STUDY INFORMATION SHEET

The effects of a curcumin extract (Curcugen®) on cognition, mood, fatigue, sleep, and menopausal symptoms in peri- and early postmenopausal women: a randomised, double-blind, placebo-controlled trial

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Background

There is some research suggesting that curcumin, a compound derived from turmeric, may help improve cognitive performance, mood, and general wellbeing in adults. However, limited research has examined its effects on these outcomes in women during the menopausal transition. This study, therefore, aims to examine the effects of 12 weeks of curcumin supplementation on cognitive performance, mood, sleep, pain, and other menopause-related symptoms in women aged 40 to 65 years who are peri- or early postmenopausal. To help understand how curcumin may work, changes in blood markers associated with inflammation, glucose regulation, and appetite-regulating hormones will also be examined.

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

Information about the funding source and declaration of interests

This study is funded by Dolcas Biotech LLC, the company that produces the curcumin extract (Curcugen®). However, this study is being conducted and managed by Clinical Research Australia in accordance with the approved protocol and applicable ethical and scientific standards.

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 takes approximately 10 minutes to complete. It provides us with information relating to the eligibility criteria. If, based on the screening questionnaire results, 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 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. 15 minutes). The purpose of this interview is to obtain relevant background information (e.g., medication use, current treatments, cognitive complaints, menopausal symptoms, general health, etc.) and assess other relevant eligibility criteria. We will also provide you with further details about the study. If you meet our eligibility criteria and agree to participate in the study, you will proceed to the next step.

Step 3: VISIT 1 (Day 0): Face-to-face assessment (total time approx. 60 to 90 mins)

The face-to-face assessment will comprise the following:

a. Measurement of vital signs and anthropometric measurements: A researcher will measure your sitting blood pressure, height, weight, and body composition (using a bioimpedance scale).

b. Blood collection: A researcher trained in venous blood collection will collect a blood sample from your vein. We will use this blood sample to measure several markers associated with inflammation, glucose and appetite regulation. We will investigate whether concentrations in these blood markers change over time.

c. Cognitive testing: You will complete several tests assessing your memory, attention, and cognitive function

d. Completion of self-report questionnaires: You will complete a series of questionnaires.

e. Provision of a 12-week supply of the study capsules: You will be given one bottle containing capsules with either Curcumin or a placebo.

f. Provision of gift voucher. You will be given a $40 gift voucher.

Step 4: DAYS 1 TO 84: Start taking your capsules

In this study, we will be using a randomised, double-blind, placebo-controlled design. This means that half of the participants will receive placebo capsules, and the other half will receive capsules containing Curcumin.

Neither you nor the investigator will know which group you have been placed in. This random allocation is important for assessing the true effects of the curcumin supplement.

You will be required to take **ONE** capsule, **TWICE** daily (morning and evening) with food. It is extremely important that you take these capsules every day.

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

Step 5: DAY 28: questionnaires (online)

You will complete online questionnaires that take approximately 10 minutes.

Step 6: DAY 56: questionnaires (online)

You will complete online questionnaires that take approximately 10 minutes.

Step 7: VISIT 2 (Day 84): Face-to-face assessment (total time approx. 60 mins)

The face-to-face assessment is similar to visit 1 and will comprise the following:

a. You will need to return your study bottles/ capsules

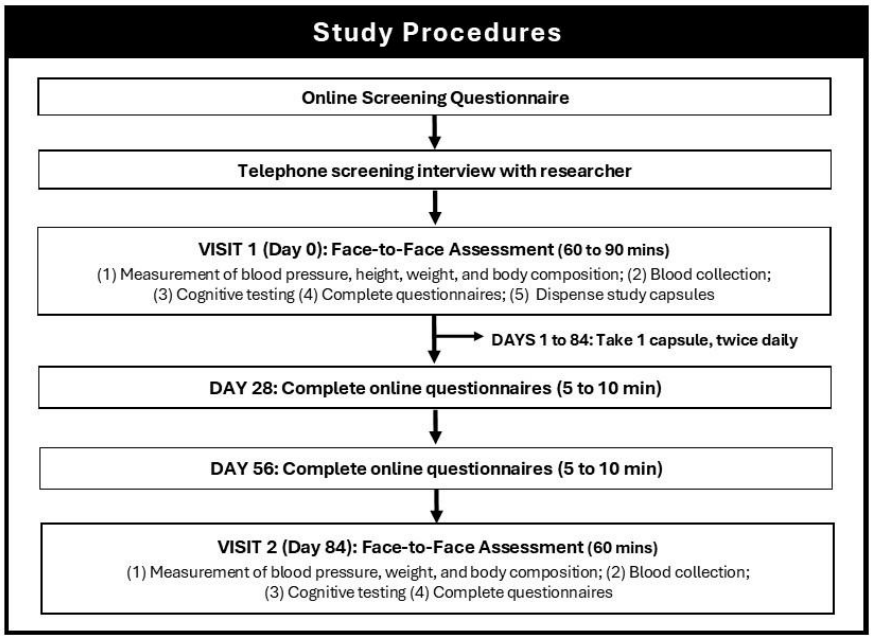
b. Measurement of vital signs and anatomical measurements: A researcher will measure your sitting blood pressure, weight, and body composition.

c. Blood collection: A researcher will collect a blood sample from you

d. Cognitive testing: You will complete several tasks assessing your memory, attention and cognitive function

e. Completion of self-report questionnaires: You will complete several questionnaires.

f. Provision of gift voucher. You will be given a $120 gift voucher



Compensation for participating in this study

To compensate participants for travel costs and time associated with participating in this study, you will receive a $40 gift voucher at visit 1 and a $120 gift voucher at visit 2. At the end of the study, volunteers in the placebo group will also be offered a complimentary 12-week supply of curcumin to try.

Criteria for inclusion/ exclusion in this study

To be eligible for this study, you must meet all of the following inclusion criteria:

1. You are a woman aged 40 to 65 years.
2. You have an intact uterus and at least one ovary.
3. You are perimenopausal, with persistent changes in your menstrual cycle consistent with the menopausal transition, or early postmenopausal, with your final menstrual period occurring no more than 6 years ago
4. If you are using menopausal hormone therapy, you have been using the same formulation, dose, and route for at least 12 weeks before baseline and do not anticipate changing treatment during the study.
5. You have self-reported difficulties with memory, concentration, attention, word-finding, or clear thinking that have been present during most weeks over the previous 3 months and began or became noticeably worse during the menopausal transition.
6. You have a body mass index (BMI) between 18 and 35 kg/m^2.
7. You understand the study requirements and are willing and able to comply with all study procedures.

You will not be eligible to participate if any of the following exclusion criteria apply:

1. Your menstrual changes are primarily attributable to pregnancy, a medical condition, or another cause unrelated to the menopausal transition.
2. You currently use hormonal contraception that prevents reliable classification of your menopausal stage.
3. You have a recently diagnosed or inadequately managed medical condition that, in the Investigator's judgement, may affect your safety, study participation, or interpretation of the study outcomes. Examples include, but are not limited to, diabetes, hypertension, cardiovascular disease, gastrointestinal disease, biliary disease, autoimmune disease, endocrine disease, or a chronic or acute pain condition.
4. You have a neurological or psychiatric disorder that, in the Investigator's judgement, is likely to materially affect cognitive performance, your safety, or adherence to study procedures. Examples include, but are not limited to, dementia, Parkinson's disease, psychotic disorders, bipolar disorder, or a significant head injury. Stable mild-to-moderate depression or anxiety will not exclude participation.
5. You have taken a supplement containing curcumin or turmeric within the previous 8 weeks.
6. You regularly use medications that are likely to materially affect cognitive performance, mood, sleep, menopausal symptoms, inflammation, or the safety or metabolism of the investigational product. Examples include benzodiazepines, anticholinergics, antipsychotics, and regular anti-inflammatory medications. Occasional analgesic use may be permitted at the Investigator's discretion if the dose and pattern of use are stable.
7. You have started or changed a medication likely to affect cognitive function, menopausal symptoms, mood, or sleep within the previous 8 weeks, or you anticipate changing such medication during the study.
8. You have started or changed a nutritional or herbal supplement likely to affect cognitive function, menopausal symptoms, mood, or sleep within the previous 4 weeks, or you anticipate changing such supplementation during the study.
9. You plan to make a major lifestyle or dietary change during the study.
10. You consume more than 14 standard alcoholic drinks per week.
11. You currently use illicit drugs regularly or have a history of regular illicit drug use within the previous 12 months.
12. You currently smoke or regularly use nicotine-containing products (defined as use on at least one day per week during the previous 3 months).
13. You are pregnant, breastfeeding, or intend to become pregnant during the study.
14. You have undergone significant surgery within the previous 6 months that affects your general health or daily functioning, or you have planned surgery during the study.
15. You have participated in another clinical trial within the previous month.

Voluntary participation and withdrawal from the study

It is essential that you understand your involvement in this study is entirely voluntary. While we appreciate your participation, 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 need to commence or change a medication, supplement, or other treatment during the study, please inform the research team. Starting or changing treatment will not necessarily require withdrawal, but the Investigator will determine whether it may affect your safety or the interpretation of the study results. Your health and access to appropriate treatment will always take priority over continued participation in the study.

Your privacy

Your participation in this study and the information you provide will be treated confidentially. Your name and other directly identifying information will not appear in any report or publication arising from the study. Study data will be assigned a unique participant identification number and stored securely. The document linking your identity with your participant identification

number will be stored separately from the study data and accessed only by authorised members of the research team. Study records will be retained and destroyed in accordance with the approved protocol and applicable research-governance requirements.

Possible benefits

During the menopausal transition, changes in memory/cognition, mood, energy, and fatigue are commonly reported. Therefore, identifying safe and effective methods to improve function in these areas is crucial. If curcumin supplementation is found to be effective, the results may contribute to the development of additional approaches for supporting cognition and wellbeing in women during the menopausal transition. You may or may not personally benefit from participating in this study.

Possible risks

Participation in this study is considered to involve low risk, and numerous measures will be in place to minimise potential risks. Curcumin, derived from the spice turmeric, is widely used as an over-the-counter supplement. Curcumin is widely available as an over-the-counter supplement and is generally well-tolerated. However, adverse effects can occur. Reported effects are usually mild and may include abdominal discomfort, bloating, nausea, diarrhoea, or headache.

In this study, we will collect a blood sample from your vein (venepuncture). Although venepunctures are very safe, there is a possibility of 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 typically disappears 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 during venepuncture. Bruising on the lower arm may develop over the next 2 to 3 days. Again, this is not dangerous and will gradually disappear over a couple of weeks. Although extremely rare, some people may have a small sensory nerve branch in the arm running over the surface of a vein. Rarely, the needle will hit this tiny nerve on the way into the vein. This may cause a 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 the formation of a small clot (thrombus) in the vein at the venepuncture site. This is noticed as a small firm lump just under the skin at the venepuncture site. The lump may be tender and typically subsides over a couple of weeks. Finally, although extremely rare, an infection can occur at the puncture site. Please notify us immediately if this occurs. To minimise these risks, blood samples will be collected by a qualified and experienced phlebotomist in accordance with current best practices.

What to do if you experience significant side effects

If you experience any significant illness, injury, or side effect that has commenced since starting your capsules, please get in touch with Dr Adrian Lopresti or Dr Stephen Smith immediately (contact details are below). You may be asked to stop participating in the study and to seek medical advice.

Dr 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 anticipated that the study results will be finalised after recruitment, follow-up, data analysis, and preparation of the study report have been completed.

Questions

If you would like to discuss any aspect of this study, please contact the principal investigator, Dr Adrian Lopresti, on 08 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: 0166E_2026). If you have any reservations or complaints 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 email hrec@niim.com.au. Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.