INFORMATION SHEET

The effect of a topical curcumin formulation (VAS101) on knee pain in adults with knee osteoarthritis: A randomised, double-blind, placebo-controlled study

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Background

Curcumin is derived from the turmeric plant and its intake is associated with several health benefits. Curcumin has anti-inflammatory effects, and in previous clinical trials, the oral intake of curcumin has been associated with reductions in pain in adults with osteoarthritis. However, its pain-relieving effects when applied topically (on the skin) have not been previously investigated.

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 Vascarta Inc., the company that produces the curcumin gel (VAS101) used in this study. However, this study is independently managed by Clinical Research Australia without external influence from Vascarta Inc.

Aim of the study

We would like to know whether the topical application of a gel containing curcumin (VAS101) for 4 weeks can improve pain and symptoms associated with knee osteoarthritis in adults aged 45 to 75 years with chronic knee osteoarthritis.

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 7 to 14 days later.

Step 3: Have an X-ray of your target knee

We will send you a referral to have an X-ray of your target knee. Before visit 1, you will need to visit your nearest SKG radiology centre to have an X-ray of your knee. This X-ray will be used to help classify the severity of your osteoarthritis.

Step 4: VISIT 1: Face-to-face assessment (approx. 90 mins)

During this visit, the following tasks will be completed:

1. Your weight, height, and blood pressure will be measured
2. You will collect a small urine sample in a collection tube
3. You will complete several tasks to assess your physical function. These include:
    a. 30-second chair stand test – From a sitting position on a chair, you stand up and then return entirely back down. This is done for 30 seconds, and the number of repetitions is counted
    b. 40-metre fast-paced walk test – You will walk 40 metres as quickly as you can, and the time to complete this is recorded
    c. Timed up and go test – you will stand up, walk to a mark 3 metres away, turn around and return to sit back on a chair. The time to complete this is recorded.
    d. Six-minute walk test – you will walk for 6 minutes as quickly as possible, and the distance covered will be recorded.
4. You will complete self-report questionnaires assessing your knee osteoarthritis symptoms
5. A researcher will apply a gel to your target knee and show you how to do this.
6. You will be given a 2-week supply of gel to apply to your knee

Step 5: application of gel (curcumin/VAS101 or placebo)

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

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 the gel on knee osteoarthritis symptoms.

You will be required to apply the gel ONCE every TWO days. A researcher will show how the gel needs to be applied. When the gel is applied, showering/bathing must be avoided for 12 hours.

* Placebo involves providing a substance with no known treatment effects. In this case, the placebo will only contain the gel and yellow dye (polyethylene glycol 400 and myristic acid 400).

It is extremely important that you apply the gel every 2 days. We will send you reminders.

Step 6: Complete daily questionnaires

After visit 1, you will complete online questions assessing your knee pain and knee symptoms. You will also complete online questions that ask if you have been experiencing any adverse effects associated with the gel application, experienced any illnesses/injuries, or changed/started any new medications. The time it takes to complete these daily questions will vary from 1 to 5 minutes.

Step 7: VISIT 2: Day 14, face-to-face re-assessment (approx. 90 mins)

Two weeks after visit 1, you will return for a second assessment. The tasks completed during this visit will be the same as those conducted during visit 1, except there will be no urine collection. You will also be required to bring your allocated study gel with you to this visit.

Step 8: continued application of gel (curcumin/VAS101 or placebo)

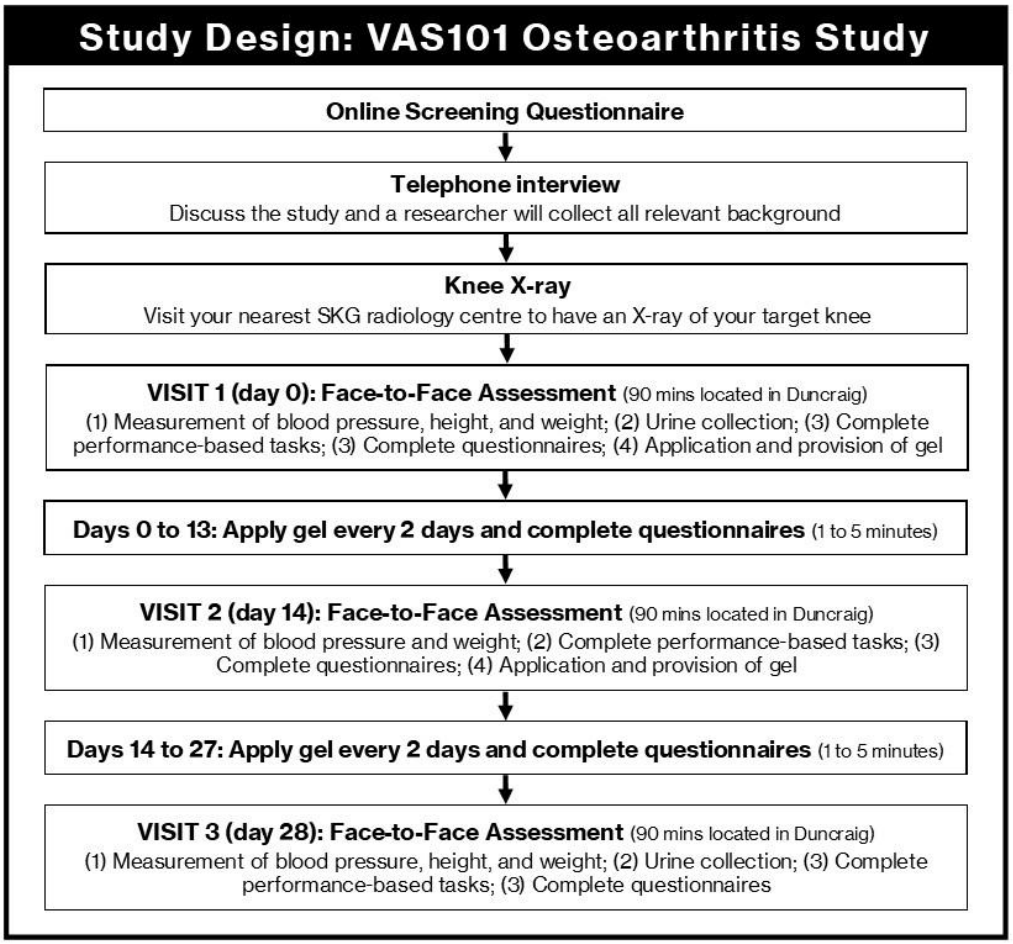
You will continue to apply the gel ONCE every TWO days

Step 9: Complete daily questionnaires

After visit 2, you will continue to complete the same daily questionnaires as previously completed

Step 10: VISIT 3: Day 28, face-to-face re-assessment (approx. 90 mins)

Two weeks after visit 2, you will return for a third assessment. The tasks completed during this visit will be the same as those conducted during visit 1. You will also be required to return your allocated study gel.



Compensation for participating in this study

To compensate you for your travel costs and time associated with participating in this study, at visits 1 and 2, we will give you a $40 gift voucher and at visit 3, a $100 gift voucher. Furthermore, participants placed in the placebo group will receive a complimentary 30-day supply of VAS101 gel at the end of the study.

Criteria for inclusion/ exclusion in this study

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

1. You are between 45 and 75 years old.
2. You experience symptoms of knee osteoarthritis.
3. You have a body mass index (BMI) between 18 and 32 kg/m^2
4. You have previously been diagnosed with osteoarthritis of the knee by a medical practitioner
5. You report a knee pain severity within our established cut-off severity
6. You have knee pain on more than 50% of days over the previous month
7. You have no plan to commence new treatments over the study period
8. You understand and are willing and able to comply with all study procedures
9. 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 suffer from recently diagnosed or unmanaged medical conditions including but not limited to hyper/hypotension, cardiovascular disease, diabetes, gastrointestinal disease, endocrine disease, neurological disease, cancer/ malignancy or other conditions that would jeopardise safety or impact validity of results (in the opinion the Investigator)
2. You suffer from arthritis of the hip or have chronic back pain that significantly affects your daily function

3. You have received intra-articular treatment/injections with a corticosteroid or hyaluronic acid within 6 months before screening
4. Have had surgery on the target knee within 6 months before screening
5. You plan to have surgery during the study period
6. You have had a clinically significant infection, injury, or illness within 28 days before screening
7. You plan to engage in heavy exercise (e.g., e.g., marathon run, heavy leg squats) within 48 hours before screening or during the study
8. Have a known allergy to curcumin-containing products
9. You have had an injury in the area of the target knee within 3 months before screening
10. You currently take curcumin-containing products
11. You have started or changed medication, herbal or vitamin supplements within 4 weeks before screening
12. You consume more than 14 alcohol standard drinks per week
13. You currently or in the last 12 months have regularly engaged in illicit drug use
14. You are pregnant, breastfeeding, or planning to fall pregnant in the next 2 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 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

The oral intake of curcumin has been shown to have anti-inflammatory and pain-relieving effects. However, there has been no investigation into its pain-relieving effects when applied topically. If topical curcumin is effective, it will provide us with a natural option to help improve knee pain in adults with osteoarthritis of the knee.

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:

- VAS101 is well tolerated and is available by prescription in the USA. Anecdotal reports indicate that it is well tolerated. Moreover, in a randomised, double-blind, placebo-controlled human safety study it was well tolerated by healthy participants, with no reported significant adverse effects. However, the topical application of VAS101 may lead to slight yellowing in the skin, and if it makes contact with clothing, it can lead to staining. The skin yellowing typically disappears 1 to 2 days after discontinuation.
- To minimise the chance of the staining of clothing, you will be asked to wear shorts, a skirt, or loose-fitting pants after each application. You will also be provided with a knee sleeve which you place over your knee and leave on for 12 hours. After this time, you can shower, which will prevent the staining of clothing.
- Further details about this VAS101 and its application are included in the ‘VAS101 Curcumin Information Sheet’.

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 that the results of this study will be finalised in early 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: 0147E_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.