INFORMATION SHEET

The effects of supplementation with a phyto-blend (Osteosine™) on makers of bone health and general wellbeing in post-menopausal women: A randomised, double-blind, placebo-controlled study

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Background

Cnidium monnieri and Cuscuta chinensis are plants used in Traditional Chinese Medicine to treat and prevent a range of health conditions. In particular, they have a history of use to support bone health. Even though there are animal studies demonstrating they may have positive effects on bone health, there have been no well-controlled, human clinical trials examining their bone-supporting benefits.

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 NuLiv Science USA Inc., the company that produces the product (Osteosine™) used in this study. However, this study is independently managed by Clinical Research Australia without external influence from NuLiv Science USA Inc.

Aim of the study

We would like to know whether supplementation with a a combination of Cnidium monnieri and Cuscuta chinensis (Osteosine™) for 6 months can improve blood markers associated with bone health and improve general wellbeing in post-menopausal women aged 50 to 80.

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 5 to 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. 10 minutes). The purpose of this interview is to obtain relevant background information (e.g., illnesses, medication use, current treatments, 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. If you meet our eligibility criteria, a face-to-face appointment at our office in Duncraig will be arranged for 3 to 14 days later.

Step 3: VISIT 1 (day 0): Blood collection and face-to-face assessment (approx. 45 mins)

During this visit, the following tasks will be completed:

1. You will visit a Western Diagnostics Pathology (WDP) collection centre located near the office of Clinical Research Australia. A blood sample will be collected from an WDP staff member to

examine blood markers associated with bone health, liver function and renal function. This blood sample needs to be collected in the morning after an overnight fast.

2. You will then visit the office of Clinical Research Australia for the following:
    a. Have your weight, height, and blood pressure measured
    b. Complete questionnaires about your general wellbeing
    c. Receive a 6 month (180 day) supply of capsules containing Osteosine™ or a placebo

Step 4: Take your capsules

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

Neither you nor the investigator will know which group you have been placed in. This random placebo allocation is important for us to assess the true effects of Osteosine™.

You will be required to ONE capsule, ONCE daily after dinner.

* Placebo involves providing a substance with no known treatment effects. In this case, the placebo will contain maltodextrin.

It is extremely important that you take these capsules every day. We will send you reminders.

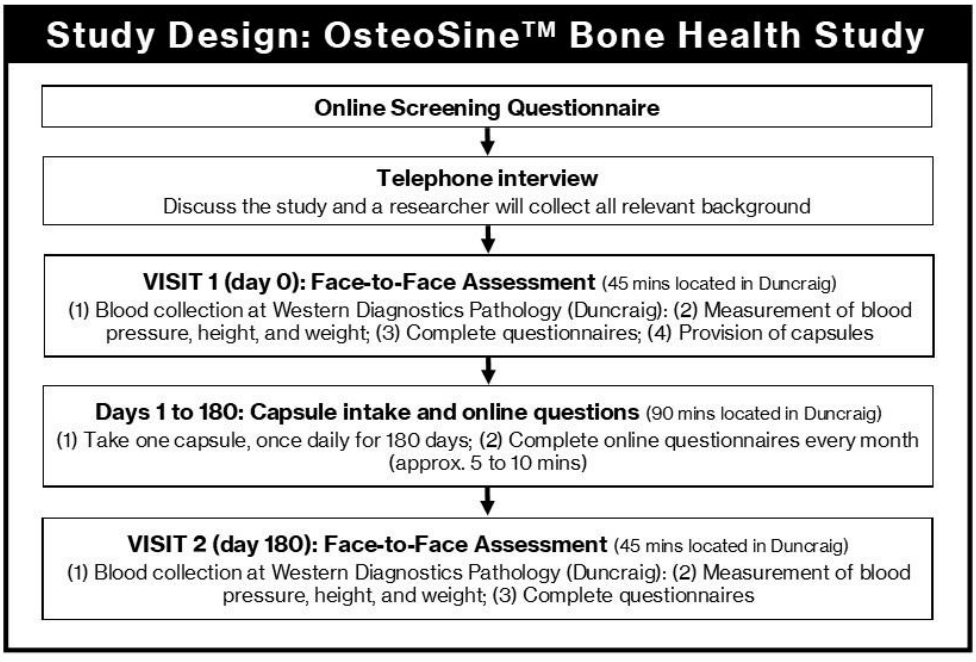
Step 5: Complete monthly questionnaires (approx. 10 mins)

Every month, you will need to complete an online questionnaire assessing your general wellbeing. You will also complete questions that ask if you have been experiencing any adverse effects associated with the intake of your capsules, experienced any illnesses/injuries, or changed/started any new medications.

Step 6: VISIT 2 (day 180): Blood collection and face-to-face assessment (approx. 45 mins)

During this visit, the following tasks will be completed:

1. You will visit a WDP located near the office of Clinical Research Australia. A blood sample will be collected from an WDP staff member to examine blood markers associated with bone health, liver function and renal function. This blood sample needs to be collected in the morning after an overnight fast.
2. You will then visit the office of Clinical Research Australia for the following:
    a. Have your weight, height, and blood pressure measured
    b. Complete questionnaires about your general wellbeing



Compensation for participating in this study

To compensate you for your travel costs and time associated with participating in this study, we will give you a $40 gift voucher at visit 1 and a $120 gift voucher at visit 2. Furthermore, at the end of the study, people placed in the placebo group will receive a free 6-month supply of Ostesine.

Criteria for inclusion/ exclusion in this study

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

1. You are a female aged between 50 and 80 years old.
2. You are postmenopausal (had no menses for at least 12 months)
3. You are a non-smoker
4. You have a body mass index (BMI) between 18 and 35 kg/m^2
5. You have no plan to commence new treatments over the study period
6. You understand and are willing and able to comply with all study procedures
7. 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 not be suitable for participation in this study:

1. You have been diagnosed with osteoporosis
2. You are diagnosed with a disease causing secondary osteoporosis within the last year, such as primary hyperparathyroidism, chronic obstructive pulmonary disease, chronic kidney disease, inflammatory bowel disease, celiac disease, or diabetes.
3. You use pharmaceutical medications including but not limited to corticosteroids, antiepileptic drugs and antiresorptive therapy, including systemic hormone replacement therapy, bisphosphonates, and strontium ranelate.
4. You have started, or changed your medication, herbal or vitamin supplements within 4 weeks before starting the study
5. You take supplements known to affect bone metabolism, including vitamin D and mineral supplements.
6. You have a recent history of fragility fractures, especially those requiring surgical intervention.
7. You plan to make major lifestyle change in the next 6 months.
8. You consume more than 14 alcohol standard drinks per week
9. You currently or in the last 12 months have regularly engaged in illicit drug use
10. You have had a significant surgery over the last year
11. You have participated in another clinical trial in the last month

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 knee pain or require treatment for any other condition during the study, this may result in withdrawal. Your health is the utmost priority, and your choice/need to commence a 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 provided 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 investigator's office 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

Bone loss occurs as we age and post-menopausal women are a population with an increased risk of osteoporosis. If Osteosine™ is found to support bone health it provides us with a natural option to support bone health as we age.

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:

- Cnidium monnieri and Cuscuta chinensis have a long history of use in Traditional Chinese Medicine and are generally well-tolerated by most users. The dose of these ingredients will supplemented at safe levels for human consumption
- Even though there have been no reports of any serious side effects associated with the intake of these ingredients, this cannot be ruled out. As with many herbal ingredients, the most likely side effects are mild digestive complaints (e.g., bloating, nausea, and loose stools).
- Further details about Osteosine™ and its intake are included in the 'Osteosine™ 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 side effects from applying the gel, please contact 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 estimated the results of this study will be finalised in mid 2026. 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 contact Dr Adrian Lopresti on 08 9448 7376.

We would like to thank you in advance for your assistance with this research project.

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: 0148E_2024). 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.