INFORMATION SHEET

An examination into the effects of a Bacopa monnieri extract (Bacumen®) on cognition and stress in healthy adults: a randomised, double-blind, placebo-controlled trial

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You are invited to participate in this study.

Background

Bacopa monnieri (Brahmi), a plant native to the wetlands of Southern and Eastern India, is traditionally used in Ayurvedic medicine as a neural tonic, sedative, memory, and learning enhancer. In this study, we are interested in examining the effects of a Bacopa monnieri extract (Bacumen®) on memory, attention, energy, and stress levels in adults.

This study will be conducted by Dr Adrian Lopresti and Stephen Smith (Clinical Research Australia).

Information about funding source and declaration of interests

This study is funded by US Pharma Lab, the company that produces the *Bacopa Monnieri* extract (Bacumen®) that will be used in this study. However, this study is independently managed by Clinical Research Australia (CRA) without external influence from US Pharma Lab.

Aim of the study

We would like to know whether taking *Bacopa Monnieri* capsules twice daily for 12 weeks can improve attention and memory, and reduce stress and fatigue in adults with self-reported attention and memory problems. We will also assess changes in blood markers associated with memory and cognitive function.

What does participation involve? **(see study flow chart on page 3)**

This study will comprise several steps as outlined below:

Step 1: Completion of initial online screening

This questionnaire consists of approximately 20 questions and takes approximately 10 minutes to complete. It provides us with information relating to the eligibility criteria. If, based on the results of the screening questionnaire, you are assessed as 'likely' eligible, you will be contacted for a phone interview. Ineligible volunteers will be informed by email that they do not fulfil the eligibility criteria.

Step 2: Phone Interview for an initial assessment of eligibility

If you are potentially eligible to participate in the study, you will be interviewed by a researcher. The interview will be conducted over the phone (approx. 20 minutes). The purpose of this interview is to obtain relevant background information (e.g., age, sex, illnesses, medication use, etc.), provide you with further details about the study and what the next step is in the qualification process, and assess other relevant eligibility criteria. This includes obtaining further details about your memory and stress levels and confirmation of your current medication and supplement intake. We will also complete a brief cognitive assessment over the phone.

If you have been assessed as eligible to participate in this study, an appointment will be arranged for a face-to-face assessment at our offices located in Duncraig.

Step 3: VISIT 1: Face-to-face assessment (approx. 90 mins)

During this meeting, the following tasks will be completed:

1. Signing of the study consent form. This must be signed before we proceed with the study.
2. Measurement of your weight, height, blood pressure, pulse, and body temperature
3. Blood sample collection: a researcher trained and accredited in venous blood collection will collect a blood sample from your vein. We will use this blood sample to measure several markers associated with memory and cognitive performance. We will investigate whether concentrations in these blood markers will change over time.
4. Completion of self-report questionnaires assessing your memory, mood, and general wellbeing
5. Completion of several computer-based and researcher-administered tests to assess your memory and attention
6. 12-week provision of capsules to take for the study

Please note: All assessments will be conducted in the morning. It is important that you:

1. DO NOT consume more than 2 standard serves of alcohol the evening before your appointment
2. DO NOT drink any caffeinated beverage in the morning of your appointment
3. DO NOT consume any food in the morning of your appointment
4. DO NOT engage in strenuous in the morning of your appointment.

We will provide you with a breakfast bar and non-caffeinated herbal tea after your blood has been collected.

Step 4: 12-week intake of capsules (Bacopa monnieri or placebo)

In this study, we will be using a randomised, double-blind, placebo-controlled design. This means that half of the participants will be placed on Bacopa Monnieri capsules, and the other half will be placed on placebo (dummy) capsules.

Neither you nor the investigator will be aware of which group you have been placed in. This random placebo allocation is important for us to assess the true effects of Bacopa on memory, attention, and mood.

You will be required to take 1 capsule, twice daily (morning and evening) with or without food.

** Placebo involves providing a substance with no known treatment effects. In this case, the placebo will contain cellulose powder (a fibre).*

It is extremely important that you take these capsules every day. We will ask you to download a simple pill reminder application on your phone to help you to remember to take the capsules every day.

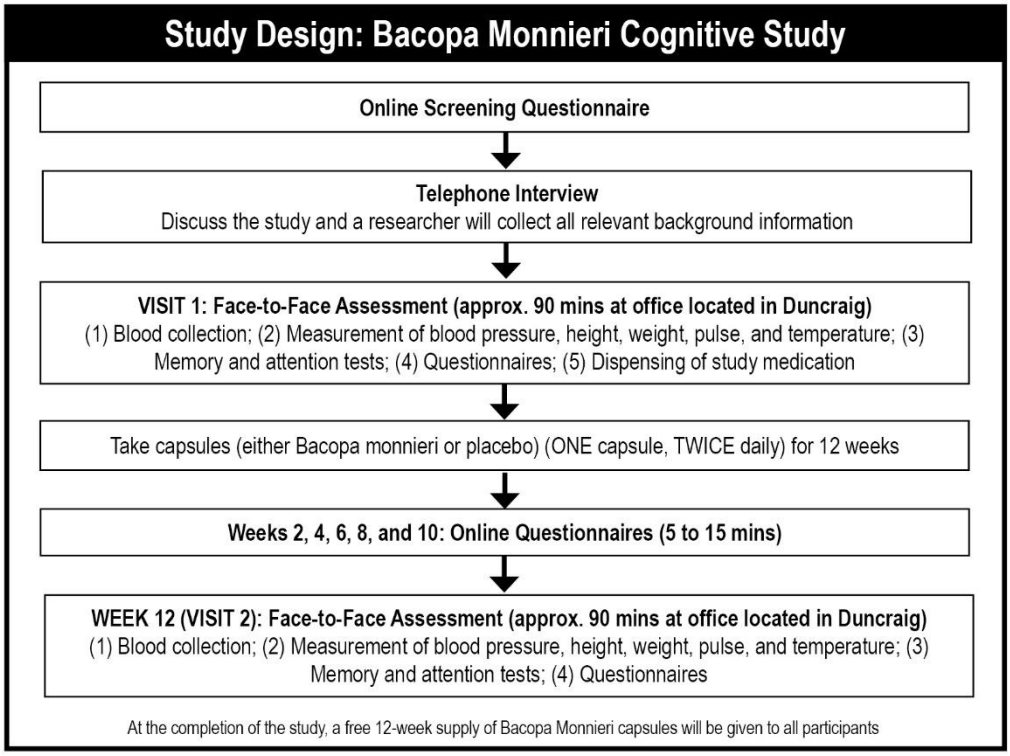
Step 5: Repeat completion of online questionnaires every 2 weeks

Every 2 weeks, you will be asked to complete online questionnaires. These are the same questionnaires that you completed during your face-to-face interview. We will also ask if you have been experiencing any adverse effects associated with your capsule intake. Questionnaires completed at weeks 2, 6, and 10 will take approximately 5 minutes to complete and questionnaires at weeks 4 and 8 will take approximately 15 minutes to complete.

Step 6: VISIT 2: Week 12, face-to-face re-assessment (approx. 90 mins)

Twelve weeks after you start taking your capsule, you will attend another face-to-face assessment where the following tasks will be completed:

1. Blood sample collection
2. Measurement of your weight, blood pressure, pulse, and temperature
3. Completion of self-report questionnaires assessing your memory, mood, and general wellbeing
4. Return of unused capsules/ pill bottles
5. Completion of several computer-based and researcher-administered tests to assess your memory and attention



Compensation for participating in this study

1. To compensate you for your travel costs and time associated with participating in this study, at the end of each face-to-face assessment (baseline and week 12), we will give you a $40 Coles Group voucher.
2. At the end of the study, all volunteers will be offered a free supply of Bacopa Monnieri capsules to try for 12 weeks.

Criteria for inclusion/ exclusion in this study

To be included in the study, the following inclusion criteria must be met:

1. You are a generally healthy adult (male and female)
2. You are aged between 40 to 70 years
3. You reside in independent living accommodation
4. You report experiencing problems with your memory or attention
5. You are a non-smoker
6. You have a body mass index (BMI) between 18 and 35 kg/m^2
7. You have no plan to commence any new treatments over the study period
8. You are willing to provide a personally signed and dated informed consent form detailing all pertinent aspects of the trial.

If any of the exclusion criteria below are met, you will <u>not</u> be suitable for participation in this study:

1. You suffer from a recently diagnosed or unmanaged medical condition including but not limited to: diabetes, hyper/hypotension, cardiovascular disease, gallbladder disease, autoimmune disease, endocrine disease, or cancer/ malignancy
2. You have been diagnosed with a psychiatric disease (other than mild-to-moderate depression or anxiety) and/or neurological condition/ disease (e.g., Parkinson's or Alzheimer's disease)
3. You have a history of paralysis, stroke, seizures, or head injury (with loss of consciousness).
4. You regularly take medications including but not limited to anticholinergics, acetylcholinesterase inhibitors, or steroid medications
5. You have changed your medication (dose or type) in the last 3 months, or you expect to change it during the study
6. You currently take supplements containing Bacopa Monnieri or other herbal ingredients that might affect the study outcomes.

7. In the last 6 months, you have commenced or changed your dose of nutritional and/or herbal supplements that may impact on treatment outcome
8. You currently (or in the last 12 months) have a problem with the use of illicit drugs
9. You drink more than 14 standard servings of alcohol per week
10. You are pregnant, breastfeeding, or intend to fall pregnant in the next 3 months
11. You fall pregnant during the study
12. You have had a significant surgery in the last 12 months
13. You do overnight shift work
14. You plan on making major lifestyle change in the next 3 months

Voluntary participation and withdrawal from the study

It is important that you understand that your involvement in this study is voluntary. While we are grateful to have you participate, we respect your right to decline. There will be no consequences to you if you decide not to participate, and this will not affect any future treatment/service. If you decide to discontinue participation at any time, you may do so without providing an explanation. If you withdraw, any assessments already conducted may continue to be used for analysis.

Please note that if you choose to commence a treatment to improve your memory or attention, or you require treatment for any other condition during the study, this may result in withdrawal from the study. Your health is the utmost priority, and your choice/need to commence new treatment before completing this study is respected and supported.

Your privacy

Your privacy is very important to us. Your participation in this study and any information will be treated in a confidential manner. Your name and identifying details will not be used in any publication arising out of the research. Following the study, the data will be kept in a de-identified format, in a locked cabinet in the office of the Investigator and will be held for statistical analysis for future publication. Re-identifying codes will be retained for 6 months in case this is needed and will then be destroyed.

Possible benefits

Like many spices, Bacopa Monnieri is a natural antioxidant and anti-inflammatory and is reported to be associated with several health benefits. If Bacopa Monnieri is found to be effective, it will provide us with a natural option to help memory, attention, and mood in adults.

Possible risks

Participation in this study carries little risk and many measures will be in place to decrease the likelihood of potential risks. Below is a list of possible risks associated with participating in this study:

- Bacopa is considered safe and is well-tolerated by most users. In traditional medicine, it has been used for centuries as a health remedy. Although reported side effects are infrequent, there have been reports of mild digestive complaints (e.g., nausea, stomach cramps, bloating, increased bowel movements, and diarrhoea). No studies have reported any serious side effects from its intake, although this cannot be totally ruled out.
- Further details about Bacopa and its intake is included in the 'Bacopa Information Sheet'.

In this study, we will collect a blood sample from your vein (venepuncture). Although venepunctures are very safe, there is a possibility of developing bruising at the site of the needle puncture. This usually appears within 24 hours and may range in size from a small spot to a large purple bruise. While bruising can be unsightly, it is not dangerous and will slowly disappear over a few days. Very rarely, a small artery that contains blood at a much higher pressure than in veins will lie unusually close to or underneath a vein. In this situation, the artery may be accidentally punctured at the time of venepuncture. Bruising on the lower part of the arm over the next 2 to 3 days will likely develop. Again, this is not dangerous and will gradually disappear over a couple of weeks. Although extremely rare, some people may have a tiny branch of one of the sensory nerves of the arm running over the surface of the vein. Rarely, the needle will hit this tiny nerve on the way into the vein. This may cause a short, sharp electric-shock type pain. This may be all that occurs but, in some cases, a tingling type of pain may persist for 1 to 4 weeks as the nerve heals. This is inconvenient and may be unpleasant, but it eventually subsides. Another rare complication is for a small clot (or thrombus) to form in the vein at the

site of the venepuncture. This is noticed as a small firm lump just under the skin at the venepuncture site. The lump may or may not be tender and will go away over a couple of weeks. Finally, although extremely rare, an infection at the site of puncture can occur. Please notify us immediately if this occurs. To minimise all these risks, blood collections will be collected by a qualified and experienced phlebotomist using current best practices.

What to do if you experience significant side effects

If you experience any significant illness, injury, or side effects from taking your supplements, please contact Dr Adrian Lopresti or Stephen Smith immediately (contact details are below). You may be asked to cease participating in the study and to seek medical advice

Stephen Smith: Ph: 9448 7376 | Mob: 0412 813 518 | Email: steve@clinicalresearch.com.au

Dr Adrian Lopresti: Ph: 9448 7376 | Mob: 0411 969 797 | Email: adrian@clinicalresearch.com.au

Feedback on study results

It is estimated the results of this study will be finalised in late-2023. A summary of the results obtained from all participants in this study will be emailed to you when they have been published in a peer-reviewed journal.

Questions

If you would like to discuss any aspect of this study, please feel free to contact Dr Adrian Lopresti on 08 9448 7376.

We would like to thank you in advance for your assistance with this research project. We look forward to hearing from you soon.

If you are interested in participating in this study, please contact Dr Adrian Lopresti on 9448 7376 or email adrian@clinicalresearch.com.au

This study has been approved by the National Institute of Integrative Medicine (NIIM) Human Research Ethics Committee (HREC) (Trial Reference Number: 0112E_2022). If you have any reservation or complaint about the ethical conduct of this research, and wish to talk with an independent person, you may contact the NIIM Research Ethics Office (Tel. 03 9804 0646) or e-mail hrec@niim.com.au). Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.