An investigation into the effects of curcumin on osteoarthritis of the knee: a randomised, double-blind, placebo-controlled study

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You are invited to participate in this study.

Background and study aims

Curcumin, derived from turmeric, has been traditionally used as a health-promoting, anti-inflammatory agent. Many studies have been conducted on turmeric as well as its main active ingredient, curcumin, demonstrating numerous health benefits. In this study, we are interested in examining the effects of curcumin on:

1. Knee pain  
2. Physical function and performance, and  
3. Quality of life

As a result, we are inviting you to participate in this 8-week, randomised, double-blind, placebo-controlled study.

This study will be conducted by Dr Adrian Lopresti, Stephen Smith (Clinical Research Australia), and Associate Professor Timothy Fairchild (Murdoch University).

Information about funding source and declaration of interests

This study is being funded by Dolcas Biotech, LLC., the company that produces the curcumin extract (Curcugen™) used in this study. However, this study is being independently managed by Clinical Research Australia (CRA) without external influence from Dolcas Biotech, LLC.

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

This 8-week study will comprise several steps as outlined below:

Step 1: Phone Interview for initial assessment of eligibility

After you have expressed an interest in participating in the study, you will be briefly interviewed by a researcher. The interview will be conducted over the phone (approx. 20 to 30 minutes). The purpose of this interview is to find out more information about your knee pain and to obtain relevant background information (e.g., age, sex, illnesses, medication use, etc.). This will allow us to see if you meet the eligibility criteria for the study.
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. This appointment will be scheduled 1 to 2 weeks after the phone interview.

**Step 2: Completion of a consent form**
Before proceeding further in the study, you will be asked to complete an online consent form to ensure that you agree to participate in the study and are aware of all the requirements in this study.

**Step 3: Face-to-face assessment (total time 30 to 45mins)**
During this meeting, the following tasks will be completed:
1. Measurement of your weight, height, and blood pressure
2. Completion of several physical performance and function tests. These include:
   a. 30-second chair stand test: in this test, we will measure how many times you can stand up to a full standing position and then sit back down on a chair
   b. 40m fast-paced walk test: in this test, we will time how long it takes to walk 40 metres
   c. Six-minute walk test: in this test, we will time how far you can walk in 6 minutes
   d. Timed up and go test: in this test, we will time how long it takes for you to rise from a chair, walk 3 metres, turn around, walk, and then sit back down
3. Completion of 2 self-report questionnaires
4. Provision of capsules to take for the study

**Step 4: 8-week intake of capsules (Curcumin or placebo)**
In this study, we will be using a randomised, double-blind, placebo-controlled design. This means that participants will be placed into ONE of the following 2 groups:
1. Placebo (dummy) tablets, or
2. Curcumin capsules

Neither you nor the investigator will be aware of which condition you have been placed in. This randomised, placebo allocation is important for us to assess the true effects of this curcumin extract (Curcugen™).

You will be required to take ONE capsule, TWICE daily with or without food. It is extremely important that you take the capsules every day.

*Placebo involves providing a substance with no known treatment effects. In this case, the placebo will contain a relatively inert substance, roasted rice powder.*

**Step 5: Complete online questionnaires every week (weeks 1 to 7)**
Throughout this study, you will be required to complete several online questionnaires every week. It will take about 15 minutes to complete the week-4 questionnaires, and about 5 minutes to complete the questionnaires on the other weeks.

**Step 6: Face-to-face re-assessment (total time 30 to 45mins)**
During this assessment, you will be required to complete the same tasks as those completed at the beginning of the study (step 3).
**Compensation for participating in this study**

1. To compensate you for your travel costs and time, you will receive a $30 gift voucher (Coles or Woolworth Group). A voucher will be given to you at the end of each face-to-face assessment session.

2. After the study, volunteers placed on placebo will be offered a free 8-week supply of curcumin capsules.

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**Criteria for inclusion/exclusion in this study**

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

1. Male and females aged 45 to 70 years
2. Meets the National Institute for Health and Care Excellence (NICE) clinical criteria for knee osteoarthritis:
   a. age 45 years or older
   b. has activity-related knee joint pain
   c. has morning knee stiffness that lasts no longer than 30 minutes
3. Osteoarthritis of the knee that has been diagnosed by a medical professional
4. Reports knee pain on most days over the previous month
5. Has experienced knee pain for 3 months or more
6. Reports knee pain during walking over the previous week
7. BMI between 20 and 35
8. Non-smoker
9. English speaking
10. No plan to commence new treatments over the study period
11. Willing to provide a personally-signed informed consent form detailing all pertinent aspects of the trial.
12. Willing and able to take prescribed capsules for 8 weeks

If any of the exclusion criteria below are met, you will not be suitable for participation in this study:
1. Experience of rapid worsening of knee symptoms or the presence of a hot swollen knee
2. Previous knee replacement on the affected side or history of significant trauma to the knee
3. Has had major surgery in the last year
4. Has had a joint injection or arthroscopy in the past 6 months
5. Current or past (3 months) use of pain-relieving medications (e.g., NSAID’s, analgesics, and corticosteroids) greater than twice a week
6. Use of anticoagulants e.g. warfarin, apixaban, ticagrelor, rivaroxaban, dabigatran within the preceding 3 months
7. Diagnosis of gout or pseudogout within the last 3 months, and/or history of gout in the knee joint
8. Diagnoses of other inflammatory arthritides (for example, rheumatoid arthritis), septic arthritis and malignancy (bone pain)
9. Diagnosis of complex pain disorder or severe immobility (e.g. complex regional pain syndrome, severe back pain, multiple sclerosis, muscular dystrophy, Parkinson’s disease, hemiplegic)
10. A recent diagnosis of and/or currently suffering from unmanaged medical conditions including but not limited to: diabetes, hyper/hypotension, cardiovascular disease, gallbladder disease/gallstones/biliary disease, endocrine disease, or malignancies
11. Diagnosis of a neurological disease (e.g., Parkinson’s disease, Alzheimer’s disease, intracranial haemorrhage, multiple sclerosis, or head/brain injury), psychiatric disorder (other than mild-to-moderate depression/anxiety)
12. Unable to walk unaided (without the use of a frame or walking stick) or is housebound due to immobility
13. Alcohol consumption > 14 standard drinks per week
14. Current or 12-month history of illicit drug abuse
15. Currently taking supplements that may impact on treatment outcome (e.g. chondroitin, glucosamine, and curcumin)
16. Pregnant women, women who are breastfeeding or women who intended to fall pregnant.

Voluntary participation and withdrawal from the study

It is important that you understand that your involvement in this study is voluntary. While we would be pleased 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 treatment for your knee pain, or you require medical 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 prior to 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 to us will be treated confidentially. Your name and identifying details will not be used in any publication arising out of this 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**

Curcumin intake may provide several health benefits, particularly due to its antioxidant and anti-inflammatory properties.

If curcumin is found to be effective at improving knee pain in people with osteoarthritis of the knee, it will provide a natural option for sufferers.

**Possible risks**

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

- Curcumin is the active ingredient found in the spice turmeric. It has a long tradition of use in Ayurvedic medicine and has been shown to be well-tolerated. Similar daily doses have been used in previous studies and have been well-tolerated. However, side effects cannot be totally ruled out and we ask you to contact us immediately if you are experiencing any adverse effects (whether you believe they are associated with the intake of the capsules or not). Further details about curcumin and its intake is included in the ‘Curcumin Information Sheet’.

**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 | Mobile: 0412 813 518 | Email: steve@clinicalresearch.com.au
Dr Adrian Lopresti: Ph: 9448 7376 | Mobile: 0411 969 797 | Email: adrian@clinicalresearch.com.au

**Feedback of study results**

It is estimated the results of this study will be finalised by mid-2021. These results will be posted on the website below. We will also notify you by email when the results have been posted on this website: www.clinicalresearch.com.au
Questions

If you would like to discuss any aspect of this study, please feel free to contact either Dr Adrian Lopresti or Stephen Smith on ph 9448 7376. Either of us would be happy to discuss any aspect of the research with you.

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) (Application Number 0072E_2020). 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.