplet size distribution, robustness to dilution, and thermodynamic and storage stability.
3. Review excipient toxicology and set a defensible dose and human-use rationale.
4. Obtain in vivo pharmacokinetic data comparing the SNEDDS with a conventional extract at matched bacoside doses.
5. Obtain ethics and regulatory approvals and register the trial.
6. Run a small randomized, placebo-controlled pilot, for example in university students, with feasibility as the primary aim and prespecified cognitive, perceived-stress and well-being outcomes.
7. Proceed to a larger trial only if feasibility, safety and pharmacokinetic data justify it.

STRENGTHS AND LIMITATIONS

Strengths. The review keeps laboratory, animal and human evidence separate, appraises the only Bacopa-SNEDDS study in full, and corrects the record on its reporting problems.

Limitations. The source set was assembled by the authors rather than retrieved by a systematic multi-database search, so relevant studies may be missing. For several trials, details came from abstracts, registry records or secondary summaries instead of full texts, and formal risk-of-bias scoring was not applied. No effect sizes were pooled. Several trials involve proprietary extracts and may share commercial sponsorship, which this review could not assess in full. The formulation checklist is not a validated instrument. A systematic review with a registered protocol, duplicate screening and RoB 2 assessment would be the proper next step.

CONCLUSION

Human evidence for conventional Bacopa extracts is suggestive but heterogeneous, mainly for memory and attention, and sparse for stress, well-being and student populations. For Bacopa SNEDDS, the available evidence is a single laboratory-level proof of concept with reporting limitations. Claims of improved bioavailability, safety or clinical superiority are not supported. A staged pathway from formulation quality to a feasibility pilot is justified.

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